

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

CENTRO DE BIOTECNOLOGIA DO ESTADO DO RIO GRANDE DO SUL

PROGRAMA DE PÓS-GRADUAÇÃO EM BIOLOGIA CELULAR E MOLECULAR

Fasciola hepatica: ESTUDO PROTEÔMICO E CARACTERIZAÇÃO DE
PROTEÍNAS RELEVANTES NA RELAÇÃO PARASITO-HOSPEDEIRO

Lucía Sánchez Di Maggio

Porto Alegre, março de 2018

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Tese submetida ao Programa de Pós-graduação em Biologia Celular e Molecular (PPGBCM) da UFRGS como parte dos requisitos para a obtenção de grau de Doutor em Ciências.

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LISTA DE ABREVIATURAS, SÍMBOLOS E UNIDADES.

ASCT	Acetato CoA-transferase
BLAST	<i>Basic Local Alignment Search Tool</i>
BSA	Albumina sérica bovina
CB	Catepsina B
CEUA	Comissão de Ética no Uso de Animais
CDC	<i>Centers for Disease Control and Prevention</i>
CL	Catepsina L
cm	Centímetro
CRP	Proteínas ricas em cisteínas
CUB	Cubilina
DNA	Ácido desoxirribonucleico
DPDx	<i>Web site</i> desenvolvido e mantido por CDC
DGSG	Grupo Técnico da Direção geral dos Serviços Pecuários
E/S ou ESP	Produtos de excreção e secreção.
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid)
FC	<i>Fold change</i>
<i>Fh</i> FABP	Proteína ligadora de ácidos graxos de <i>Fasciola hepatica</i>

<i>Fh</i> -KTM	Inibidor de tipo Kunitz de <i>Fasciola hepatica</i>
<i>Fh</i> SAP	Saposina de <i>Fasciola hepatica</i>
HSP	Proteína de choque térmico
LAP	Leucina amino peptidase
LC-MS/MS	Cromatografia líquida acoplada à espectrometria de massas em <i>tandem</i>
Mb	Mioglobina
MGAP	Ministério da agricultura, pecuária e pescas de Uruguai
µm	Micrometro
NCBI	<i>National Center for Biotechnology Information</i>
NEJ	Juvenil recentemente desencistado
NSAF	<i>normalized spectral abundance factor</i>
PES	Produtos de excreção e secreção
PBS	Solução salina tamponada com fosfato
pH	Potencial hidrogeniônico
RPMI	Meio de cultura Roswell Park Memorial Institute
SSP	Proteínas somáticas solúveis.

RESUMO

Fasciola hepatica é o parasito causador da fasciolose, doença transmitida através dos alimentos, que afeta a produção pecuária e a saúde humana. Embora a doença seja tratada com anti-helmínticos, as possibilidades de reinfecção e o desenvolvimento de resistência ao triclabendazol exigem novas estratégias de controle. Os produtos de excreção/secreção liberados pelo parasito durante a infecção auxiliam a sobrevivência do parasito, protegendo-o das respostas do hospedeiro, permitindo sua sobrevivência durante um longo período no hospedeiro vertebrado e a finalização do ciclo larval no hospedeiro intermediário. Este trabalho teve como objetivo gerar uma análise proteômica dos estágios intra-mamífero, adulto e NEJ (juvenil recentemente desencistado), de *F. hepatica*. Até o momento, os dados gerados representam o maior número de proteínas identificadas para este parasito. A classificação funcional revelou a presença de proteínas envolvidas em diferentes processos biológicos, muitos dos quais representam achados originais para este organismo. Além disso, os padrões de infecção dos parasitos são frequentemente ligados ao comportamento do hospedeiro intermediário, o qual pode desempenhar um papel na distribuição e acumulação dos parasitos. Os dois proteomas analisados neste trabalho possuem diferenças em abundância de proteínas individuais e entre as categorias funcionais. Estas diferenças podem ser causadas pelas características do ciclo biológico do parasito em cada hospedeiro (duração do ciclo de vida, quantidade de cercárias geradas, durabilidade das metacercárias, competição com outros parasitos), aspectos biológicos (como idade ou espécie) ou variações ambientais (temperatura, umidade, estação). A compreensão dos mecanismos moleculares subjacentes à interação com os hospedeiros intermediário e definitivo pode fornecer dados que auxiliem a busca de novos alvos no diagnóstico e controle da fasciolose.

ABSTRACT

Fasciola hepatica is the agent of fasciolosis, a foodborne zoonosis that affects livestock production and human health. Although flukicidal drugs are available, re-infection and expanding resistance to triclabendazole demand new control strategies. Parasite compounds released during infection, known as excretory/secretory products, mediate parasite survival within the host. ESP are thought to protect parasites from host responses, allowing them to survive for a long period in the vertebrate host and complete their larval cycle in the intermediate host. This work provides in-depth proteomic analysis of *F. hepatica* intra-mammalian stages, adult and NEJ (newly existed juvenile), and represents the largest number of proteins identified to date for this parasite. Functional classification revealed the presence of proteins involved in different biological processes, many of which represent original findings for this organism and are can be vital for parasite survival within the host. In addition, infection patterns of parasites are often tied to host behavior, and intermediate host behavior can play a role in shaping the distribution and accumulation of parasites. . The two proteomes analyzed here have differences in protein abundance, categories and individual proteins. The differences found here could be due to differences in the biological cycle of the parasite in the host (as duration of the life cycle, amount of cercariae generated, durability of metacercariae, competition with other parasites), biological aspects (as age or species) or environmental variabilities (as temperature, humidity, season). Understanding the molecular mechanisms underlying the complex interaction with the intermediate and definitive host could provide relevant clues, aiding the search for novel targets in diagnosis and control of fasciolosis.

1 INTRODUÇÃO:

A fasciolose é uma doença zoonótica que afeta herbívoros e seres humanos causada principalmente pelos parasitos trematóides digeneos *Fasciola hepatica* e *Fasciola gigantica*. Comumente conhecidos como baratas do fígado, *F. hepatica* possui uma distribuição mundial, enquanto a *F. gigantica* possui uma distribuição restrita a regiões tropicais da África e Ásia (Mas-Coma et al., 2005). A doença causa grandes perdas econômicas na pecuária, estimadas em mais de US\$ 3 bilhões em todo o mundo, incluindo redução no ganho de peso, diminuição da fertilidade, produção de leite em bovinos e lã nos ovinos (Spithill et al., 2012).

O principal método utilizado no controle da fasciolose é o uso de anti-helmínticos (Armour, 1975; Mitchell, 2003). No entanto, o tratamento é de alto custo e ocorrem reinfeções e resistência (Aguilera-Luiz MM, 2012; Molina-Hernandez et al., 2015; Olaechea et al., 2011). Assim, há necessidade de desenvolver estratégias de controle alternativas, mais efetivas e de menor custo. Por isso, é importante melhorar o conhecimento da biologia do parasito e de sua relação com o hospedeiro.

1.1 O parasito *Fasciola hepatica*.

O parasito *F. hepatica* pertence ao filo *Platyhelminthes* (do grego *platy*: achatado e *helminthes*: vermes) alguns têm vida livre e outras espécies parasitam vertebrados e invertebrados. As características principais deste filo são animais triblásticos, simetria bilateral, acelomados, e corpo achatado dorsoventralmente. O intestino termina em fundo cego e a única abertura do trato digestivo é a boca. O sistema excretor é protonefridial, e sua função é principalmente de regulação osmótica sendo que os produtos de excreção são eliminados principalmente pela superfície do corpo (Walker, 2001). Alguns dos parasitos deste filo estão incluídos na classe *trematoda*. Os vermes desta classe

apresentam adaptações para a vida parasitária, alguns das quais facilitam a sobrevivência e infestação do hospedeiro, tais como: ventosas, tegumento com cutícula protetora, ausência de órgãos sensoriais e produção de grandes quantidades de ovos. A *F. hepatica* pertence à subclasse *digenea* (*di*: dois, *genea*: vidas), o nome faz referência a um ciclo de vida heteróximo com dois hospedeiros: intermediário e definitivo (Olson et al., 2003). No hospedeiro intermediário, geralmente um molusco do gênero *Lymnaea*, habitam os estágios larvais do parasito e no hospedeiro definitivo, geralmente mamíferos, habitam os estágios reprodutores (Andrews, 1999).

A *F. hepatica* adulta é um verme achatado com forma de folha que mede de 1,5 a 5 cm de comprimento e 1,5 a 5 cm de largura na parte mais espessa do corpo. O corpo apresenta cor rosa, mas o intestino apresenta cor marrom pela presença de bile e sangue. Na porção anterior do corpo há duas ventosas: a oral, ao redor da boca, que é utilizada para ingestão de alimento e adesão e a ventosa ventral para adesão; e um poro genital. O corpo está recoberto pelo tegumento, formado por um sincício anucleado limitado por uma membrana dupla e possui microvilosidades. Sob o sincício há uma membrana basal e uma camada de fibras musculares, que asseguram a locomoção do helminto, e o parênquima. No parênquima estão incluídos os sistemas digestório, excretor e nervoso. O sistema digestório é altamente desenvolvido e ramificado, e como a *F. hepatica* não tem sistema circulatório, este sistema é responsável pela distribuição de nutrientes para as células. No estágio adulto, a *F. hepatica* é um parasito hematófago. Os ovos eliminados nas fezes do hospedeiro definitivo possuem 150 x 90 µm, cor amarelo-marrom, e têm um opérculo por onde emerge o miracídio. São compostos por células vitelínicas ao redor de um óvulo fertilizado (Andrews, 1999). Do ovo eclode uma larva chamada de miracídio (130x28 µm), sendo o corpo em forma de cone e coberto de cílios (Malek, 1980; Valero

et al., 2009). O NEJ é o estágio invasivo da *F. hepatica*. A migração até o fígado e os canais biliares leva aproximadamente 8 semanas, nas quais os NEJ crescem e desenvolvem-se em adultos atingindo o tamanho completo em 12-14 semanas após infecção (Boray, 1969).

1.2 Ciclo biológico da *Fasciola hepatica*.

Os hospedeiros definitivos da *F. hepatica* são infestados quando ingerem vegetação contendo larvas latentes encercadas, chamadas de metacercárias, em terrenos alagados ou perto de cursos de água (Mas-Coma et al., 2014). Seres humanos são infestados ao ingerirem plantas aquáticas ou água contaminada com metacercárias (Figura 1). Os NEJ eclodem no duodeno, atravessam rapidamente a parede intestinal, entram na cavidade peritoneal e migram até atingir o parênquima hepático. Após um período de alimentação e crescimento, deslocam-se para seu destino final dentro dos canais biliares, onde amadurecem e produzem ovos. Os ovos são liberados a partir dos canais biliares até o intestino grosso pelos fluídos biliares e são eliminados pelas fezes, contaminando as pastagens. Quando as condições ambientais de luz e temperatura são adequadas, começa o período de maturação e eclodem os miracídios. Esta larva tem capacidade natatória e infecta o hospedeiro intermediário, gastrópodes pertencentes à família *Lymnaeidae* no caso da *F. hepatica*. No gastrópode, o miracídio perde os cílios e forma um esporocisto. O esporocisto é uma massa celular germinativa onde cada célula multiplica-se e produz uma redia. As redias crescem até estourar a parede do esporocisto e são liberadas no caramujo. As redias multiplicam-se e produzem cercarias (fase larvária final), que emerge do caramujo para encistar na vegetação que fica perto ou na superfície da água, começando o estágio de metacercária. Como consequência, durante a migração e o desenvolvimento nos hospedeiros, os parasitos encontram diferentes tecidos,

macromoléculas, microambientes fisiológicos dinâmicos e respostas imunes do hospedeiro (Andrews, 1999).

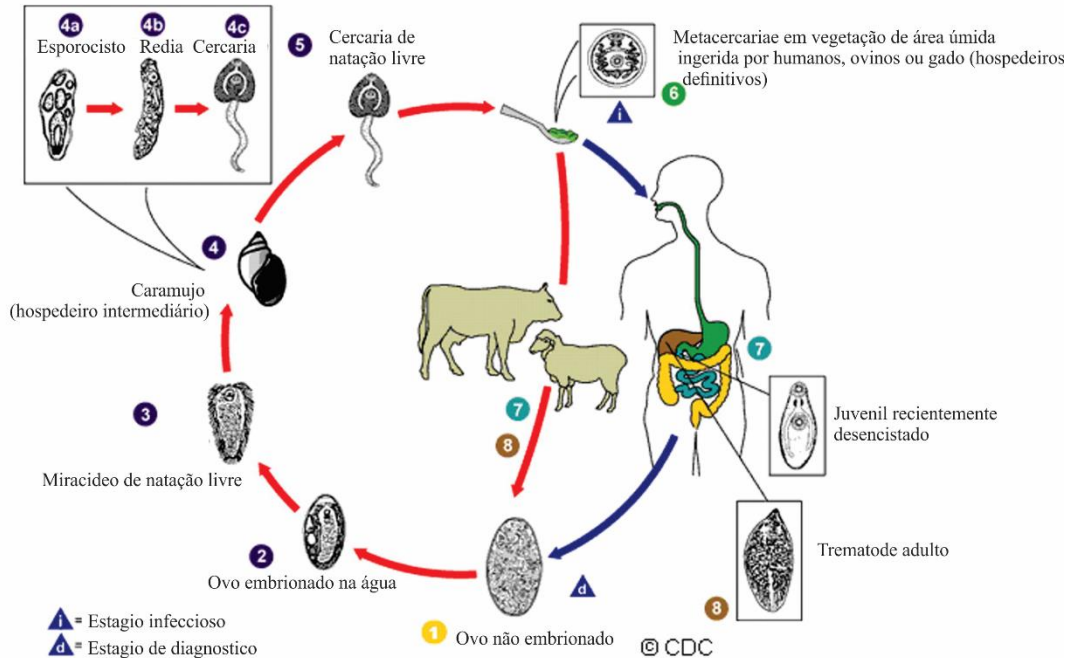


Figura 1. Ciclo biológico do parasito *Fasciola hepatica*. Adaptado de DPDx – CDC.

1.3 Fasciolose

A fasciolose é reconhecida como um problema de saúde pública no mundo; em seres humanos a doença foi considerada de importância secundária até o final da década de 1980, devido ao pequeno número de casos. Apenas 2000 casos foram relatados em seres humanos nos 25 anos anteriores a 1990 no mundo (Chen e Mott, 1990). No início da década de 1990, a fasciolose foi reconhecida pela Organização Mundial da Saúde como doença negligenciada. Atualmente, as estimativas para todos os continentes atingem 17 milhões de pessoas infectadas, sendo esta uma subestimativa, pois existe falta de dados relativos a vários países asiáticos e africanos (Mas-Coma, 2005). No Brasil, a doença em bovinos é monitorada a nível estadual e federal, sendo a maior prevalência observada nos estados da região Sul (Santa Catarina e Rio Grande do Sul com 4,5% e

14,4% da prevalência, respectivamente), existindo focos ao longo do litoral desses estados (Figura 2) (Bennema et al., 2014). Um fator importante dos dados coletados no país é que o monitoramento das inspeções (estaduais e federais) no abate não é padronizado. Isso gera grandes diferenças no tipo de inspeção e fazem com que a distribuição espacial dos dados não seja comparável entre regiões, ou que algumas regiões como o norte e nordeste não estejam contempladas nos dados públicos da doença (Bennema et al., 2014).

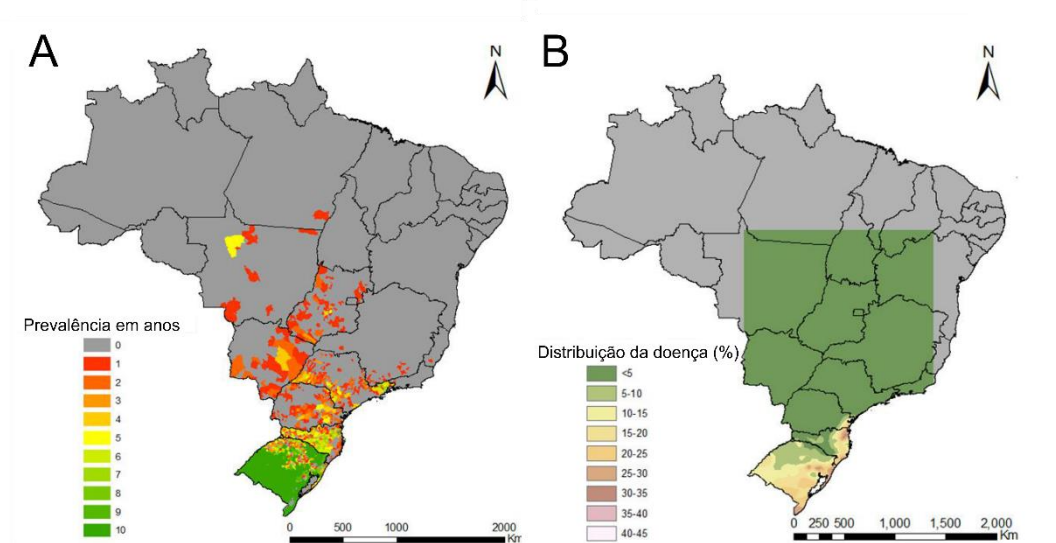


Figura 2. Distribuição da fasciolose no gado bovino no Brasil. A: Prevalência da fasciolose em gado por municípios no período de 2002 a 2011. B: Distribuição espacial (%) da prevalência de *F. hepatica* em fígados de gado abatido por município no período de 2002 a 2011. Adaptado de Bennema (2014).

1.4 Patologia, diagnóstico e prevenção da doença.

1.4.1 Patologia.

Entre 8 e 10 semanas após a ingestão de metacercárias, haverá vermes adultos nos canais biliares do fígado do hospedeiro definitivo. Os vermes adultos fixam-se às paredes dos canais biliares e alimentam-se de sangue. O padrão de alimentação multi-sítio combinado às espinhas do tegumento da *F. hepatica* irritam e machucam os canais biliares, o que provoca espessamento nas paredes dos canais. A irritação crônica pode levar à calcificação das paredes dos ductos biliares e o comprometimento a função

hepática. Quando a carga parasitária é grande, pode causar anemia, devido a ingestão de sangue. Os vermes adultos produzem prolina em grandes quantidades, o que incrementa o espessamento das paredes dos canais biliares e também é capaz de destruir glóbulos vermelhos (Isseroff et al., 1979; Torgerson, 1999).

1.4.2 Diagnóstico

O diagnóstico da fasciolose é desafiador, já que grande parte dos infestados não apresentam sintomas. Quando sintomática há febre, tremor, dor na zona do fígado, hepatomegalia e/ou eosinofilia. Nos casos em que a doença é aguda, pode acontecer icterícia, necrose no fígado e anemia. Em geral, os sinais clínicos de fasciolose podem ser facilmente confundidos com infecções de nematoides, porém sinais clínicos não precisam estar presentes para que a produtividade do hospedeiro seja afetada. O diagnóstico é possível após 3 meses da infecção inicial. As técnicas geralmente utilizadas são exames coproparasitológicos ou sorológicos (Alvarez Rojas et al., 2014; Braun et al., 1995; Mezo et al., 2004).

1.4.3 Prevenção

Os métodos de controle da *F. hepatica* são focados na redução da doença em animais, evitando perdas econômicas. O método de controle mais utilizado é o tratamento do ruminante com anti-helmínticos, ou o controle biológico do caramujo (Torgerson, 1999). Pelo tratamento com moluscidas é possível controlar a população de hospedeiros intermediários com sucesso e com uma boa relação custo-benefício. No entanto, essa abordagem não é muito aceita devido ao risco de contaminação ambiental, particularmente com populações econômica e biologicamente importantes, como peixes ou caranguejos. No caso dos anti-helmínticos, diferentes compostos são utilizados

dependendo da espécie infestada, do preço e da segurança (Sanyal, 1995). Um problema que limita o uso de drogas no tratamento da doença é o aumento de resistência aos anti-helmínticos nas populações de parasitos e a presença de resíduos xenobióticos em alimentos e no meio ambiente (Tsiboukis et al., 2013; Wolstenholme and Martin, 2014). Além disso, há demanda de vários mercados, estimulando a busca de novos métodos de controle. Uma alternativa ao uso de anti-helmínticos e moluscidas são as vacinas. E para procurar alvos biológicos é necessário incrementar o conhecimento da relação parasito-hospedeiro.

1.4.1 Interação parasito-hospedeiro

Alguns parasitos facilitam a sua sobrevivência no hospedeiro pela secreção ou excreção de moléculas solúveis que degradam, interagem ou manipulam o sistema imune do hospedeiro (Lightowers and Rickard, 1988). A caracterização destas moléculas, que desempenham um papel importante nas interações parasito-hospedeiro, é fundamental na descoberta de alvos para o diagnóstico e tratamento contra os parasitos. As técnicas de proteômica, junto com a caracterização de vários genomas de parasitos, permitiram identificar e caracterizar proteínas importantes na relação parasito-hospedeiro em vários parasitos. As análises proteômicas vão além de simples listagem de proteínas, elas fornecem de indícios da dinâmica dos processos metabólicos, de sinalização e regulatórios necessários para a correta função celular. Além disso, mostraram como que esses processos mudam quando a célula ou os organismos sofre patologias, manipulações ou administração de drogas.

No caso da *F. hepatica*, e outros endoparasitos, os estudos proteômicos enfatizam os PES (De la Torre Escudero et al., 2011; Di Maggio et al., 2016; Robinson et al., 2013), proteínas de superfície/tegumento (Wilson et al., 2011) ou vesículas extracelulares

(Cwiklinski et al., 2015b). No estudo feito pela equipe de Robinson (2013) foram combinados dados transcriptômicos e proteômicos. Com a abordagem transcriptômica foram preditas 160 proteínas secretadas; no entanto, apenas 22 proteínas foram encontradas em vermes adultos e 29 proteínas foram detectadas nas secreções dos NEJ utilizando a abordagem proteômica 2-DE. Em outro estudo proteômico realizado com o verme adulto, 29 das 60 proteínas mais proeminentes na amostra foram identificadas, também usando uma abordagem 2-DE (Jefferies et al., 2001). Em outro trabalho de PES de NEJ utilizando LC-MS/MS, apenas 16 das 54 proteínas que foram sugeridas como secretadas foram identificadas (De la Torre Escudero et al., 2011). Em um estudo de 2010 sobre proteínas expressas no estágio de NEJ, os autores encontraram 40 proteínas de *F. hepatica* usando LC-MS/MS (Hernandez-Gonzalez et al., 2010). Em 2011, o estudo de Wilson et al sobre o secretoma do tegumento identificou-se 63 proteínas, enquanto que em um artigo publicado recentemente (Cwiklinski et al., 2015b), os autores identificaram 69 proteínas em vesículas extracelulares de *F. hepatica*.

Os PES em *F. hepatica* são compostos majoritariamente por enzimas digestivas, envolvidas na reprodução e produção de ovos (Sotillo et al., 2017). Um exemplo são as proteases digestivas, categoria principal de proteínas encontradas nos PES de helmintos, que quando secretadas, possuem atividade na invasão do parasito e na degradação de tecido, imunoglobulinas e quimiocinas do hospedeiro (Culley et al., 2000; McKerrow et al., 2006; Williamson et al., 2006). Além de proteases, os PES possuem proteínas envolvidas na modulação da resposta imune do hospedeiro (Zhang et al., 2005) e envolvidas na alimentação (Martinez-Sernandez et al., 2014). Porém, essas proteínas devem ter uma função na relação parasito-hospedeiro para haver a liberação das mesmas para fora do parasito.

2 OBJETIVOS

2.1 Objetivo geral

O principal objetivo deste trabalho consistiu na caracterização do perfil proteico do helminto parasito *Fasciola hepatica* em diferentes estágios do ciclo de vida.

2.2 Objetivos específicos.

Realizar a análise comparativa das proteínas presentes nos PES nos diferentes estágios intra-mamíferos (NEJ e adulto) do ciclo de vida do parasito

Realizar a comparação de proteínas e suas abundâncias relativas nos PES de NEJ de *F. hepatica* provenientes de diferentes hospedeiros intermediários

Estabelecer possíveis funções na relação parasito-hospedeiro das proteínas identificadas

Determinar proteínas e grupo de proteínas de importância biológica visando um interesse no diagnostico, tratamento ou controle deste parasito

3 PARTE EXPERIMENTAL E RESULTADOS.

A tese é composta por dois capítulos, contendo artigos científicos que contem a descrição do trabalho experimental realizado no período de execução do doutorado.

Capítulo 1: *Across intra-mammalian stages of the liver fluke Fasciola hepatica: a proteomic study.* Artigo publicado no periódico científico Scientific Reports no 2016 (doi: 10.1038/srep32796).

O material suplementar do capítulo é disponibilizado digitalmente.

Os dados brutos do proteoma estão disponibilizados no site ProteomeXchange Consortium. Número identificador: PXD004418.

Capítulo 2: *The host factor: comparison between F. hepatica newly excisted juvenile from different intermediate hosts.* Manuscrito em fase de discussão de dados e redação do artigo.

O material suplementar do capítulo é disponibilizado digitalmente.

3.1 Capítulo I.

Across intra-mammalian stages of the liver fluke *Fasciola hepatica*: a proteomic study

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Across intra-mammalian stages of the liver fluke *Fasciola hepatica*: a proteomic study

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Fasciola hepatica is the agent of fasciolosis, a foodborne zoonosis that affects livestock production and human health. Although flukicidal drugs are available, re-infection and expanding resistance to triclabendazole demand new control strategies. Understanding the molecular mechanisms underlying the complex interaction with the mammalian host could provide relevant clues, aiding the search for novel targets in diagnosis and control of fasciolosis. Parasite survival in the mammalian host is mediated by parasite compounds released during infection, known as excretory/secretory (E/S) products. E/S products are thought to protect parasites from host responses, allowing them to survive for a long period in the vertebrate host. This work provides in-depth proteomic analysis of *F. hepatica* intra-mammalian stages, and represents the largest number of proteins identified to date for this species. Functional classification revealed the presence of proteins involved in different biological processes, many of which represent original findings for this organism and are important for parasite survival within the host. These results could lead to a better comprehension of host-parasite relationships, and contribute to the development of drugs or vaccines against this parasite.

Fasciolosis is a zoonotic foodborne disease caused mostly by the digenean trematode parasites *Fasciola hepatica* and *Fasciola gigantica*. *F. hepatica* has a worldwide distribution, while *F. gigantica* is found in tropical climates, with a much more focal distribution in parts of Africa and Asia, where these species overlap¹. The disease causes significant economic losses in livestock production worldwide, also having increased relevance to human health in developing countries¹.

Current control relies mainly on the use of anthelmintic drugs, eradication of the intermediate host with molluscicides, as well as improving drainage systems to limit snails habitat². Nevertheless, emerging resistance to anthelmintic drugs and the presence of xenobiotic residues in food and environment have stimulated the search for novel control methods. Immune control through the development of vaccines has emerged as a promising alternative; however, vaccines have to reach an appropriate level of efficacy to make them commercially viable³. Increasing efficacy is most likely to come through the discovery of additional and relevant vaccine antigens.

The definitive, mammalian host of *F. hepatica* is orally infected by metacercariae on plants. Newly excysted juveniles (NEJ) emerge in the duodenum and migrate to the liver. Following a period of blood feeding and growth in the liver, they move to the bile ducts, where they obtain blood by puncturing the duct wall, undergo maturation, and produce eggs⁴. Although adult flukes are reproductively active and the major responsible for the pathology in mammalian hosts, NEJ are the cause of significant damage to host tissues when migrating from the gut lumen to the bile ducts⁴. During migration and development, parasites encounter different host tissues and macromolecules, dynamic physicochemical microenvironments, and host responses such as blood coagulation, complement activation, in addition to other innate and acquired immune responses⁵.

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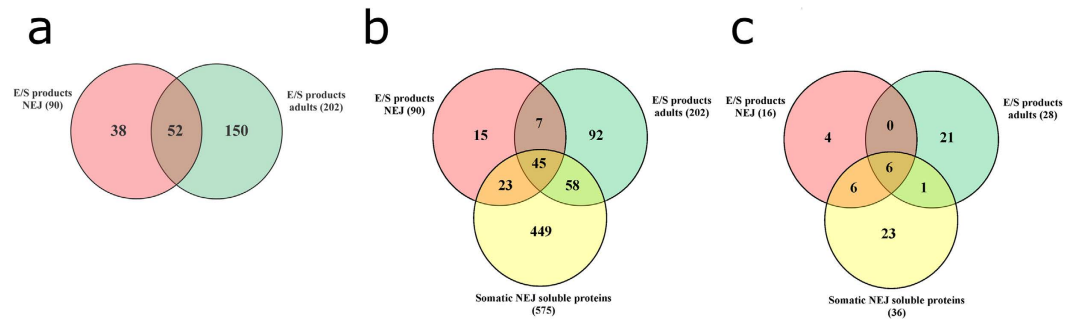


Figure 1. Distribution of proteins among *Fasciola hepatica* stages. (a) Comparison of *F. hepatica*-derived proteins identified in NEJ E/S products and adult E/S products. (b) Comparison of *F. hepatica*-derived proteins identified in NEJ E/S products, adult E/S products, and somatic NEJ soluble proteins. (c) Comparison of *Bos taurus*-derived proteins identified in NEJ E/S products, adult E/S products, and somatic NEJ soluble proteins. The overlap region between the circles shows proteins present in two or more stages.

Parasite excretory/secretory (E/S) products are the collective material comprising proteins and other compounds secreted from the fluke's gut, excretory pores and surface tegument; they are released by parasites within the host, or during *in vitro* culture⁶. These compounds play major roles in the parasite-host interface, since they are secreted during infection and protect the parasite from the host defensive responses^{7,8}. Identifying E/S proteins secreted by parasites and understanding their associated functions within the host will improve our knowledge of their roles in parasite-host relationship, generating new insights into parasite biology.

The purpose of the present study was to perform a proteomic analysis of the intra-mammal stages of *F. hepatica*, comparing protein expression in E/S products from adults and NEJ, and somatic soluble proteins from NEJ. The results obtained here present new information for future studies on the discovery of diagnostic, therapeutic, and/or vaccine targets for this important foodborne disease.

Results and Discussion

Overview of the *F. hepatica* proteome. In this study, a total of 689 *F. hepatica* proteins were identified (Fig. 1). This is the largest number of proteins identified so far for the intra-mammal stages of *F. hepatica*^{7,9–11}. One concern about the E/S products produced *in vitro* is if they are actually secreted into the host tissue by flukes. Comparing NEJ somatic proteins with NEJ E/S products we could clearly observe that protein profiles are quite different (Fig. 2a,b); for instance some proteins, such as the cytoskeletal ones, are enriched in the NEJ somatic soluble fraction over the NEJ E/S products. Thus, demonstrating NEJ E/S products are indeed excreted/secreted by the parasite, and not the result of a rupture of the parasites during cultivation.

In NEJ and adult E/S products, 240 proteins were identified: 90 from NEJ, 202 from adult flukes, and 52 proteins present in both stages (Fig. 1a). Of those shared proteins, a total of 14 (blue dots in Fig. 3a) were found to be differentially expressed in the two stages: the levels of 13 proteins were found to be higher in NEJ E/S products, whereas only one protein (a stefin) was found at higher levels in adult E/S products (Fig. 3a and Supplementary Table S1).

In the proteomic analysis of somatic soluble NEJ proteins, 575 proteins were identified, of which 68 proteins are shared with NEJ E/S products and 103 proteins are shared with adult E/S products (Fig. 1b). A core of 45 proteins is observed among the three samples (Fig. 1b). In terms of differential expression, we found that 29 proteins are differentially expressed comparing NEJ E/S products and somatic soluble NEJ proteins (blue dots at Fig. 3b). The expression levels of 17 proteins were found to be higher in NEJ E/S products, and 12 proteins were at higher concentration in somatic soluble NEJ extracts (Fig. 3b and Supplementary Table S2).

Host-derived proteins were identified in all samples. NEJ and adult E/S products presented 16 and 28 host-derived proteins, and 36 host-derived proteins were identified in somatic soluble NEJ extracts (Fig. 1c). Two host-derived proteins were found differentially expressed between NEJ E/S products and somatic soluble NEJ proteins (Fig. 3b and Supplementary Table S6).

Proteinases. Relative expression analysis showed that the most abundant class of proteins in E/S products samples from NEJ and adults are proteinases, representing 83% and 73% of the total proteins in each sample, respectively (Fig. 2b,c).

In the somatic soluble NEJ sample, proteinases represented 16% of the total protein content (Fig. 2a). Cathepsins L and B represented 51% of the total proteinase content (25.7% each), followed by legumains (20%), metalloproteinases (17%), serine-proteinases (8%), and calpains (2.8%) (Fig. 4a). Seven metalloproteinases and three serine-proteinases were detected in the somatic soluble NEJ sample (Supplementary Table S3). Concerning leucine aminopeptidases, the analysis showed three matches in our database; however, contigs BN1106_s617B000566 and BN1106_s617B000567 represented, respectively, the C-terminal and N-terminal fragments of the same protein, *FhLAP*. The third leucine aminopeptidase sequence (*FhLAP-2*) is a novel protein among somatic soluble proteins from NEJ, and shows similarity with LAP-1 from other helminths.

In the NEJ E/S products sample, contrary to what was previously described¹², the cathepsin L family was the most significantly represented group within cysteine proteinases, comprising 50% of all proteinases, followed by cathepsin B (25%) and legumain (24%) (Fig. 4b). We identified 12 cathepsin L proteins and 9 cathepsin B proteins

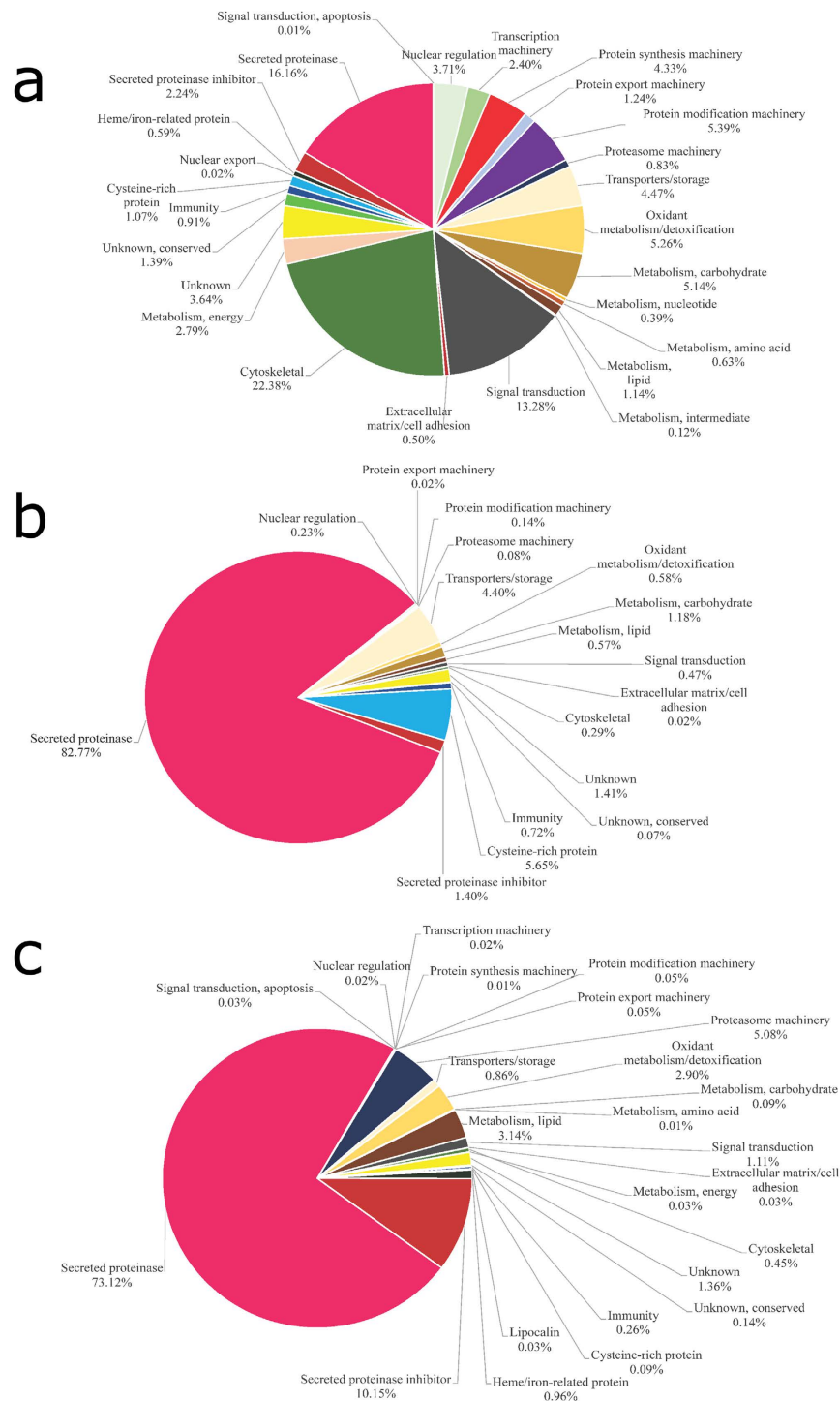


Figure 2. Functional classification of *F. hepatica*-derived proteins. Functional classification of *F. hepatica*-derived proteins identified in (a) somatic NEJ soluble proteins, (b) NEJ E/S products, and (c) adult E/S products. Pie charts represent the percentage of proteins found in each group with respect to normalized spectral counting (NSAF) for each sample.

(Supplementary Table S3, Supplementary Fig. S1 and Supplementary Fig S2). In addition, six legumains and one leucine amino peptidase (*Fh*LAP already described for *F. hepatica*)¹³ were found.

In the adult E/S products, the most abundant class of proteinases was also related to the cysteine proteinase family, with cathepsins L accounting for 44% of the total proteinase content, followed by cathepsins B (26%) and legumains (15%) (Fig. 4c and Supplementary Table S3). This is in agreement with previous reports^{7,14,15}, however, in this study a higher number of cathepsin L-like proteins were identified. We found nine cathepsin L-, five cathepsin L1-, one cathepsin L2-, one cathepsin L3-, and one cathepsin L4-like proteinases (Supplementary Table S3). Furthermore, considering the 17 cathepsins L detected, it was identified at least one representative protein of each

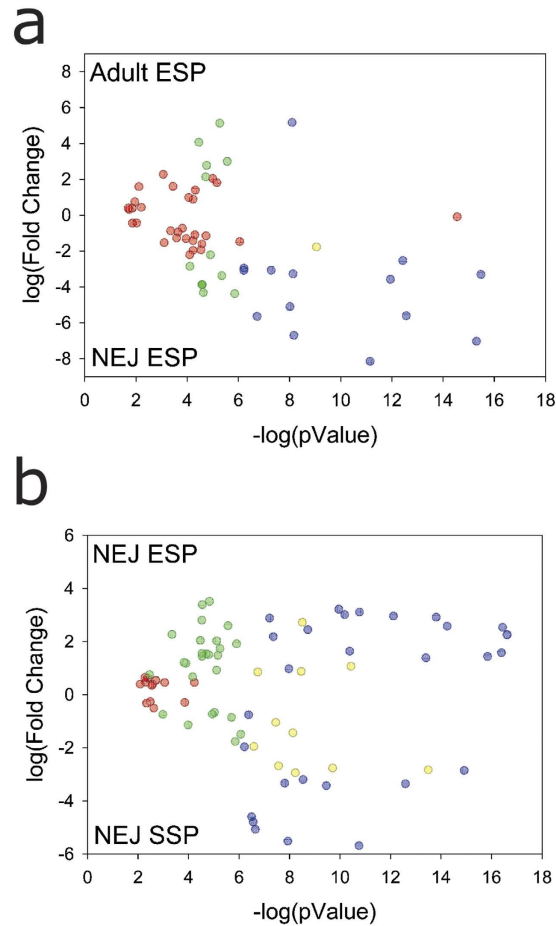


Figure 3. Volcano plot showing differentially expressed proteins. The volcano plot shows the results of differentially expressed proteins based on fold change versus t-test probability. (a) Plot obtained with the proteomic approach when comparing *F. hepatica*-derived proteins identified in E/S products from NEJ stage (NEJ ESP) with E/S products from the adult stage (Adult ESP) and (b) *F. hepatica*-derived proteins identified in E/S products from NEJ stage (NEJ ESP) with the somatic NEJ soluble proteins (NEJ SSP). Each protein is represented as a dot and is mapped according to its fold change on the ordinate axis (y) and t-test p-value on the abscissa axis (x). Proteins are represented by: (blue dot) if had an identification that satisfied both fold and statistical criteria; (yellow dot) had an identification that was filtered out by the L-stringency; (green dot) had an identification satisfied the fold criteria but, most likely, this happened by chance; and (red dot) had identification did not meet the fold and p-value criteria.

cathepsin L clade (CL1–CL4). Interestingly, clades CL3 and CL4 were previously described as NEJ-specific¹⁶. In adult E/S products, 10 cathepsins B, six legumains, three carboxypeptidases, one leucine aminopeptidase, and one dipeptidyl peptidase of the M24 family were identified (Supplementary Table S3).

All proteins that were found to be differentially expressed between NEJ and adult E/S products are proteinases, except for an alpha-glucosidase and CD59 (Fig. 3a and Supplementary Table S1). Eleven proteinases (legumains and cathepsins) exhibited higher levels in NEJ E/S products, in the range of 5- to 280-fold increase (Supplementary Table S1).

Cathepsins are secreted in the gut lumen following ingestion of host blood and liver tissue, to perform the digestion of host tissues and degradation of extracellular matrix, suggesting a role during invasion¹⁷. A role during the feeding process could be inferred based on the ability of cathepsin to degrade fibrinogen. Furthermore, since cathepsin L is able to cleave immunoglobulins, a possible function in the host immune system evasion could be assumed^{18,19}. Liver flukes possess a blind-ending intestine, and the gut content is emptied by regurgitation⁷. Accordingly, proteinases once released may carry out additional important functions for the parasite-host relationship, since liver fluke cathepsins L can cleave interstitial matrix proteins such as fibronectin, laminin, and native collagen¹⁷. More recently, it was proposed that the secreted cathepsin L may be involved in suppression and/or modulation of Th1 immune responses and induction of non-protective host Th2 responses²⁰.

Proteinase inhibitors. The proteinase inhibitors identified among NEJ E/S products represented 1% (four different proteins) of the total protein content (Fig. 2b), two of which were Kunitz-type inhibitors, one was a stefin, and one an inhibitor belonging to the I63 family (Supplementary Table S3). The proteinase inhibitors in the

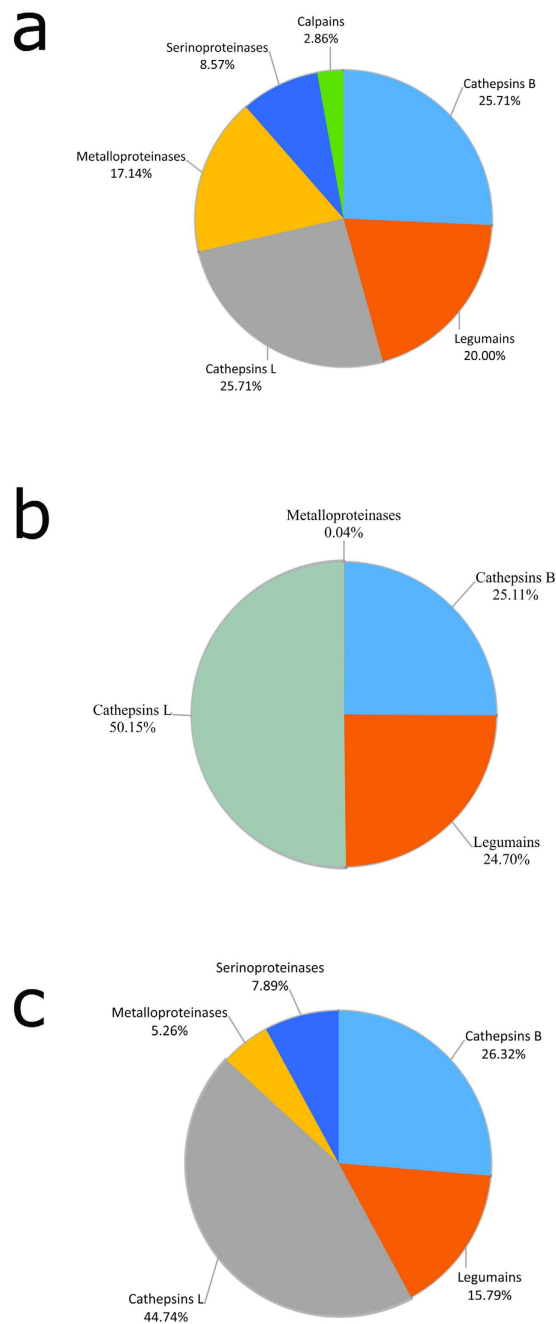


Figure 4. Functional classification of *F. hepatica*-derived proteinases. Proteinases identified in (a) somatic NEJ soluble proteins, (b) NEJ E/S products, and (c) adult E/S products were classified based on amino acid sequence similarity according to MEROPS definition. Pie charts represent the percentage of proteins found in each group with respect to normalized spectral counting (NSAF) for each sample.

adult E/S products sample represented about 10% of the total protein content, being the second most-represented class (Fig. 2c). Three cysteine proteinase inhibitors and seven serine proteinase inhibitors (five serpins and two Kunitz-type inhibitors) were identified. In the NEJ somatic soluble sample, 2% of total proteins were proteinase inhibitors (two cystatins, one stefin, five serpins and one Kunitz-type inhibitor) (Fig. 2a).

Since proteinases are important to accomplish physiological processes and have a wide spectrum of activity within the parasites, they have to be tightly regulated, or else they could be harmful to both parasite and host²¹. In addition, it has been demonstrated that proteinase inhibitors may modulate host defenses against ecto- and endoparasites^{22,23}.

Kunitz-type inhibitors are low-molecular-weight, competitive serine proteinase inhibitors that behave in a substrate-like manner and form stable complexes with their target proteases²⁴. There is to date only one Kunitz-type inhibitor described for *F. hepatica* (*Fh*-KTM)²⁵. It was described in the adult stage only, and its activities include trypsin inhibition and suppression of pro-inflammatory cytokine production by dendritic cells²³. In

our study, another Fh-KTM-like protein was found also in the E/S products from NEJ and adults (Supplementary Table S3), sharing 44% identity in amino acid sequence with Fh-KTM (data not shown).

Five serpins (serine protease inhibitors) were identified in adult E/S products and somatic soluble NEJ (Supplementary Table S3). Serpins are irreversible inhibitors of serine proteinase mediators of host defense pathways²⁶. Several serpin-encoding cDNAs from parasites have been cloned and characterized^{27,28}, although no data has been published about these proteins from *F. hepatica*. Some studies have shown that parasite-encoded serpins are functional inhibitors likely associated with evasion of host defenses, displaying anticoagulant and immunomodulatory properties^{29,30}, a characteristic that could be important for *F. hepatica* establishment and survival in the host.

Cystatin is a superfamily of cysteine protease inhibitors. In the adult E/S products and somatic soluble NEJ proteins, one stefin (family-I cystatin) and two cystatins (family-II cystatins) were identified. In NEJ E/S products only one stefin was identified (Supplementary Table S3). This stefin represents the only up-regulated protein in adult E/S products, 35.8-fold higher when compared with NEJ E/S products (Supplementary Table S1 and Supplementary Table S5). It shares 93% similarity with the one described in *F. gigantica* adult E/S products³¹. This stefin was partially found in complex with cathepsin L, suggesting a role in the regulation of cysteine proteinases activity and/or protection against extracellular proteolytic damage to the parasite intestinal tissue³¹.

Hemoglobin metabolism and heme-related proteins. In adult E/S products and somatic soluble NEJ extract, five proteins were identified which are related to hemoglobin metabolism, including: one myoglobin, three ferritins and MF6p/FhHDM-1^{7,9,32} (Fig. 2a,c and Supplementary Table S3). Two of the ferritins are novel protein descriptions for *F. hepatica*. The main source of nutrients necessary for the survival of hematophagous parasites in the host comes from the digestion of host hemoglobin, by proteolytic proteinases within the lumen of the parasite gut³³. Hemoglobin degradation releases the iron-containing prosthetic group heme, which is toxic when free in biological systems³⁴, and has pro-inflammatory properties³⁵. To avoid this, blood feeders have developed strategies for detoxifying excess heme, such as the crystallization of heme into hemozoin³⁶. It is assumed that adult *F. hepatica* releases heme and other waste molecules directly in the biliary ducts³⁷, but its capacity to form hemozoin remains unknown, although it has been described for other trematodes³⁸. Therefore, heme-binding proteins such as MF6p/FhHDM-1 and myoglobin could be used during adult *F. hepatica* blood feeding process as free-heme ligands, as a way to release excess heme and prevent heme-induced inflammation. On the other hand, heme is also a cofactor required by most living organisms to form heme proteins, which are involved in several biochemical processes³⁹. Most eukaryotic cells have enzymes that enable complete *de novo* heme biosynthesis, but it is generally accepted that hematophagous parasites have a total or partial loss of the *de novo* heme biosynthesis pathway³⁴. These parasites have had to develop heme intake, transport, and storage mechanisms, while protecting their tissues from the putative toxic effects of such molecules⁴⁰. Proteins that belong to this class were not identified in NEJ E/S products. Little is known about the diet of NEJ; it is suggested to comprise mainly host tissue cells, although some blood could be also ingested⁴¹. Therefore, the identification of heme-binding proteins exclusively in somatic soluble NEJ extract (but not in NEJ E/S products) indicates that they may contribute in the storage and supply of heme to NEJ metabolism, but are not secreted in NEJ E/S products as a way to release excess host heme.

Myoglobin (Mb) is a heme-protein described in trematodes which may have a role in host-parasite interactions, but its physiological functions are still in debate⁴². Globins of non-vertebrate species show higher variability in their structures, which might reflect their adaptations to specific functions, when compared with their vertebrate homologs⁴³. Indeed, adult parasitic helminths live mainly in a semi-anaerobic environment, and their hemoglobin-like proteins display such a high oxygen affinity that they are unlikely to serve only as O₂ transporters. In platyhelminthes, other functions for these proteins have been described, such as oxygen scavenging, heme reserve for egg production, and NO dioxygenase^{44,45}. Thus, they are functional molecules with considerable affinity for oxygen, and their role in oxygen transport and supply should be critical under the low-oxygen conditions typical of the host microenvironment. Consumption of oxygen is associated with energy metabolism; in *F. hepatica*, the Krebs cycle, which is by far the major energy-yielding pathway of NEJ and migrated juvenile flukes, is gradually replaced by aerobic acetate formation, and finally by anaerobic dismutation reactions in adult liver flukes⁴⁶.

Energy Metabolism. A total of 16 proteins with a role in energy metabolism were found, representing 3% of the total protein content in somatic soluble NEJ extracts (Fig. 2a and Supplementary Table S3). Also, one protein of this functional class, a glyceraldehyde-3-phosphate dehydrogenase, was found in the adult E/S products sample. This could suggest that energy requirements differ between stages of the same parasite.

A cytochrome C proximal sequence identified in the soluble NEJ proteins sample presents high similarity with cytochrome C from other trematodes such as *Schistosoma japonicum* and *Opisthorchis viverrini* (78% and 76% of sequence similarity, respectively; data not shown). Cytochrome C oxidase is a large transmembrane protein complex and it is the last enzyme in the mitochondrial respiratory electron transport chain, a crucial process for hypoxic response in aerobic organisms. However, hypoxia adaptation mechanisms in mitochondria are still poorly understood⁴⁷. Moreover, the high homology with a Tibetan bird cytochrome C protein suggests a similar role in *F. hepatica*. They are able to improve physiological performance by enhancing oxygen transport capacity, and have yielded important insights into the genetic basis of adaptation involving the critical oxygen carrier, hemoglobin⁴⁸.

Among somatic soluble NEJ proteins we identified one acetate/succinate CoA transferase (Supplementary Table S3) previously characterized in the mitochondria of adult fluke⁴⁹. As discussed above, the availability of oxygen is limited during all or part of the parasite life cycle; therefore, it requires ATP-synthesis pathways that are independent of O₂ as the terminal electron acceptor. The formation of acetate as an end-product from acetyl-CoA is a metabolic route present in parasites that survive in hypoxic or anoxic habitats⁵⁰. Formation and excretion of

acetate as an end-product of energy metabolism are catalyzed by a cytosolic acetyl-CoA synthetase (ACS) or by an organellar acetate:succinyl CoA-transferase (ASCT)⁵¹. In *F. hepatica*, ASCT catalyzes these reactions, indicating that acetate is synthesized in NEJ through the ASCT pathway. Given that acetate is not formed by mammalian hosts, acetate production might harbor novel targets for the development of anti-parasitic drugs.

Cysteine-rich proteins. In this group we found proteins belonging to the superfamily CAP (Cysteine-rich secretory protein, Antigen 5, and Pathogenesis-related-1 proteins), and to the CRP (Cysteine-rich protein) family. The CAP superfamily members are found in a remarkable range of organisms, and have been described in helminths⁵², as well as in other parasites⁵³. These proteins are generally secreted with a broad range of functions, including: regulation of the extracellular matrix, proteases or protease inhibitors, ion channel regulation, reproduction, and cellular adhesion⁵⁴.

In the NEJ E/S proteins sample, we identified four proteins (5% of the total protein content) corresponding to the peptidase inhibitor 16 subfamily (PI16). They share similarity with *Clonorchis sinensis* PI16 proteins, and two of them were also detected among somatic soluble NEJ proteins (1% of the total proteins) (Fig. 2 and Supplementary Table S3). However, PI16 subfamily is not well characterized, and it remains to be established whether these proteins have proteinase inhibitory activity.

Concerning the adult E/S products, two proteins of the glioma pathogenesis related-1 (GLIPR1) subfamily were identified, both of which are novel sequences with similarity to *C. sinensis* proteins. GLIPR1 proteins represent the second best-characterized CAP subfamily in mammals. In a previous transcriptomic analysis, some proteins of this subfamily were predicted *in silico* for different trematodes⁵⁵. In that study, the authors predicted two proteins with double cysteine domains, up-regulated in juvenile stages of *F. hepatica*, and other nine proteins with only one domain. Nonetheless, our work is the first to experimentally identify GLIPR1 proteins in *F. hepatica* secretome. In *Ancylostoma caninum*, proteins belonging to this class are related to neutrophil and platelets aggregation inhibition, and participate in gastrointestinal hemorrhage and iron deficiency anemia⁵⁶.

In the somatic soluble NEJ proteins, one protein was identified belonging to the CRP family. These proteins mediate protein–protein interactions and are important for cell differentiation, cytoskeletal remodeling, and transcriptional regulation⁵⁷. Further analysis and experimental data should help to understand the biological function of all these proteins in parasites.

Transport/Storage. Transport proteins represented 4% of the total protein content in both samples from NEJ (Fig. 2a,b). On the other hand, they represented less than 1% of the total proteins in adult E/S products (Fig. 2c). In NEJ E/S products, the majority of the transport proteins found belong to the cubilin family (Supplementary Table S3). Cubilins are peripheral membrane glycoproteins without transmembrane segments, having CUB domains that indicate potential binding sites for various ligands⁵⁸. These proteins, in complexes with megalin or RLP2, could work as endocytic receptors for a variety of proteins, including hemoglobin, albumin, ferritin, vitamin-carriers, and lipoproteins⁵⁹. In a recent study in mice, cubilin was apparently responsible for binding ferritin, while megalin was the protein responsible for iron uptake by the cells⁶⁰. Megalin was not found in our samples; the lack of this protein in *F. hepatica* possibly implicates cubilin binding as a way to excrete heme from hemoglobin digestion without generating an immune response from the host. In the adult E/S sample, we found some proteins related to exosomes⁶¹, ABC transporters, and calmodulins, as well as one glucose transporter.

Lipid Metabolism. Lipid metabolism is the least-studied metabolic pathway in *F. hepatica*, as the total lipid content of adult fluke represents only the 1.2% of its dry tissues⁶². From this functional class, 13 proteins were identified in adult E/S products, 3 in NEJ E/S products and 11 in the soluble components of NEJ (Supplementary Table S3). In adult E/S products, the most abundant components were the fatty acid binding protein type 2 (*FhFABP*), a saposin-like protein, and a Niemann-Pick protein. The FABP detected has a 191-aa-long sequence that matches *F. hepatica* FABP2; however, there was no match in our data for FABP1 and FABP3, in contrast to other proteomic studies^{7,9}. Two saposin-like molecules, *FhSAP-1* and *FhSAP-2*, were already described for *F. hepatica*^{63,64} and a third saposin, named *FhSAP-3*, was described for *F. gigantica*⁶⁵. In accordance with those previous reports, three saposin-like proteins were identified in the E/S products of adult flukes, but only one of them, *FhSAP-1*, was observed in NEJ samples. Other proteins found were Niemann-Pick proteins, which are involved in the transport of cholesterol within the late endosomal-lysosomal compartment⁶⁶. Besides the first description of the genes in *Caenorhabditis elegans*, the NPC2 protein has been found as one of the most abundant proteins in *Schistosoma mansoni* eggs⁶⁷, and also present in extracellular vesicles of adult *F. hepatica*⁶¹. Our results are in accordance with the previous reports. However, from the five Niemann-Pick proteins detected in adult E/S products, one was also found at high abundance in NEJ E/S products.

In the somatic soluble NEJ proteins we also identified an enzyme related to the arachidonic acid pathway: the prostamide/prostaglandin F synthase, which includes a thiolase domain in its sequence (Supplementary Table S3). To date, this proteins have been described only in protozoan parasites such as *Trypanosoma brucei*, which produces prostaglandin F₂ α ⁶⁸. Prostaglandins of the 2-series are synthesized from arachidonic acid, and their function in mammals is to modulate different physiological processes⁶⁹. The role of this prostamide/prostaglandin F synthase in *F. hepatica* is unknown, but since they produce PG₂, we could hypothesize a role in parasite-host relationship, as immunomodulators, in vacuole formation, or as signal transducers for apoptosis^{70,71}.

Miscellaneous. The alpha-glucosidase found in our study is up-regulated in NEJ E/S products, when compared to adult E/S products (Fig. 3 and Supplementary Table S5). Alpha-glucosidase is a protein involved in the hydrolysis of starch and disaccharides to glucose, which has been reported in other blood-sucking species in association with hemozoin formation, but so far never described in helminth species⁷². Glucosidase activity was described in adult E/S products from *F. hepatica*⁷³; however, β -glucosidase was not found in our

analysis. As long as it is assumed that *F. hepatica* does not have the capacity to form hemozoin, we suggest that the role of alpha-glucosidase in this parasite could be as part of a strategy to overcome heme toxicity in the host. Furthermore, alpha-glucosidase could take part in the conversion and transport of complex sugars into simpler ones, and their presence in the E/S products could mean that gastrodermis also has a role in glucose uptake.

We were also able to find proteins related to the proteasome machinery in the samples (Fig. 2). In the adult E/S products, we identified two proteins that represented 5% of the total protein (Fig. 2c), and were among the most abundant proteins in the sample (Supplementary Table S3). Concerning their presence in NEJ samples, we identified 2 proteins in NEJ E/S products and 15 proteins in somatic soluble NEJ proteins (Fig. 2 and Supplementary Table S3). The proteasome and its associated proteins have not been well studied in trematodes, but in *S. mansoni* it was demonstrated the presence of a functional proteasome⁷⁴. Protein ubiquitination is responsible for the regulation of various biological processes through covalent modification of proteins and transcription factors. During its life cycle, the parasite is exposed to physical and chemical stress. Free-living stages are subjected to threats, such as chemical pollutants, variations in temperature, and solar radiation, while parasitic stages are exposed to oxidative stress and the host immune system. The proteasome represents the main cytoplasmic proteolytic machinery for the degradation of damaged proteins⁷⁵, and is responsible for the maintenance of protein homeostasis during oxidative stress⁷⁶. Apart from these various antioxidant defense systems, we also identified superoxide dismutase, peroxiredoxins, glutathione peroxidase, cytochrome C, glutathione S-transferase, glutathione reductase, and thioredoxin glutathione reductase in *F. hepatica* (Supplementary Table S3). These findings suggest that the proteasome machinery is important across different intra-mammal stages, though it seems to have a fundamental role in the adult fluke.

Only one lipocalin protein was identified in adult E/S products (Supplementary Table S3). Lipocalins are proposed to be members of a superfamily of proteins named calycins, which comprises proteins with a β -barrel that binds small, lipophilic ligands⁷⁷. This superfamily includes fatty acid binding proteins (FABP), avidin, metalloproteinase inhibitors, and triabin⁷⁸. There is still no evidence of the function of lipocalins in trematodes, but they are a well-studied family of proteins in other blood-sucking arthropods, like ticks⁷⁹. In ticks, lipocalins are present in saliva, and part of their role could be that of antihemostatic and immunomodulatory molecules, helping to maintain parasite attachment to host tissues and to overcome the host immune system. Like ticks, flukes are blood feeders which depend upon attachment to host tissues, thus lipocalins could perform a similar function in *F. hepatica*.

Other novel proteins found in the somatic soluble NEJ sample are the actin-associated proteins (Supplementary Table S3). It is known that several actin-associated proteins are required to maintain the high rates of actin filament disassembly and turnover that drive biological processes. Rapid cycles of actin assembly and disassembly require actin-binding proteins, including beta-thymosins, actin-binding competitor profilin⁸⁰, and the depolymerization factors cofilin⁸¹ and coronin⁸². Their role may be associated with vesicular trafficking in the tegumental syncytium of NEJ, as well as to other intracellular events in muscle tissue or nervous system development which require formation and/or depolymerization of actin. In particular, coronins are highly conserved proteins involved in actin dynamics across eukaryotic systems, including filament binding and bundling. They generally bind to F-actin and apparently are involved in proliferation, locomotion, and phagocytosis⁸³. A major actin binding protein, called beta-thymosin, was described in *Trichinella spiralis* and it is so far the best-studied actin-associated protein from helminth parasites⁸⁴. It sequesters beta-actin to regulate its polymerization, functions as an angiogenic factor which is up-regulated during *T. spiralis* nurse cell formation, and is co-localized with beta-actin within infected host muscle⁸⁴. Nevertheless, the role of those proteins in *F. hepatica* biology remains to be elucidated. However, it comes as no surprise that NEJ possesses this battery of actin-binding proteins that might be used in morphogenesis, tissue remodeling, and/or in exocytosis/endocytosis events during its development into the larger immature stages.

Furthermore, proteins with potential roles in exosomal membrane structure were identified in both, adult and NEJ E/S products samples (Supplementary Table S1)^{10,85}. This is the first identification of exosome-related proteins among NEJ E/S products. Considering all the new data about the components of E/S products, including host and exosomal proteins, maybe it is time to formally revise the definition and composition of helminth E/S products.

Host-derived proteins. Host-derived proteins (based on a *B. taurus* database) were identified in all samples, including 16 proteins in NEJ E/S products, 28 proteins in adult E/S products, and 36 proteins in somatic soluble NEJ extract (Fig. 1c and 5 and Supplementary Table S4). Based on relative abundance, most of them are blood-related proteins. During adult E/S products collection, only adult flukes that had visibly emptied their guts were used; however, they may still have had mammal blood proteins in them. Interestingly, we were not able to find albumin or hemoglobin, the major proteins in blood, proposing that the host-derived proteins identified here are more than contamination agents due to parasite regurgitation. In agreement with this hypothesis, some of the host proteins described here have been found in secreted exosome vesicles of *F. hepatica*¹⁰, suggesting that their presence in parasite secretions may be a real and common recycling system, not a result of contamination during sample collection. This finding is in accordance with previous studies that investigated parasite secretion from other blood-feeding parasites⁷⁹. It remains to be clarified whether these proteins are returned to the host as intact proteins or products of partial hydrolysis.

Host-derived proteins with a role in regulation of host defense pathways against parasites were detected in adult E/S products, including: antithrombin III (thrombin inhibitor), alpha-1-antitrypsin and serpin B1 (neutrophil elastase inhibitor), immunoglobulin (humoral response), alpha-2-macroglobulin (blood coagulation), fibrinogen (blood coagulation and platelet aggregation), and kininogen-2 (inflammation and coagulation) (Supplementary Table S4). Liver fluke adults establish contact with the host immune and hemostatic systems, and have to evade them in order survive. Thus, one possible explanation for the presence of host-derived proteins in

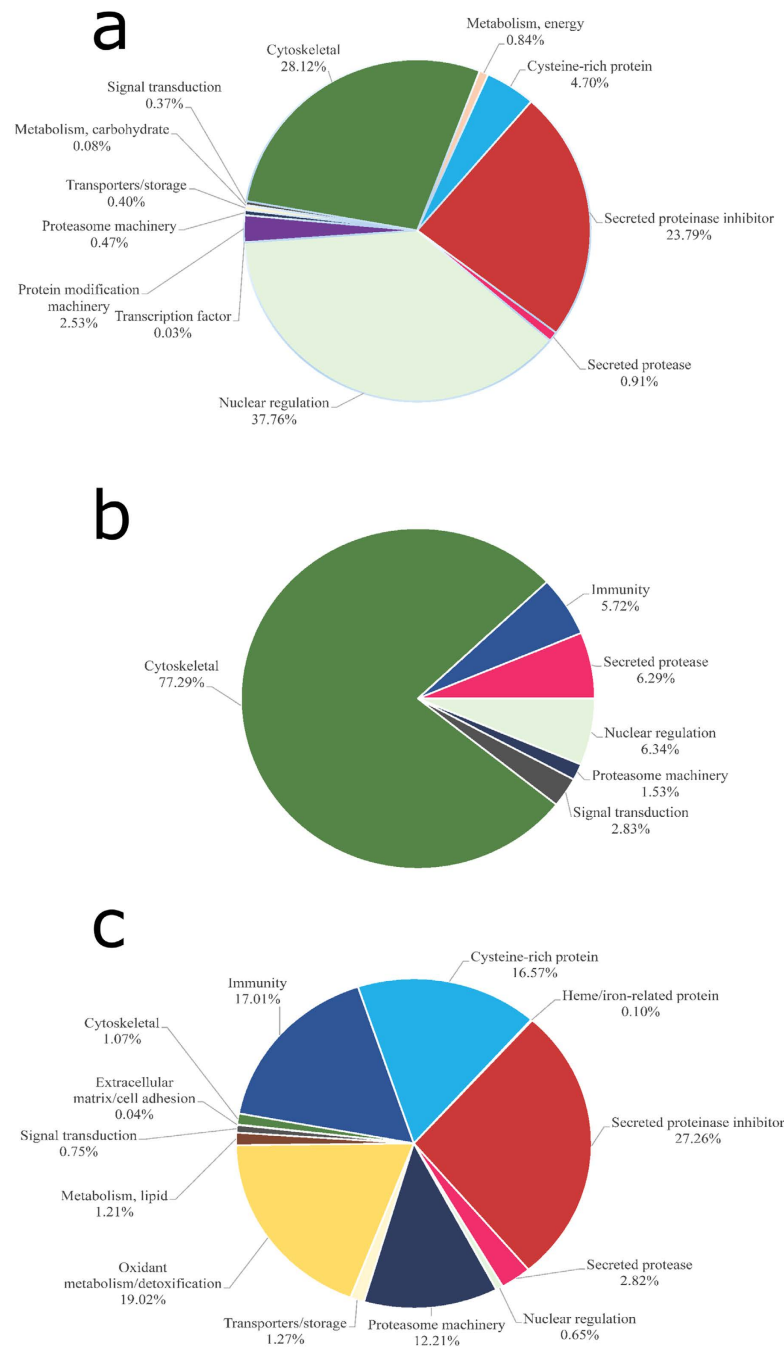


Figure 5. Functional classification of *Bos taurus*-derived proteins. Functional classification of *B. taurus*-derived proteins identified in (a) somatic NEJ soluble proteins, (b) NEJ E/S products, and (c) adult E/S products. Pie charts represent the percentage of proteins found in each group with respect to normalized spectral counting (NSAF) for each sample.

parasite secretion is that parasites recycle pivotal host proteins in order to subvert their role in the host and/or use host proteins in specific parasite physiologic systems. Alpha-1-antiprotease, serpin B1, and antithrombin III were identified in adult E/S secretions. These proteins regulate proteinases such as neutrophil elastase and thrombin, and thus it would be interesting to find out whether these host proteins have the potential to inhibit their own serine proteinases. In turn, the presence of immunoglobulin chains could be explained as a parasite self-defense system, in a process leading to removal of host immunoglobulins. In addition, a recent study demonstrated the use of host-derived transferrin in the tick *H. longicornis*. This host-derived transferrin moves particularly from the midgut via hemolymph to the tick's ovary, raising the possibility that it functions as an iron source in this organ⁸⁶

Host-derived proteins were also found in NEJ samples (Fig. 5a,b and Supplementary Table S4). This is a quite interesting finding, since NEJ hatched from metacercariae *in vitro* are not expected to have host proteins

as contaminants. In the NEJ stage, the host-derived proteins identified are mainly represented by cytoskeletal and nuclear proteins such as histone H2A, histone H4, actin-2, tubulin, and HSP 70. These proteins are largely conserved across species, and these signals could have been derived from parasite proteins instead. Accordingly, to further control the origin of the putative host-derived proteins identified, we compared these host protein sequences with proteins from *F. hepatica* (data not shown). Indeed, a great part of the detected host proteins is highly conserved. For example, mammalian histone is 89% identical to *F. hepatica* histone, while host actin and tubulin are 93% and 92% identical to the liver fluke proteins, respectively. Many proteins show similarity >65% to liver fluke proteins, and thus their origin cannot be determined. The mammalian keratin found in all samples could represent a major contamination from laboratory manipulation⁸⁷.

Despite reports of host-derived proteins in parasite exosomes⁸⁵, this remains a neglected issue in the study of parasite biology. The demonstration of these proteins in the present work raises several questions to be further explored, and may reveal novel insights into parasite-host relationship.

Conclusions

The purpose of this study was to characterize the protein composition of mammal-related stages of the endo-parasite *F. hepatica*. The liver fluke secretes/excretes proteins which are qualitatively and quantitatively different during its intra-mammal life stages, likely reflecting different locations within the host. The use of LC-MS/MS approach allowed us to identify proteins previously found in other proteomic studies, as well as other proteins described here for the first time in *F. hepatica*.

Comparing our data with previous studies, the proteomic strategy used here allowed us to identify proteins that are not abundant in the samples (Fig. 2, Supplementary Tables S3 and S4). We identified 575 proteins in the soluble NEJ extract, 90 proteins in the E/S products from NEJ, and 202 proteins in adult E/S products. In a recent study combining transcriptomic and proteomic data, 160 secreted proteins were predicted in the transcriptomic approach; however, only 22 proteins were found in adult flukes and 29 proteins were detected in NEJ secretions using a 2-DE proteomic approach⁷. In another study on secreted proteins from adult fluke, 29 out of 60 prominent proteins were identified, also using a 2-DE approach¹⁴, while in a study using LC-MS/MS, only 16 out of 54 proteins from NEJ were suggested to be secreted⁸⁸. In a study from 2010 on proteins expressed by freshly excysted parasites, or NEJ, the authors found a total of 40 *F. hepatica* proteins using LC-MS/MS¹¹. In 2011, a study on the adult fluke secretome identified 63 proteins, whereas in a recently published article the authors identified 69 proteins in *F. hepatica* extracellular vesicles^{9,10}. Comparing these studies, we found that all share a common group of proteins, but with some differences (Supplementary Table S7). These differences could maybe be explained based on the different technical procedures and materials used in each study. Another point to keep in mind is that, even though the *F. hepatica* adults used in these studies belong to the same species, they are subject to different environments (weather conditions, soil, cattle, etc.), which may influence the amount and variety of secreted proteins.

In general, another concern is about the biological relevance of the proteins identified by a proteomic analysis. In a previous proteomic study of bile from *F. hepatica*-infected animals, had shown that the major *F. hepatica* proteins present in the host were proteases, as well as, in the *in vitro* culture¹⁵. In addition, it was demonstrated that E/S products can be used for diagnosis of human fascioliasis^{89,90}. Therefore, proteins identified in the present study are physiologically relevant since them, besides being identified in other proteomic studies, were also previously validated as secreted proteins in natural infections.

Methods

Ethical statement. This study was conducted in accordance to the ethic and methodological aspects preconized by the International and National Directives and Norms by the Animal Experimentation Ethics Committee of the UFRGS. The protocols were approved by the Comissão de Ética no Uso de Animais - CEUA and UFRGS (No. 28309). Cattle livers were collected from a local abattoir immediately after slaughter. Natural liver fluke infections were diagnosed at abattoir by independent trained meat inspectors and the biological material discarded by the local abattoir protocol. The abattoir authorized by the Ministry of Agriculture and Fisheries of Uruguay (MGAP), complies with the National Animal Welfare Act No. 18471 of 2009 law of protection, welfare and possession of animals, regulated by: Decree No. 62/014 14.03.2014; and with the good animal welfare practices concerning transport and slaughter of cattle and sheep, prepared by the Technical Group of the Directorate General of Livestock Services (DGSG-MGAP) in 2005, according with the recommendations of the 73rd General Session of the OIE-World Organisation for Animal Health on 27 May 2005.

Preparation of *F. hepatica* E/S products. *F. hepatica* metacercariae (Oregon strain) were purchased from Baldwin Aquatics Inc. (Monmouth, OR, USA). In order to obtain E/S products, metacercariae were activated *in vitro* to allow eclosion of NEJ, as previously described⁹¹, and the process was monitored under a binocular stereo zoom microscope. The emerging active parasites were washed with sterile PBS, then 600 to 800 NEJ were picked up and incubated at 37 °C, 5% CO₂ in 1 ml of sterile culture medium, composed of RPMI 1640 supplemented with 30 mM HEPES pH 7.2, 2% glucose and 10% antibiotic/antifungal mixture (Penicillin/Streptomycin/Amphotericin B Mix). NEJ were maintained alive in culture for 48 h; every 12 h, the supernatant containing the E/S products was collected under a security cabinet with laminar flow, and replaced with fresh sterile medium. During medium exchange, NEJ integrity was evaluated by motility visualization. All samples were pooled under laminar flow, syringe-filtered through sterile filter (0.22 µm), processed for buffer exchange against sterile PBS, and concentrated using centrifugal filter units of 3,000-Da cut-off. Aliquots were lyophilized and stored at -80 °C until use.

Adults flukes (n = 50) were collected from the bile ducts of four different infected cattle from a local abattoir in Montevideo, Uruguay, and E/S products were obtained cultivating flukes into 1 mL of culture medium per fluke following incubation at 37 °C. After 3 hours, a total of 50 mL of supernatant was collected and filtered

esterilized¹⁹. The product was stored at -80°C until use. To verify the absence of contaminating proteins in the samples, the taurocholic acid used during the excystment procedure was analyzed by LC-MS/MS as a control.

Preparation of *F. hepatica* NEJ soluble extracts. NEJ ($n=400$) were collected (as described under item 2.1) in a sterile 1.5-mL tube, washed 3 times in PBS with protease inhibitor cocktail, and sonicated for 5 min with 60-s bursts at 20% power followed by 30-s pauses, using a tissue homogenizer. The homogenate was centrifuged at 48,000 g for 10 min at 4°C . The obtained supernatant was stored at -80°C until use. Protein extracts were quantified at 280 nm in a Nanodrop 1000 spectrophotometer (Thermo Fisher Scientific, USA).

Protein digestion and sample preparation. Protein samples were digested in solution with trypsin. Samples were diluted in 8 M urea/0.1 M Tris, pH 8.5, reduced with 5 mM Tris (2-carboxyethyl) phosphine hydrochloride, and alkylated with 25 mM iodoacetamide. Proteins were digested overnight at 37°C in 2 M urea/0.1 M Tris pH 8.5, 1 mM CaCl_2 with trypsin at a final ratio of 1:20 (w/w) (enzyme:substrate). Digestion reactions, at a final protein concentration of $0.15\ \mu\text{g}/\text{mL}$, were quenched with formic acid (5% final concentration) and centrifuged at 17,000 g for 5 min at 4°C for removal of debris.

Pre-columns and analytical columns. Reversed phase pre-columns were prepared in $250\ \mu\text{m}$ ID/ $360\ \mu\text{m}$ OD capillaries with a Kasil frit at one end. Pre-columns were packed in-house with 2 cm of a $5\text{-}\mu\text{m}$ ODS-AQ C18 particle slurry in methanol. Analytical reversed phase columns were prepared by pulling a silica capillary ($100\ \mu\text{m}$ ID/ $360\ \mu\text{m}$ OD) to a $5\text{-}\mu\text{m}$ ID tip, and packing 20 cm of the above mentioned particles directly onto the pulled tip. Reversed phase pre-columns and analytical columns were connected using a zero-dead volume union.

LC-MS/MS. Peptide mixtures were analyzed by nanoflow LC-MS using an Easy NanoLC II coupled to a Q Exactive mass spectrometer (Thermo Fisher Scientific, USA). Solutions A and B consisted of 5% acetonitrile/0.1% formic acid and 80% acetonitrile/0.1% formic acid, respectively. The flow rate was set to 400 nL/min. Protein samples ($1.5\ \mu\text{g}$ per injection) were separated in 155-min chromatographic runs, as follows: 1–10% B in 10 min, 10–40% B in 100 min, 40–50% B in 10 min, and 50–90% B in 10 min. The column was held at 90% B for 10 min, then brought to 1% B and re-equilibrated prior to the next injection. Peptides eluted from the analytical column were electrosprayed directly into the mass spectrometer.

The mass spectrometer was operated in a data-dependent mode, collecting a full MS scan from 400 to 1,200 m/z at 70,000 resolution and AGC target of 1×10^6 . The 10 most abundant ions in each scan were selected for MS/MS at 17,500 resolution, with AGC target of 2×10^5 , and an underfill ratio of 0.1%. Maximum fill times were 20 ms and 120 ms for MS and MS/MS scans, respectively, with dynamic exclusion of 15 s. Normalized collision energy was set to 25.

Data Analysis. Tandem mass spectra were extracted from Thermo RAW files using RawExtract 1.9.9.2⁹², and searched with ProLuCID⁹³ against a non-redundant database containing coding sequences from *Fasciola hepatica* genome⁹⁴ (33,454 entries), concatenated with a *Bos taurus* Uniprot reference database (23,804 entries), in addition to reverse sequences of all entries. Searches were done using Integrated Proteomics Pipeline (IP2, <http://www.integratedproteomics.com>). The search space included all fully-tryptic and half-tryptic peptide candidates. Carbamidomethylation of cysteine was used as static modification. Data were searched with 50-ppm precursor ion tolerance and 20-ppm fragment ion tolerance.

The validity of the peptide spectrum matches (PSMs) generated by ProLuCID was assessed using Search Engine Processor (SEPro) module from PatternLab for Proteomics platform⁹⁵. ProLuCID XCorr, DeltaCN, DeltaMass, Z-score, number of matched peaks, and secondary rank values were used to generate a Bayesian discriminating function. A cut-off score was established to accept a false discovery rate (FDR) of 1% based on the number of decoys. A minimum sequence length of six residues per peptide was required. Results were post-processed to only accept PSMs with precursor mass error <10 ppm.

A Volcano plot was generated by pairwise comparison between NEJ and adults E/S products, and between NEJ E/S products and NEJ somatic soluble extract, using the PatternLab's TFold module⁹⁵. NSAF (normalized spectral abundance factor) was used for data normalization⁹⁶. NSAF for a given protein is the number of spectral counts (SpC) identified for that protein, divided by the protein's length (L), divided by the sum of SpC/L of all protein in the experiment. The following parameters were used to select differentially expressed proteins: proteins were grouped by maximum parsimony, spectral count data were normalized using NSAF values, and two nonzero replicate values were required for each condition (at least two out of three replicates). A BH q-value was set at 0.02 (2% FDR). A variable fold-change cut-off for each individual protein was calculated according to the t-test p-value using an F-stringency value automatically optimized by the TFold software. Low-abundance proteins were removed using an L-stringency value of 0.4.

Protein functional annotation and classification. To manually curate *F. hepatica* and *B. taurus* protein database annotation, BLASTP searches against several databases were performed. To functionally classify the protein sequences, a program developed and provided by Dr. José M. C. Ribeiro was used⁹⁷. The functionally annotated catalog for each dataset was manually curated and plotted on a hyperlinked Excel spreadsheet (Supplementary Tables S3 and S4).

Relative abundance and graphical visualization. Proteomic profiles were compared across samples as functional classes or individual proteins. To determine the relative abundance of proteins, NSAF was used in a label-free relative quantification approach⁹⁸. Mean NSAF values from the two or three replicates were determined and combined according to functional class, and then divided by the total NSAF for the respective sample.

NSAF as an index for relative protein abundance was input in Microsoft Excel as percentage of the total NSAF for respective samples, and visualized on pie charts according to protein classes.

Data availability: The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD003214.

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Author Contributions

Conceived and designed the experiments: L.S.D.M., L.T., A.F.M.P., J.K.D., J.R.Y., U.B., C.C., I.d.S.V. and P.B. Performed the experiments: L.S.D.M., L.T., J.K.D. and P.B. Contributed reagents/materials/analysis tools: A.F.M.P., J.R.Y., C.C., I.d.S.V. and P.B. Drafting the article: L.S.D.M., L.T., A.F.M.P., C.C., I.D.S.V. and P.B. Critical revision of the article: L.S.D.M., L.T., A.F.M.P., J.K.D., J.R.Y., U.B., C.C., I.d.S.V. and P.B.

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3.2 Capítulo II.

The host factor: comparison between *F. hepatica* newly excisted juvenile from different intermediate hosts.

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The host factor: comparison between *Fasciola hepatica* newly excisted juvenile derived from two intermediate hosts

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Abstract

The characteristics of parasitic infections are often tied to host behavior. Although most studies have investigated definitive hosts, intermediate host also can play a role in shaping the distribution and accumulation of parasites. This is important particularly in the larval stages, where the intermediate host behaviour could interfere in the molecules that parasite will secrete during the infection. In an attempt to answer this question, excretion/secretion products (ESP) of newly excisted juvenile (NEJ) *Fasciola hepatica* derived from two intermediate host species, *Lymnaea viatrix* and *Lymnaea columella*, were analyzed. The two proteomes analyzed here have shown differences in protein abundance, functional classification and individual proteins that could be due to differences in the biological cycle of the parasite in the host, biological aspects, and/or host-dependent factors. Categories such as protein modification machinery, protease inhibitors, signal transduction, and cysteine-rich proteins have different abundance between samples. In addition, differences in abundance of individual proteins such as peptidyl-prolyl cis-trans isomerase, thioredoxin, cathepsin B, cathepsin L, and Kunitz-type inhibitors were identified. Based on the differences identified between the NEJ ESP samples, we can conclude that the intermediate host is capable of interfere in the proteomic profile of ESP in *F. hepatica*.

Keywords: *Fasciola hepatica*, secretome, parasite-host interaction.

Introduction

Fasciola hepatica is the causative agent of fasciolosis, a zoonotic foodborne disease of livestock that cause economic losses worldwide and, in developing countries, it constitutes a treat to human health¹. The parasite has a broad host-range, and depending on the definitive host species, including sheep, cattle, wild mammals, and humans, the illness has different progression. Acute fasciolosis is present primarily in ovines and may lead to the death of the animal, whereas chronic fasciolosis is often fatal in ovines, could be asymptomatic in cattle². The snails, which function as intermediate host of this parasite, belong to the family *Lymnaeidae*, and the specie varies between world regions. In America, the most common genus are *Lymnaea columella* and *Lymnaea viatix*, while in Europe is *Galba truncatula*. However, nowadays these species could be found in other regions as well^{3,4}. In the snail, which inhabits temporary steams bordered by aquatic vegetation and grass⁵, miracidium complete the asexual phase of the parasite and exit the host as a cercariae to later become a metacercariae. The definitive mammalian host becomes infected ingesting vegetation containing metacercariae. Newly excysted juveniles (NEJ) emerge in the duodenum and migrate to the liver and bile ducts, where undergo maturation, and produce eggs⁶. Immature eggs are discharged in the biliary ducts and in the stool, each egg release a miracidium which invade the intermediate host. The number of ingested metacercariae usually determines the course of pathology, since it is related to the intensity of mechanical destruction of tissues during NEJ migration, that in addition to tissue destruction caused during migration, can cause localized or generalized toxic and allergic reactions⁷. The NEJ stage is important since they migrate though the parenchyma in the definitive host causing significant tissue injuries that can lead to pathologies. As NEJ migrate, they have to deal with host defenses⁸ that affect the parasite

survival. As a consequence, parasite has to develop ways to interact with and neutralize them⁹. Some of the proteins and other compounds secreted/excreted from the parasite that interacts with the host are called excretory/secretory products (ESP). Although ESP from NEJ *F. hepatica* has been studied in the past, the purpose of the present study was to perform a comparative proteomic analysis of the NEJ stage of *F. hepatica* derived from different intermediate hosts, *L. columella* and *L. viatrix*. The results obtained here provides clues to better understand the response of *F. hepatica* to different host environments, which could be useful for future studies on parasite control.

Methods

Collection of *F. hepatica* ESP

F. hepatica metacercariae cysted from cercariae developed in the snail *L. viatrix* were purchased from the laboratory DILAVE "Miguel C. Rubino" (Montevideo, Uruguay). *F. hepatica* metacercariae cysted from cercariae developed in the snail *L. columella* were purchased from Baldwin Aquatics Inc. (Monmouth, OR, USA). Metacercariae were activated *in vitro* and NEJ were allowed to excyst as previously described¹⁰. About 600 emerging NEJ were removed from the excystement medium, washed with sterile phosphate-buffered saline (PBS, pH 7.4), and maintained at 37 °C, 5 % CO₂ in 1 mL of sterile culture medium (RPMI 1640, 30 mM HEPES, pH 7.2, 2 % glucose and 10 % penicillin/streptomycin/amphotericin B mix). After incubation for 12 h, the supernatant containing the ESP was collected, and vial-containing NEJs was filled with fresh sterile medium where evaluation of the NEJ integrity was assessed under the microscope. All ESP supernatant samples were pooled, syringe-filtered (0.22 µm), and concentrated using centrifugal filter units of 3,000-Da cut-off. Aliquots of the samples were lyophilized and stored at - 80 °C until use.

Protein digestion, liquid chromatography and tandem mass spectrometry analysis.

ESP sample obtained in the previous step was diluted in a buffer containing 8 M urea/0.1 M Tris, pH 8.5, reduced with 5 mM Tris (2-carboxyethyl) phosphine hydrochloride, and alkylated with 25 mM iodoacetamide. Digestion with trypsin (at a final ratio 1:20, enzyme: substrate) was performed overnight at 37 °C in 2 M urea/0.1M Tris pH 8.5, 1 mM CaCl₂ buffer. After digestion, 0.15 µg/mL of the sample was quenched with formic acid (5 % final concentration) and centrifuged at 17,000 g for 5 min at 4 °C for debris removal.

Reversed phase pre-columns were prepared in 250 µm ID/360 µm OD capillaries with a Kasil frit at one end. Pre-columns were packed in-house with 2 cm of a 5-µm ODS-AQ C18 particle slurry in methanol. Analytical reversed phase columns were prepared by pulling a silica capillary (100 µm ID/360 µm OD) to a 5-µm ID tip, and packing 20 cm of the above mentioned particles directly onto the pulled tip. Reversed phase pre-columns and analytical columns were connected using a zero-dead volume union.

Peptide mixtures were analyzed by nanoflow LC-MS/MS using an Easy NanoLC II coupled to a Q Exactive mass spectrometer (Thermo Fisher Scientific, USA). Solutions A and B consisted of 5 % acetonitrile/0.1 % formic acid and 80 % acetonitrile/0.1 % formic acid, respectively. The flow rate was set to 400 nL/min. Protein samples (1.5 µg per injection) were separated in 155-min chromatographic runs, as follows: 1-10 % B in 10 min, 10-40 % B in 100 min, 40-50 % B in 10 min, and 50-90 % B in 10 min. The column was held at 90 % B for 10 min, then brought to 1 % B and re-equilibrated prior to the next injection. Peptides eluted from the analytical column were electrosprayed directly into the mass spectrometer.

The mass spectrometer was operated in a data-dependent mode, collecting a full MS scan from 400 to 1,200 m/z at 70,000 resolution and AGC target of 1×10^6 . The 10 most abundant ions in each scan were selected for MS/MS at 17,500 resolution, with AGC target of 2×10^5 , and an underfill ratio of 0.1 %. Maximum fill times were 20 ms and 120 ms for MS and MS/MS scans, respectively, with dynamic exclusion of 15 s. Normalized collision energy was set to 25.

Data Analysis

Tandem mass spectra were extracted from Thermo RAW files using RawExtract 1.9.9.2⁹⁰, and searched with ProLuCID⁹¹ against a non-redundant database containing coding sequences from *Fasciola hepatica* genome⁹² (33,454 entries), concatenated with a *Bos taurus* Uniprot reference database (23,804 entries, compiled October 2017) in addition to reverse sequences of all entries. Integrated Proteomics Pipeline (IP2, <http://www.integratedproteomics.com>) were used to search for proteins with fully-tryptic and half-tryptic peptide candidates included. Carbamidomethylation of cysteine was used as static modification. Data were searched with 50-ppm precursor ion tolerance and 20-ppm fragment ion tolerance.

The validity of the peptide spectrum matches (PSMs) generated by ProLuCID was assessed using Search Engine Processor (SEPro) module from PatternLab for Proteomics platform⁹³. ProLuCID XCorr, DeltaCN, DeltaMass, Z-score, number of matched peaks, and secondary rank values were used to generate a Bayesian discriminating function. A cut-off score was established to accept a false discovery rate (FDR) of 1 % based on the number of decoys. A minimum sequence length of six residues per peptide was required. Results were post-processed to only accept PSMs with precursor mass error < 10 ppm.

Volcano plots were generated by pairwise comparisons between PES from *L. viatrix* and *L. columella* NEJ, in Excel 2013 (Microsoft; Redmond, WA). Three technical replicates were performed for each ESP sample and proteomic differences were evaluated for statistical significance ($p < 0.05$) by student t-test. Means were calculated for the replicates and fold-changes were determined by dividing the mean intensity value of the *L. viatrix* sample by that of the *L. columella* sample for each shared protein. The fold change and p -value were transformed using the log₂ function, so that the data is centered around zero for volcano plot scaling.

Protein functional annotation, relative abundance, graphical visualization and comparison between samples.

To manually annotate the matched proteins, BLASTP searches against several databases were performed. A program developed by Dr. José M. C. Ribeiro was used to functionally annotate the protein sequences retrieved from the databases¹¹. The functionally annotated proteins for each dataset was manually curated and plotted on a hyperlinked Excel spreadsheet (Supplementary Table S1). Proteomic profiles were compared between samples, *L. viatrix*- and *L. columella*-derived NEJ, as functional categories or individual proteins. For data comparison results from our previous published study with ESP from NEJ derived from *L. columella* snails metacercariae, with 90 proteins identified were used¹². NSAF was used as a label-free relative quantification approach. Mean NSAF values from, at least two replicates were determined and combined according to functional categories and then divided by the total NSAF for the respective sample. The NSAF values, in percentages and as an index for relative protein

abundance, were plotted in a Microsoft Excel spreadsheet and visualized on pie charts or tables according to protein categories.

Results and Discussion

NEJ is a stage in the *F. hepatica* cycle that causes damage in the definitive mammalian host tissues during the migration through the parenchyma to the liver. Hence, expanding the knowledge of this stage of the *F. hepatica* cycle is crucial to understanding the mechanism that this parasite uses to invade, migrate, grow and survive in the hosts. In an attempt to do that, we analyzed whether the intermediate host snail species where cercariae develops could affect the abundance and/or profile of proteins present in the NEJ ESP. In order to compare samples from different hosts, NEJ ESP samples obtained from *L. viatrix*-derived metacercariae were compared with ESP NEJ retrieved from metacercariae obtained from *L. columella* snails.

In our previous study about ESP in the intra-mammalian stages of *F. hepatica*¹², 90 *F. hepatica* proteins were identified in the NEJ derived from *L. columella* intermediate host. Here, we used NEJ ESP data from Di Maggio *et al* (2016) to compare with the present results, where the intermediate host was *L. viatrix*. From *L. viatrix*-derived NEJ ESP sample, 57 *F. hepatica*-derived proteins were identified (Figure 1A). Overall, three and thirty-six proteins are unique for *L. viatrix*- and *L. columella*-derived NEJ ESP, respectively (Figure 1A). Both analyzed NEJ ESP samples share 54 proteins (Figure 1A). In the *L. viatrix* NEJ ESP sample, 78.8% of the total proteins belongs to the secreted protease class, followed by secreted protease inhibitors (5.0%), transporters/storage (4.3%) and oxidant metabolism/detoxification (2.2%) (Figure 2A). While in the *L. columella* NEJ ESP the most abundant categories are proteases (83%), cysteine-rich proteins (5.6%) and transporters/storage (4.4%) (Figure 2B). Figure 2B shows

comparison on functional abundance of proteins between *L. viatrix* and *L. columella*-derived NEJ ESP.

From those 54 protein shared between intermediate hosts, 16 of them were found to be differentially abundant between samples (blue dots in Figure 3), all of those being up-regulated in the ESP sample from *L. viatrix*-derived NEJ (Figure 3 and Table 1).

Proteases. Comparison of the ESP proteome from NEJ derived from two different intermediate hosts shows that proteases are the most abundant class of proteins (79% and 83% from *L. viatrix*- and *L. columella*-derived ESP, respectively). This class of proteins is required in various stages of the life cycle of parasitic and non-parasitic organisms¹³. In *F. hepatica*, proteases are the most well studied and abundant family of proteins, and their potential as chemotherapeutic or vaccine targets is promising^{14,15}. It is known that they are secreted into the ESP from the gut lumen of the parasite and that their functions are varied, acting in processes such as tissue and extracellular matrix digestion, excystment, and immunomodulation¹⁶. Relative abundance analysis showed this is the most abundant class in *L. viatrix*- and *L. columella*-derived NEJ ESP. All proteins belonging to secreted protease class are part of the cysteine proteases family, comprising 09 cathepsins L, 08 cathepsins B and 06 legumains (Figure 2 and Supplementary Table S1). Members of the cysteine protease family are the most abundant expressed proteins in juvenile and adult stages of *F. hepatica*^{12,17}. Several of them are described as differentially expressed between intra-mammal stages of *F. hepatica*. The function of these proteins is not yet fully understood. Cathepsins B were first identified as NEJ-specific proteins and is known that they can digest type I collagen, fibronectin, and immunoglobulins^{18,19}. When silenced, NEJ ability to penetrate host tissues was reduced²⁰. Altogether, these findings suggest that cathepsins B could be involved in excystment,

tissue penetration and evasion of the host immune system^{21,22}. Cathepsins L are divided into clades according to their sequences, and some of them are specific for NEJ (clade 4) or adults (clades 1, 2 and 5)²³. Cathepsins L have a broad range of possible functions, including cleavage of extracellular matrix proteins and immunoglobulins, suggesting roles in tissue degradation and evasion of host immune system. The ability to secrete proteases involved in extracellular matrix degradation is a common feature in parasitic organisms²⁴.

From 23 proteases identified in *L.viatrix*-derived NEJ sample, 05 are differentially abundant, including 02 cathepsins B (BN1106_s5163B000012, FC=1.22 and BN1106_s4482B000044, FC=0.65), 02 cathepsins L (BN1106_s6995B000048, FC=1.29, and BN1106_s5602B000083, FC=2.20), and a legumain (BN1106_s9069B000006, FC=1.72) (blue dots in Figure 3). All of them are highly abundant in the *L.viatrix*-derived NEJ sample.

Protease inhibitors. As proteases are a family of proteins with a wide spectrum of functions, their functions have to be tightly regulated, avoiding damages to host and/or parasite²⁵. Protease inhibitors are key to control the activity of parasite or host proteases. In both ESP samples, the relative abundance of this category is different: abundance is higher in the ESP from *L. viatrix*-derived NEJ (5.0 %) in respect to ESP from *L. columella*-derived NEJ sample (1.4 %) (Figure 2A). Both samples have three protease inhibitors already described in *F. hepatica*, including two Kunitz-type inhibitors and one stefin. These protease inhibitors display variable relative abundance (Figure 3 and Table 1). Stefins are included in the cystatin superfamily of cysteine protease inhibitors, while members of the Kunitz-type family are inhibitors of a large number of serine proteases, including pro-coagulant and pro-inflammatory proteases²⁶⁻²⁸. In cestodes, Kunitz-type

inhibitors could act as cation channels blockers that can help in the establishment and persistence of the parasite in the host. Stefin is one of the major component in *F. gigantica* adult ESP, being identified in complex with cathepsin L. It is suggested that this protein has important extracellular functions, since this protein represents about 50% of total secreted protein²⁹. It is possible that steffin has other functions than inhibition of parasite proteases as demonstrated in nematodes, where it modulates cytokine responses and antigen processing and presentation, inducing an anti-inflammatory environment³⁰. The well-studied members of the Kunitz-type family act as serine protease inhibitors, but some inhibitors can have cross-activity on aspartic and cysteine proteases as in *Rhipicephalus microplus*, *Stichodactyla helianthus* and some inhibitors from plants³¹⁻³⁴. Serine proteases such as pro-coagulant, pro-inflammatory, and complement proteases have a role in these host defense responses to parasite infection³⁵⁻³⁸. The Kunitz-type inhibitor, the higher relative expression inhibitor in the ESP samples (BN1106_S318B000274, Supplementary Table S1) is a cathepsin-L inhibitor and do not have activity against serine proteases or cathepsin B³⁹. This was the first Kunitz-type that inhibits exclusively cysteine proteases. During migration through the definitive host parenchyma, the NEJ secretes large amounts of cathepsin L and B, which helps in penetration and evasion from the host immune system, but these enzymes has to be tightly regulated to ensure the survival of the parasite. Therefore, the function of this secreted Kunitz-type inhibitor could be the regulation of proteases secreted from the parasite into the host.

Transporter/storage. The five proteins identified in this category are cubilins and they represent 4.3% of ESP from *L. viatrix*-derived NEJ and the 4.4% in the ESP *L. columella*-derived NEJ sample (Figure 2 and Supplementary Table S1). One important function of the excreted/secreted proteins for parasites could be to take nutrients available

from the host cells. Cubilins are involved in the endocytic uptake of lipoproteins, vitamins, enzymes, and hormones⁴⁰. They are the receptors for intrinsic factor/vitamin B12 complex, and in schistosomes this vitamin is essential for growth and division of the larval stages of the parasite⁴¹. One cubilin (BN1106_s7307B000022) is highly abundant in both ESP samples (Table 1, Figure 3 and Supplementary Table S1). As NEJ is a juvenile stage into the life cycle of *F. hepatica* the presence of this protein, and other, that can act as carriers for host proteins could explain the way this parasite intake host proteins and transport nutrients from one compartment to another.

Oxidant metabolism and detoxification. This class represents 2.2% of the total protein content of the *L. viatrix* ESP (Figure 2A) and 0.6% in the *L. columella* ESP sample. The composition of this category remains the same in both samples (Supplementary Table S1) with the exception of carbonic anhydrase that is only present in the *L. columella*-derived NEJ ESP sample (Figure 2B). On the other hand, thioredoxin peroxidase (BN1106_s4026B000080) is one of the most differentially abundant protein, displaying a FC 2.26 fold change in the *L. viatrix*-derived NEJ ESP sample (Figure 3 and Table 1) compare with the *L. columella*-derived NEJ ESP sample.

Carbonic anhydrase is a zinc-containing metallo-enzyme, which catalyze reversible hydration of CO₂ in forming HCO₃. In *Plasmodium falciparum*, inhibition of carbonic anhydrase affects the growth of the parasite⁴². This protein was not found in the *L. viatrix*-derived NEJ ESP sample. For endoparasites, the maintenance of redox homeostasis is an important factor in the parasite-host interaction and adaptations. Without it, the host reaction against the parasite, with innate or adaptative mechanisms, could neutralize or kill the parasite⁴³. As the parasite have to deal with the reactive oxygen species (ROS) of their cellular metabolism and from the immune cells of the host, they

must have a system that control and remove ROS to avoid harmful consequences. Platyhelminthes possess a simplified thiol-redox system based on the enzyme thioredoxin glutathione reductase, that supplies electrons to oxidized glutathione and thioredoxin⁴⁴. Parasitic flukes have a limited set of antioxidant proteins but their functions are important to the survival of the parasite, and for that these class of proteins appears to be a good target to study for parasite control. If the increase or decrease of these proteins in each sample is related to each other or related to other proteins that have modified their abundance is something that needs to be addressed.

Metabolism. Proteins related to lipid and carbohydrate metabolism were also identified in ESP from NEJ derived from two different intermediate hosts. They represent 1.2% and 1.8% of the total protein content in *L. viatrix*-derived NEJ ESP and the 0.6% and 1.2% in the *L. columella*-derived NEJ ESP sample, respectively (Figure 1). In the carbohydrate metabolism from the *L. viatrix*-derived NEJ ESP sample proteins five proteins were identified, in both samples the most abundant protein in this class is an alpha-glucosidase (Supplementary Table S1). Alpha-glucosidases are common proteins in hematophagous parasites, and one important function is to induce hemozoin formation in a way to overcome heme toxicity⁴⁵⁻⁴⁷. Hemozoin was not described in *F. hepatica* but is assumed that, as in other hematophagous parasites, it release metabolic wastes into the hosts tissues during migration. Heme is an important cofactor for biochemical processes, however some hematophagous parasites have lost the capacity to biosynthesis heme, and they had to develop ways to uptake, process and store this cofactor⁴⁸⁻⁵⁰.

From the lipid metabolism the most abundant components were saposin-like (SAP-3) and a Niemann-Pick protein. SAP-3 was already described in *F. gigantica*⁵¹ and *F. hepatica*, whereas the Niemann-Pick proteins are cholesterol-binding proteins and are

present in the *Schistosoma mansoni* eggs^{52,53}. In *Toxoplasma gondii*, mutated parasites for these proteins presents large lipid bodies, abnormalities membrane biosynthesis and parasite replication, suggesting that Niemann-Pick proteins regulates the state of various lipids to ensure the proper development of the parasite⁵⁴.

Cysteine-rich proteins. The relative protein abundance for this category is increased in the *L. columella*-derived NEJ ESP sample (5.6%) when compared to the *L. viatrix*-derived NEJ ESP sample (0.4%) (Figure 1). In both samples, the only member of this superfamily is the peptidase inhibitor 16, corresponding to the peptidase inhibitor 16 subfamily (PI16). This subfamily contains inhibitors of serine and metalloproteases^{55,56} but its function in *F. hepatica* remains to be addressed⁵⁷. The presence of possible serine or metalloproteases inhibitors in samples that do not contain these classes of proteases in the ESP (Supplementary Table S1) could be that they act on another proteases, have another function or they act modulating host proteins.

Definitive host proteins. In *L. viatrix*-derived NEJ ESP sample we identified 12 proteins matching definitive host proteome database (Figure 1B and Table S3). Keratins were also found in both host-derived proteins NEJ ESP samples, these proteins are abundant on the skin, hair and nails, and a represent a common source of contamination in proteomic analysis⁵⁸. From those, 07 proteins are represented by keratin (Supplementary Figure S2). The other proteins identified are a trypsin, a polyubiquitin C, an actin, and histones. The same definitive host-derived proteins were found in the *L. columella*-derived NEJ ESP sample from our previous study¹² with the exception of actin, complement C1q receptor, tubulin and a GTPase (Supplementary Table 2 and Supplementary table S3). We compared these proteins with an NCBI snail database with 1544 entries (compiled in February 2018) and we were not able to find entries for trypsin

of polyubiquitin. The presence of polyubiquitin C in both samples is intriguing; various cellular processes uses proteins involved in ubiquitination, such as protein stability or intracellular localization. Apart from that, ubiquitination is involved in cell communication and adhesion⁵⁹. What effects or functions these host-secreted proteins have in the parasite remains to be determined. However, as the database for intermediate host contain few proteins, we cannot exclude that these proteins have an intermediate host origin.

Shared proteins between the NEJ ESP samples. When we compared specific proteins shared between both samples, the most abundant proteins are the cathepsins B and L. In the *L. viatrix*-derived NEJ ESP sample, the six most abundant proteins are a legumain, two cathepsin L3-like and three cathepsin B (B, B3 and B2-like). For the *L. columella*-derived NEJ ESP sample, the most abundant proteins are two cathepsin B (B2 and B3-like), two cathepsin L3-like, one legumains and a cubilin. (sequence details in Supplementary Table S1). In terms of different abundance, the 16 proteins that satisfied both fold change and statistical criteria have been identified (Figure 3 and Table 1) are highly abundant in the *L. viatrix*-derived NEJ ESP sample. From them, those with the higher fold change values are peptidyl-prolyl cis-trans isomerase, thioredoxin and cathepsin L4. The peptidyl-prolyl cis-trans isomerase is similar to the cyclophilin A from *Clonorchis sinensis*⁶⁰ and it is more abundant in the *L. viatrix*-derived NEJ ESP sample. It is a multifunction protein capable of performing roles in protein folding, trafficking signal transduction or apoptosis⁶⁰. The localization of this protein within the ESP may indicate that is involved in ion fluxes regulation in analogy to the renal system of the vertebrates.

The differences in protein abundance and composition founded here could be due to the different hosts, but little is known about the influence of the intermediate hosts in the ESP proteome from helminths. The metacercariae used here completed their cycle within the intermediate host in different species. The metacercariae that came from Oregon (USA) encyst from cercariae developed in *L. columella* and the metacercariae from Montevideo (Uruguay) came from *L. viatrix* snails. Although the parasite-intermediate host relationship is not well explored, there is evidence about the recognition of the parasite by the intermediate host immune system⁶¹. It is known that in the intermediate host the parasite has to locate, penetrate, establish, and persist into host until transmission by the next stage. For that, parasite has to have ways to control or manipulate the host responses and evade the immune responses and other mechanisms of defense. For example, *Schistosoma mansoni* has the ability to release ACTH (adrenocorticotrophic hormone) and β -endorphin that could act as immunosuppressors, directly or indirectly, on immune system host cells and mask the presence of the worm⁶². In Benin strains of *Schistosoma haematobium*, there is evidence of local adaptations to their hosts, as cercarial production is optimized when the local snail is used as intermediate host⁶³. In particular, in *F. hepatica* was demonstrated that the level of hemocytes circulating on hemolymph varies between infected and non-infected snails⁶⁴. Another study suggests that the decrease in hemocytes in infected snails could be due to the migration of these cells to the site of penetration of the miracidia⁶⁵. Thus, miracidia has to deal with the snail immune system, as the NEJ does with the definitive hosts, the developmental process within the snail will have an effect in the kind or amount of proteins the NEJ will later express in the definitive host. All that could explain why in some snails genus or species the prevalence of *F. hepatica* infection is higher than in others, even when

different snail species share the same habitat⁶⁶. In the cycle inside the intermediate host, one important feature is to maximize the fitness of the progeny that involves establishment, growth potential, mortality and survival rates. For that, taxon-specific mechanism arouse providing parasites with morphological characteristics, secretions, or another advantages that help colonizing an specific intermediate host. Besides that, in some regions, different parasites or strains of the same parasite has to compete inside the host to finish their cycle⁶⁷. That is the case of *F. hepatica* and *Paramphistomum daubneyi* co-infection, when they co-infect a snail the number of rediae generated are lower than when the snail is infected with only one parasite⁶⁸. In the same study, they compare if differences in snail nutrition affects the rediae generation and they show that the kind of food indeed affects the amount of rediae generated during the cycle.

Concluding remarks. Since environmental impact that usage of molluscicides brings, there is a need for more specific way to control or remove the intermediate host from the areas of transmission. As well as control against the introduction of these intermediate host in new regions. Accordingly, differences in the proteomes between the NEJs are relevant to highlight the different intermediate hosts. The differences in protein abundance, categories and individual proteins, could be due to differences in the biological cycle of the parasite in the host, as well as duration of the life cycle, amount of cercariae generated, durability of metacercariae, competition with other parasites, response to snail immune response, among others. Accordingly, differences in the proteomes between the NEJs are relevant to highlight host-induced variations in NEJ secretion. As the parasite inside the intermediate host, before delivery a cercariae into the water to encyst, must undergo across selective pressure (as snail immune system, tissue

micro-environment, environmental factors, etc.) and this, may have an impact in the expression of proteins that are secreted from NEJ.

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Legends

Figure 1. Venn diagram of NEJ ESP identified in *Lymnea columella* and *Lymnea viatrix* samples. The overlap between the circles represent the shared proteins between samples.

A: *Fasciola hepatica* database. **B:** *Bos taurus* database.

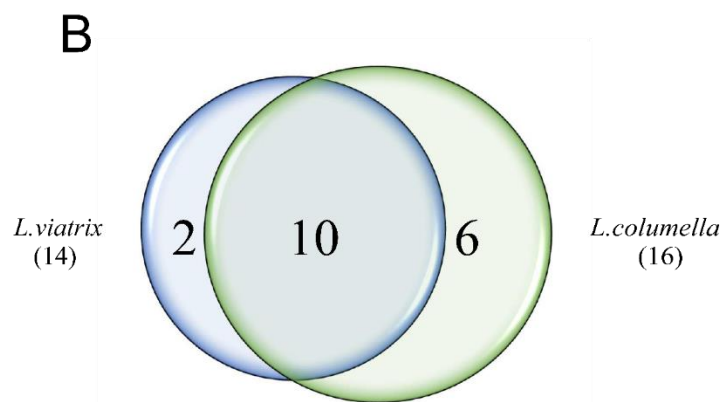
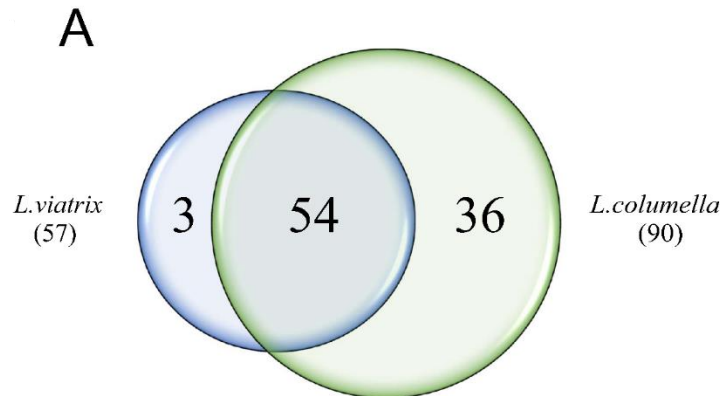


Figure 2. A: Functional classification of *F. hepatica* NEJ ESP identified *Lymnea viatrix* NEJ ESP sample. Pie chart represent the percentage of proteins found in each group with respect to their normalized NSAF classified according to their function and/or protein family. **B:** Percentages of the total protein abundance for both NEJ ESP samples within a functional category.

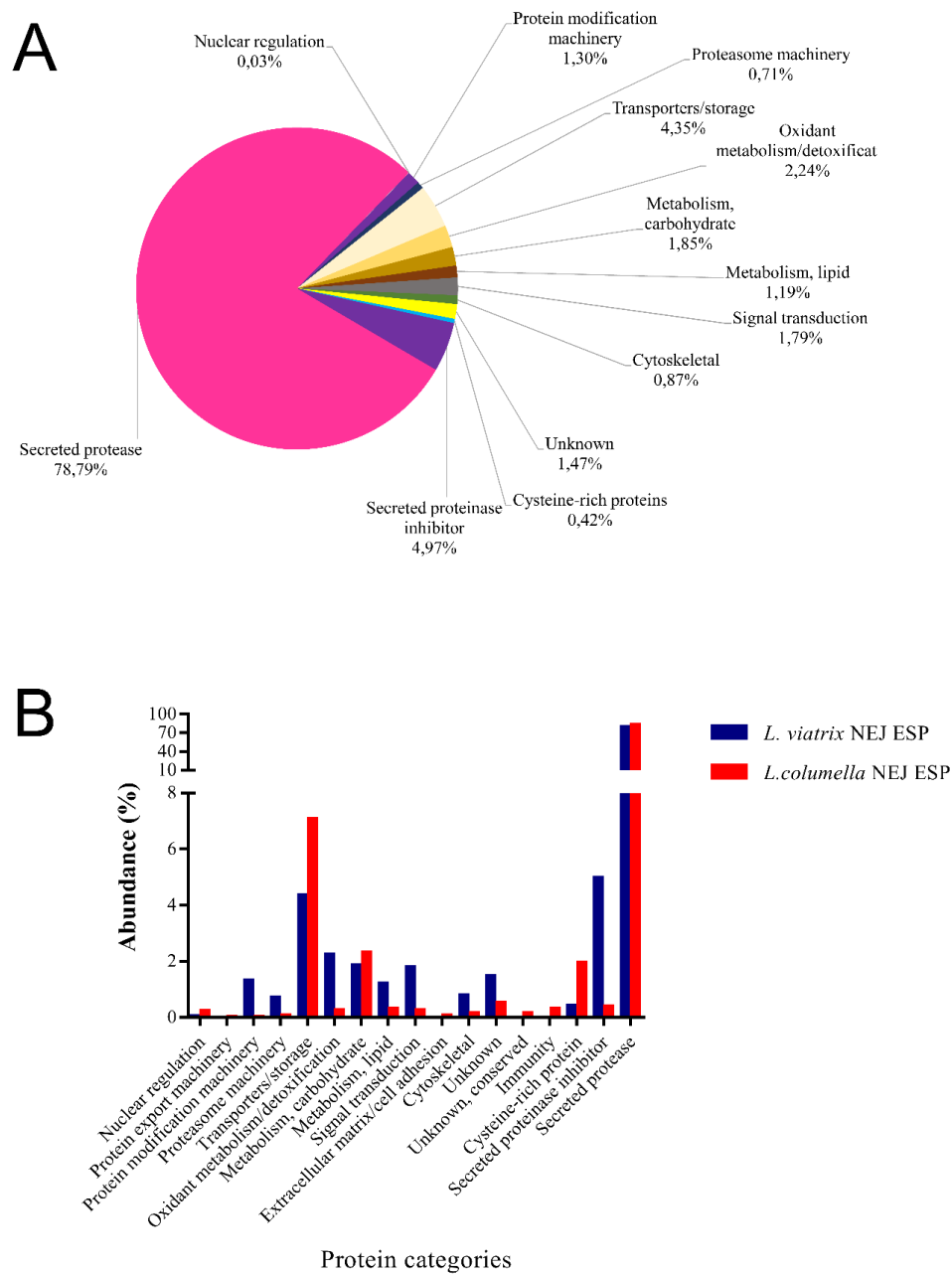


Figure 3. Volcano plot of the shared *F. hepatica* identified both samples: in *Lymnea columella* and *Lymnea viatrix* NEJ ESP samples. Each point, representing one individual protein, represents the difference in expression (\log_2 fold difference, abscissa axis) between samples plotted against the level of statistical significance (\log_2 p-value, ordinate axis). Proteins represented by blue dots have a relative abundance that satisfied both fold change and statistical criteria; yellow dots have an identification that was filtered out by the statistical criteria; green dots have an identification satisfied the fold criteria but, most likely, happened by chance; and red dots when the identification did not meet fold change and p-value criteria.

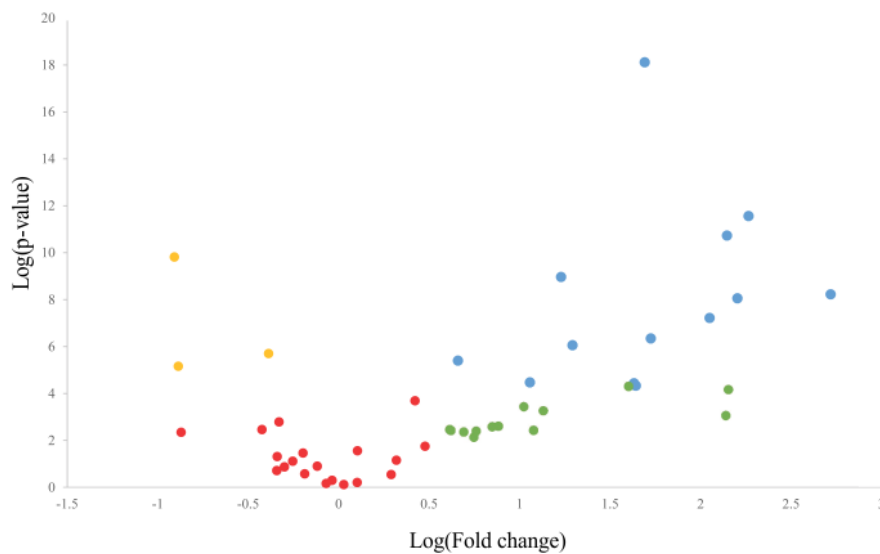


Table 1. Differential protein abundance of *Lymnea columella* and *Lymnea viatrix* NEJ ESP (determined using the TFold and pvalue). In blue, proteins with identification that satisfied both fold change and statistical criteria; in yellow proteins that satisfied statistical criteria only; in green, proteins that satisfied the fold criteria but, most likely, happened by chance; and in red when the identification did not meet fold change and p-value criteria.

Contig ^a	Annotation	p-value	Fold change ^b
BN1106_s9189B000015	Peptidyl-prolyl cis-trans isomerase	0.003342154	2.7185806
BN1106_s4026B000080	Thioredoxin	0.000330162	2.2647091
BN1106_s5602B000083	Cathepsin L4	0.003754325	2.2030655
BN1106_s4B000834	Calcium-binding protein	0.000588114	2.1450494
BN1106_s8826B000029	Kunitz-type proteinase inhibitor	0.006690459	2.0495541
BN1106_s9069B000006	Legumain-1	0.012266922	1.7243626
BN1106_s6840B000044	Polyubiquitin-A	3.50727E-06	1.6906129
BN1106_s318B000274	Kunitz-type proteinase inhibitor	0.049506705	1.6414831
BN1106_s2907B000133	Actin-2	0.046083345	1.6318037
BN1106_s2907B000134	Actin-2	0.046067964	1.6318037
BN1106_s101B000531	Actin-2	0.046067184	1.6318037
BN1106_s455B000331	Actin-2	0.046067184	1.6318037
BN1106_s6995B000048	Cathepsin L	0.0150011	1.2919247
BN1106_s5163B000012	Cathepsin B4	0.001996026	1.2282861
BN1106_s5689B000026	Natterin-4	0.04488283	1.0560709
BN1106_s4482B000044	Cathepsin B2	0.023677796	0.6588513
BN1106_s7353B000023	Niemann-Pick protein	0.055376513	2.1524778
BN1106_s4651B000094	Stefin-1	0.119515378	2.1379569
BN1106_s1444B000095	Dynein	0.050394853	1.6008411
BN1106_s373B000290	Cathepsin B	0.103553653	1.129531
BN1106_s2385B000108	Lysosomal alpha-glucosidase	0.184304573	1.0754525
BN1106_s1110B000106	Cubilin-like	0.091875185	1.0220858
BN1106_s666B000200	Mannosidase, alpha, class 2B	0.163340809	0.881786
BN1106_s1614B000280	Thioredoxin peroxidase	0.166145234	0.8475696
BN1106_s7443B000031	Unknown product	0.189273863	0.7586605
BN1106_s6635B000017	Legumain-1	0.226116276	0.7458397
BN1106_s3001B000132	Cubilin-like	0.193736208	0.690637
BN1106_s6995B000049	Cathepsin L	0.184982867	0.6191792
BN1106_s1657B000161	Tetraspanin-CD63 receptor	0.180677549	0.6126403
BN1106_s6570B000050	Cathepsin B1	0.019159598	-0.3874135
BN1106_s17622B000002	Cubilin-like isoform 1	0.02791595	-0.8865502
BN1106_s10890B000012	Cysteine-rich secretory protein family	0.001109935	-0.9081878
BN1106_s3173B000376	Alpha-glucosidase	0.297366259	0.4766813
BN1106_s7307B000022	Cubilin	0.077458717	0.4216493
BN1106_s3001B000132	Cubilin-like	0.448390507	0.3188559
BN1106_s8462B000006	Cathepsin B4	0.683106284	0.2900186

BN1106_s7612B000030	Legumain	0.338601007	0.1039702
BN1106_s3227B000227	Enolase	0.865489485	0.1022563
BN1106_s5172B000090	Unknown product	0.92037348	0.0276297
BN1106_s2087B000065	Legumain-1	0.812848	-0.036736
BN1106_s1840B000150	Cathepsin B4	0.891235095	-0.0691718
BN1106_s3008B000074	Cathepsin L3	0.534926598	-0.1183949
BN1106_s10139B000014	Cathepsin 1L	0.670597257	-0.1879076
BN1106_s4187B000061	Cathepsin L3	0.363449752	-0.1974395
BN1106_s7612B000031	Legumain	0.462921538	-0.2540623
BN1106_s4187B000060	Cathepsin L-like proteinase	0.544998955	-0.2999439
BN1106_s6570B000051	Cathepsin B3	0.1445975	-0.3296382
BN1106_s5100B000033	Cathepsin B4	0.402202737	-0.3398618
BN1106_s2303B000143	Cathepsin L	0.60950223	-0.3423143
BN1106_s8881B000009	Cathepsin L	0.181330126	-0.424283
BN1106_s1985B000403	Ectonucleotide pyrophosphatase/phosphodiesterase	0.196147665	-0.8709993

^a. Accession numbers of *F.hepatica* proteins identified as differentially expressed (Cwiklinski et al., 2015)

^b, Positive values represent the fold increased expression in the *L. viatrix* NEJ ESP. Negative

Supplementary Table S1. *Fasciola hepatica*-derived proteins identified by LC-MS/MS.

Protein functional classification and data generated in Bird's eye view from PatternLab for Proteomics platform (Carvalho et al., 2012a; Carvalho et al., 2012b) are provided in the accompanying spreadsheet (Hyperlinked Excel spreadsheet, zipped). Protein functional classification was manually curated using BLASTP searches against several databases. Accession number of *F. hepatica*-identified proteins, classification based in function and/or protein family, and accession numbers in addition to other parameters of best match identities obtained using BLASTP are provided ("Annotation" sheet). Data generated in the LC-MS/MS analyzes such as unique peptide, peptide count, spectral count, NSAF, and coverage are also provided for all triplicates from all three samples (in separated sheets).

Supplementary Table S2. *Bos taurus*-derived proteins identified by LC-MS/MS. Protein functional classification and data generated in Bird's eye view from PatternLab for Proteomics platform (Carvalho et al., 2012a; Carvalho et al., 2012b) are provided in the accompanying spreadsheet (Hyperlinked Excel spreadsheet, zipped). Protein functional classification was manually curated using BLASTP searches against several databases. Accession number of *B. taurus*-identified proteins, classification based in function and/or protein family, and accession numbers in addition to other parameters of best match identities obtained using BLASTP are provided ("Annotation" sheet). Data generated in the LC-MS/MS analyzes such as unique peptide, peptide count, spectral count, NSAF, and coverage are also provided for all triplicates from all three samples (in separated sheets).

Supplementary table S3 *Bos taurus*-derived proteins identified by LC-MS/MS in *Lymnea columella* and *Lymnea viatrix* NEJ ESP samples. The * indicated the presence of the protein in the sample.

Accession number	Description	<i>L.viatrix</i>	<i>L. columella</i>
sp A1L595 K1C17_BOVIN	Keratin, type II cytoskeletal 80		*
sp P00760 TRY1_BOVIN	Cationic trypsin	*	*
sp P06394 K1C10_BOVIN	Keratin	*	*
sp P08728 K1C19_BOVIN	Keratin, type I cytoskeletal 19		*
sp P0CH28 UBC_BOVIN	Polyubiquitin-C	*	*
sp P68138 ACTS_BOVIN	Actin, alpha skeletal muscle	*	
sp Q29S21 K2C7_BOVIN	Keratin type II cytoskeletal 7	*	*
tr E1BGJ5 E1BGJ5_BOVIN	Complement component C1q receptor		*
tr E1BJB1 E1BJB1_BOVIN	Tubulin		*
sp Q5XQN5 K2C5_BOVIN	Keratin, type II cytoskeletal 5	*	
tr F1MC11 F1MC11_BOVIN	Keratin		*
tr F1MFW9 F1MFW9_BOVIN	Keratin	*	*
tr F1MIH7 F1MIH7_BOVIN	Small GTPase mediated signal transduction		*
tr F1MUY2 F1MUY2_BOVIN	Keratin	*	*
tr F2Z4I6 F2Z4I6_BOVIN	Histone H2A	*	*
tr G3N0V2 G3N0V2_BOVIN	Keratin	*	*
tr M0QVY0 M0QVY0_BOVIN	Keratin	*	*
tr Q17QG8 Q17QG8_BOVIN	Histone H2A	*	*

4 DISCUSSÃO GERAL

É reconhecido o impacto causado pelo helminto parasito *F. hepatica* na produção animal (Cwiklinski et al., 2016), já que a fasciolose causa grandes prejuízos na economia dos países produtores de carne e derivados (Spithill et al., 2012). A importância da busca por um método de controle tornou-se uma prioridade devido aos regulamentos impostos pelos mercados internacionais. Já na saúde humana, a doença tornou-se importante nos países não desenvolvidos, onde é associada às comunidades rurais mais pobres e com menor sanidade e higiene alimentar.

Os helmintos parasitos têm se adaptado a viver em diferentes ambientes dentro do hospedeiro e para isso devem migrar pelos tecidos do hospedeiro até atingir o destino final (Andrews, 1999; Chubb et al., 2010). Para facilitar essa migração, o helminto secreta um conjunto de moléculas que além de facilitarem a migração, ajudam no estabelecimento final no hospedeiro. Com isso, o objetivo geral desta tese foi identificar proteínas secretadas de importância na relação parasito-hospedeiro.

No primeiro capítulo, comparamos o proteoma dos estágios intra-mamíferos (NEJ a adulto) da *F. hepatica*, com o foco na comparação de proteínas dos PES entre estágios e das proteínas somáticas solúveis e PES no NEJ. No segundo capítulo, o foco foi a comparação de amostras de PES entre NEJ que foram desencistados de metacercárias que se desenvolveram de diferentes hospedeiros intermediários. A essência dos estudos foi a comparação de categorias de proteínas presentes em cada amostra, classificadas segundo as bases de dados de proteínas de parasito e de hospedeiro, e sugere possíveis funções biológicas na relação parasito-hospedeiro. Todos os resultados apresentados neste trabalho demonstram que os PES, assim como as proteínas somáticas solúveis de NEJ, são amostras complexas e, de acordo com o estágio do ciclo de vida, variam as proteínas

secretadas. Uma categoria de proteínas presente em grande abundância nas amostras de PES são as proteases, representando o 83% e 73% da abundância total de proteínas nas amostras de PES de NEJ e adulto, respectivamente. Dentro desta categoria, o grupo majoritário é o das catepsinas que pertencem às cisteíno-proteases. Esses dados estão de acordo com outras análises de proteomas de *F. hepatica* já publicados (Cwiklinski et al., 2015b; Jefferies et al., 2001; Morphew et al., 2007; Robinson et al., 2009; Wilson et al., 2011). Além do número de proteínas e categorias funcionais encontradas neste trabalho, este é o primeiro a utilizar o genoma da *F. hepatica* (Cwiklinski et al., 2015a) para a procura das proteínas e anotação funcional. A função das catepsinas é muito estudada em *F. hepática* e elas estão envolvidas em várias funções importantes na relação parasito-hospedeiro. Essas proteínas são secretadas na luz do intestino do parasito após a ingestão de sangue e tecido hepático, realizando as funções de degradação de tecido e matriz extracelular, sugerindo uma contribuição na capacidade de invasão do parasito (Berasain et al., 2000). As catepsinas também poderiam estar envolvidas na alimentação e proteção do parasito, já que tem a capacidade de degradar fibrinogênio e imunoglobulinas e suprimir ou modular a resposta Th1 do hospedeiro (Berasain et al., 2000; Dalton et al., 2003; Dowd et al., 1995). Outra classe de proteínas encontradas nos PES são as envolvidas no metabolismo de heme, sendo algumas delas as mais abundantes nas amostras dos PES. Sendo que o parasito é hematófago, e que o heme livre é tóxico para as células, é previsto a existência de proteínas relacionadas com a degradação da hemoglobina, como mioglobinas ferritinas, e a proteína MF6p/FhHDM-1. Também foram encontradas proteínas envolvidas no metabolismo energético, proteínas ricas em cisteínas, inibidores de proteases, proteínas transportadoras, metabólicas e proteínas desconhecidas com/sem domínio conservado. Do grupo de proteínas que possuem

abundância diferencial entre as amostras de PES nos diferentes estágios, a grande maioria pertence as cisteíno proteases, inibidores de proteases, imunidade, transportadores, metabolismo de citoesqueleto e desconhecidas. Várias destas proteínas, após serem secretadas ou excretadas, poderiam ter uma função biológica diferente do que nas células em que foram produzidas. Estas proteínas que realizam mais de uma função fisiologicamente relevantes, e não sendo produto de fusão genica, *splicing* ou efeitos pleiotrópicos, são chamadas de proteínas *moonlight* (Huberts and van der Klei, 2010). Um exemplo é a tioredoxina de *Escherichia coli* que aumenta a taxa de replicação do DNA do bacteriófago T7 favorecendo a infecção da bateria (Bedford et al., 1997). Outro exemplo são as metaloproteases de matriz (MMP) que tem função de degradação de matriz extracelular, mas, atualmente são reconhecidas como transdutores de sinais e fatores de transcrição (Jobin et al., 2017).

A infestação por *F. hepática* libera grande quantidade de prolina no hospedeiro definitivo que pode ser parcialmente responsável, pela anemia e hiperplasia dos ductos biliares que muitas vezes acompanha a infecção com esse trematoide (Coffin et al., 1984; Isseroff et al., 1977). Este aminoácido tem um papel importante como fonte de energia em parasitos hematófagos. *F. hepatica* não possui as enzimas responsáveis pela metabolização de prolina mas possui altos níveis da enzima envolvida na sua síntese. A prolina pode ser um produto do catabolismo do aminoácido arginina, e esteja envolvida na manutenção do equilíbrio redox devido a regeneração de NAD (Kurelec, 1975).

Além de procurar proteínas de *F. hepatica*, nos estudos proteômicos foram utilizadas bases de dados com proteínas do hospedeiro definitivo. Baseados na abundância relativa das proteínas de hospedeiro nas amostras, a grande maioria é de proteínas do sangue. Muitas vezes a presença de proteínas do hospedeiro é considerada

contaminação, mas a grande presença de proteínas do sangue e a ausência de albumina ou hemoglobina é um indício que podem fazer parte de alguma função biológica. Em *F. hepatica* os exosomos são vesículas altamente estudadas (Cwiklinski et al., 2015b; de la Torre-Escudero and Robinson, 2017; Marcilla et al., 2012). Dentro dos exosomos foram encontradas várias proteínas do hospedeiro, o que sugere que a presença de proteínas do hospedeiro nas secreções do parasito não é causada pela regurgitação do conteúdo do intestino e sim como parte de um sistema de reciclagem de proteínas. Com essa reciclagem o parasito poderia utilizar proteínas do próprio hospedeiro para evadir o sistema imune ou em processos fisiológicos próprios. Isto também é sugerido em outros parasitos hematófagos, como o carrapato *Rhipicephalus microplus* (Tirloni et al., 2014), ou *Schistosoma japonicum* (Liu et al., 2007).

As pesquisas em *F. hepatica* estão focadas em estudos que envolvem os estágios dentro do hospedeiro definitivo. No entanto, em *Schistosoma heamatobium* existem evidências de uma adaptação do parasito ao hospedeiro intermediário local, onde aumenta o número de metacercarias produzidas pelo caramujo (Ibikounle et al., 2013). Assim, no segundo capítulo da tese o foco foi a biologia da *F. hepatica* no hospedeiro intermediário. Neste estudo, foram encontradas categorias de proteínas que estão em proporções iguais entre as amostras que provêm de diferentes hospedeiros intermediários. Assim como proteases, proteínas transportadoras, de regulação nuclear, envolvidas no proteosoma, metabólicas e de citoesqueleto. Enquanto que as categorias de inibidores de proteases, maquinaria de modificação de proteínas, metabolismo de lipídeos, transdução de sinais e proteínas ricas em cisteínas apresentam diferenças na abundância entre as amostras. No que refere a abundância das proteínas compartilhadas, na amostra de NEJ de *L. viatrix* e *L. columela* existem diferenças nas proteínas majoritárias. As seis proteínas mais

abundantes na amostra de NEJ de *L. viatrix* são proteases, sendo uma legumina a mais abundante, seguida de catepsinas L e B e um inibidor de proteases tipo Kunitz. Para a amostra de *L. columella* as proteínas mais abundantes são catepsinas B e L e uma cubilina. Ter proteases como as proteínas mais abundantes nas amostras não é surpreendente. Mais do 70% do número total de proteínas do proteoma (57 e 90 proteínas nas amostras de *L. viatrix* e *L. columella*, respectivamente) é composto por proteases e eles tem funções importantes na migração e penetração de tecidos do NEJ permitindo a degradação de matriz extracelular, colágeno e na evasão do sistema imune (Dzik, 2006; Law et al., 2003; Moerman, 1999; Wilson et al., 1998). O inibidor tipo Kunitz, ao ser considerado inibidor de serino proteases, é uma proteína que não se esperava estar presente em grande quantidade quando a amostra é composta 70% por cisteíno proteases. No entanto, esse Kunitz tem atividade específica sobre catepsina L e não sobre serino proteases (Smith et al., 2016), com isso sua abundância nos PES pode estar associada à regulação dessas proteases do parasito. As diferenças nos proteomas entre os NEJ desencistados são relevantes para salientar os diferentes hospedeiros intermediários. As diferenças poderiam encontrar-se no ciclo biológico do parasito no hospedeiro (assim como duração do ciclo de vida, quantidade de cercarias geradas, durabilidade da metacercarias, concorrência com outros parasitos, entre outros) e influenciar as proteínas que serão secretadas após o desenciste no hospedeiro definitivo. Isso já foi estudado em outros parasitos como *Toxoplasma gondii*, onde o parasito manipula o comportamento do hospedeiro intermediário para melhorar a transmissão para o hospedeiro definitivo (Webster, 2007). Outro ponto a ser considerado é a competição entre parasitos pelo hospedeiro intermediário. Um exemplo é *Calicophoron daubneyi*, que já demonstrou sua capacidade em adaptar-se progressivamente a um hospedeiro intermediário em um novo

ambiente. No entanto, quando há co-infecção de *C. daubneyi* e *F. hepatica*, o primeiro é menos eficiente em infectar e desenvolver-se no hospedeiro (Jones et al., 2017).

5 CONCLUSÕES

Os PES dos helmintos endoparasitos representam um conjunto de proteínas e outras moléculas, secretadas pelo tegumento, poros, e intestino do parasito e secretados no hospedeiro. Esses compostos desempenham papéis importantes na interface parasito-hospedeiro, uma vez que são secretados durante a infecção e protegem o parasito das respostas defensivas do hospedeiro. Com isso, espera-se que os dados gerados nestes trabalhos possam contribuir melhorando os conhecimentos sobre a biologia e as interações do parasito com o hospedeiro, e que seja o ponto de partida a novas descobertas no controle do parasito e a doença.

6 PERSPECTIVAS

- Análises proteômicas de tecidos do verme adulto: tegumento, intestino e órgãos reprodutivos.
- Estudos *in silico* de caracterização funcional de categorias de proteínas presentes nos PES.
- Elucidação de interações parasito-hospedeiro, determinantes de especificidade de hospedeiro
- Caracterização de proteínas candidatas a alvos vacinais

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Anexo A

CURRICULUM VITAE

DI MAGGIO, L.L.S.

1. DADOS PESSOAIS

Nome: Lucía Laura Sánchez Di Maggio

Local de nascimento: Montevideo - Uruguai

Data de nascimento: 11/05/1983

Endereço profissional: Laboratório de Imunologia Aplicada a Sanidade Animal
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Endereço eletrônico: lsanchezdimaggio@gmail.com

2. FORMAÇÃO

- 2002-2009 Graduação em Ciências Biológicas.
Universidad de la Republica Oriental del Uruguay. UDELAR.
Montevideo, Uruguai.
Monografia: “Es *Ctenomys rionegrensis* uma espécie estritamente solitária? Evaluación de las relaciones de parentesco de individuos procedentes de capturas multiples.”
Orientador: Ivanna Tomasco
- 2011-2013 Mestrado em Biología Molecular, Celular y Genética.
Universitat de València. Comunidad Valenciana, Espanha.
Dissertação: “Expresión diferencial de factores angiogénicos em líneas celulares y muestras de pacientes de cáncer de mama. ”
Orientador: Pilar Eroles Asensio.
- 2015-atual Doutorado em Biologia Celular e Molecular.
Universidade Federal do Rio Grande do Sul. UFRGS. Porto Alegre, Brasil.
Orientação: Itabajara da Silva Vaz Jr.

Bolsista: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES.)

3. FORMAÇÃO COMPLEMENTAR

2014 Ferramentas de bioinformática aplicadas às análises. (Carga horária: 80h).

Laboratório Nacional de Computação Científica, LNCC, Brasil.

2013 Proteomas de parásitos. Fundamentos y aplicaciones. (Carga horária: 50h).

Universidad de la Republica Uruguay, UDELAR, Uruguai.

2010 Uso y manejo de animales tradicionales y no tradic. (Carga horária: 40h).

Universidad de la Republica Uruguay, UDELAR, Uruguai.

4. ARTIGOS COMPLETOS PUBLICADOS

Di Maggio, L. S. et al. Across intra-mammalian stages of the liver fluke *Fasciola hepatica*: a proteomic study. *Sci. Rep.* 6, 32796; doi: 10.1038/srep32796 (2016).

5. RESUMO E TRABALHOS APRESENTADOS EM CONGRESSOS

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DI MAGGIO, L. L. S.; TIRLONI, L.; BENAVIDES, U.; PINTO, A.F.M; DIEDRICH, J.; YATES, J.R; CARMONA, C.; BERASAIN, P.; da SILVA VAZ Jr, I. The secretome of intra mammal stages of *fasciola hepatica*: new clues unveiled in the bovine host-parasite interaction. In: 23rd Congress of the International Union for Biochemistry and Molecular Biology, 2015, Foz do iguaçu. Abstracts Book, 2015.

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DI MAGGIO, L. L. S.; ALVITE, G.; CANCLINI, L.; GARRIDO, N.; ESTEVES, A. Contribución de la región amino terminal en el plegamiento de las FABPs. In: XIII Jornadas de la Sociedad Uruguaya de Biociencias, 2010, Piriapolis. Libro de resúmenes SUB2010, 2010.

DI MAGGIO, L. L. S.; TOMASCO, I.; LESSA, E.. Assessment of Parentage Relationships Among Burrow-sharing Individuals of *Ctenomys rionegrensis* using

microsatellites. In: IMC-10 International Mammalogical Congress, 2009, Mendoza. IMC-10 International Mammalogical Congress, 2009.

6. ORIENTAÇÕES E SUPERVISÕES

Iniciação científica.

Leticia Kinappe. Proteínas ligadoras de heparina em larvas de carrapato *Rhipicephalus (Boophilus) microplus*. 2015 (Veterinaria). Universidade Federal do Rio Grande do Sul.

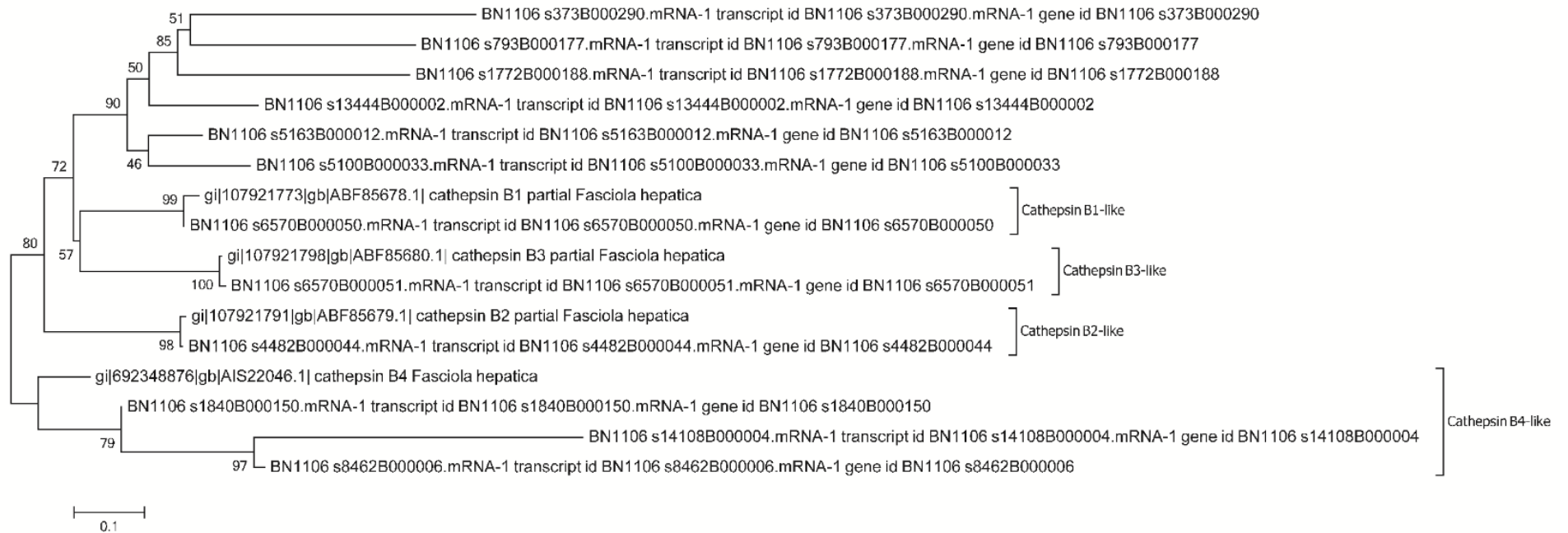
Anexo B

Material suplementar do capítulo I.

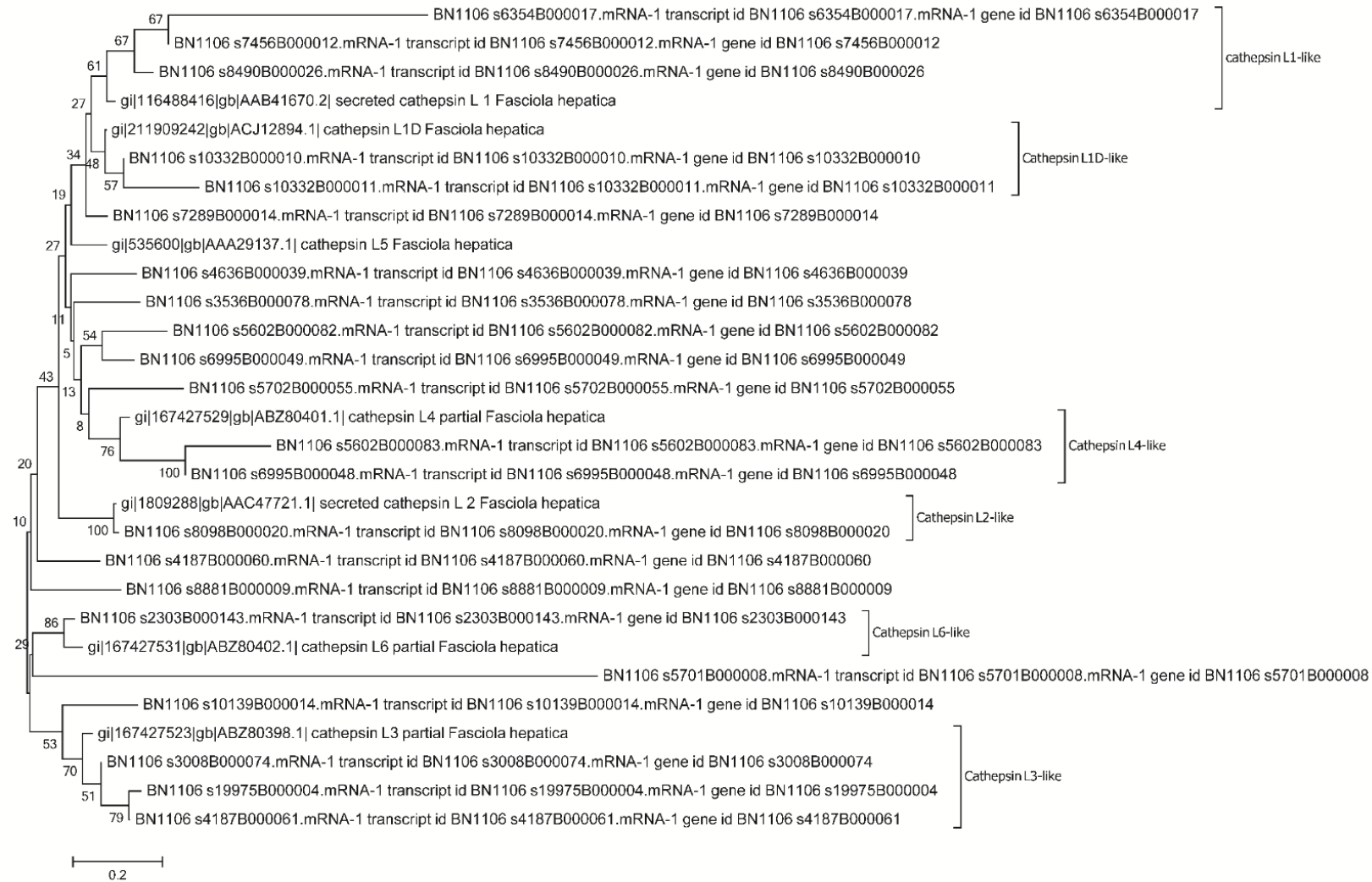
Across intra-mammalian stages of the liver fluke *Fasciola hepatica*: a proteomic study

Sánchez Di Maggio, L.; Tirloni, L.; Pinto, A.F.M.; Driedrich, J.K.; Yates III, J.R.; Benavides, U.; Carmona, C.; da Silva Vaz Jr; Berasain, P.

Supplementary Information.



Supplementary Fig. S1. Phylogenetic relationships of the cathepsin B family amino acid sequences presented here is a bootstrapped (1,000 replicates) neighbor-joining phylogenetic unrooted tree. The percentages in the nodes represent bootstrap values and branch lengths are proportional to distances.



Supplementary Fig. S2. Phylogenetic relationships of the cathepsin L family amino acid sequences presented here is a bootstrapped (1,000 replicates) neighbor-joining phylogenetic unrooted tree. The percentages in the nodes represent bootstrap values and branch lengths are proportional to distances.

Supplementary Table S1. Differentially expressed proteins based on t-fold analyses comparing E/S products from NEJ stage with E/S products from the adult stage.

Accession number ^a	Description	Class	Fold Change ^b	p-value ^b	Regulation ^c	
					Adult E/S	NEJ E/S
BN1106_s6635B000017.mRNA-1	Legumain-1	Proteinase	5.78	0.00018		↑
BN1106_s9069B000006.mRNA-1	Legumain-1	Proteinase	7.77	0.01352		↑
BN1106_s5100B000033.mRNA-1	Cathepsin B-like	Proteinase	8.39	0.00645		↑
BN1106_s8462B000006.mRNA-1	Cathepsin B4 -like	Proteinase	8.40	0.01357		↑
BN1106_s6720B000015.mRNA-1	CD59-like protein	Immunity	9.67	0.00357		↑
BN1106_s2087B000065.mRNA-1	Legumain-1	Proteinase	9.88	0.00002		↑
BN1106_s5163B000012.mRNA-1	Cathepsin B-like	Proteinase	11.89	0.00026		↑
BN1106_s373B000290.mRNA-1	Cathepsin B-like	Proteinase	34.31	0.00390		↑
BN1106_s4651B000094.mRNA-1	Stefin-1	Proteinase inhibitor	35.86	0.00367	↑	
BN1106_s8881B000009.mRNA-1	Cathepsin L-like	Proteinase	48.74	0.00017		↑
BN1106_s3173B000376.mRNA-1	Alpha-glucosidase	Metabolism. carbohydrate	49.96	0.00947		↑

BN1106_s3008B000074.mRNA-1	Cathepsin L3-like	Proteinase	103.97	0.00349	↑
BN1106_s6570B000051.mRNA-1	Cathepsin B3-like	Proteinase	130.50	0.00002	↑
BN1106_s7612B000030.mRNA-1	Legumain	Proteinase	283.68	0.00044	↑

^aAccession numbers of *Fasciola hepatica* proteins identified as differentially expressed (blue dots in Fig. 3B) (Cwiklinski et al., 2015a).

^bFold change and p-value of *Fasciola hepatica* proteins identified as differentially expressed (blue dots in Fig. 3B).

^cArrows are representing up-regulation (↑) of proteins identified as differentially in E/S products from NEJ stage or E/S products from the adult stage.

Supplementary Table S2. Differentially expressed proteins based on t-fold analyses comparing E/S products and somatic soluble proteins from NEJ stage.

Accession number ^a	Description	Class	Fold Change ^b	pValue ^b	Regulation ^c	
					NEJ E/S	Somatic NEJ
BN1106_s2907B000134	Actin-2	Cytoskeletal	-27.62	0.01065		↑
BN1106_s2907B000133	Actin-2	Cytoskeletal	-33.58	0.01004		↑
BN1106_s101B000531	Actin-2	Cytoskeletal	-45.75	0.00411		↑
BN1106_s455B000331	Actin-2	Cytoskeletal	-51.43	0.00058		↑
BN1106_s6570B000050	Cathepsin B1-like	Proteinase	4.78	0.00001	↑	
BN1106_s4482B000044	Cathepsin B2-like	Proteinase	5.82	0.00001	↑	
BN1106_s6570B000051	Cathepsin B3-like	Proteinase	6.00	0.00005	↑	
BN1106_s5163B000012	Cathepsin B-like	Proteinase	7.84	0.00023	↑	
BN1106_s5100B000033	Cathepsin B-like	Proteinase	7.40	0.00680	↑	
BN1106_s14108B000004	Cathepsin B-like	Proteinase	-1.68	0.01210		↑
BN1106_s3008B000074	Cathepsin L3-like	Proteinase	8.12	0.00086	↑	
BN1106_s4187B000061	Cathepsin L-like	Proteinase	9.32	0.00102	↑	
BN1106_s6720B000015	CD59-like protein	Immunity	4.56	0.00614	↑	
BN1106_s63B000399	CD59-like protein	Immunity	-10.06	0.00448		↑

BN1106_s7307B000022	Cubilin-like	Transport/storage	4.81	0.00001	↑	
BN1106_s17622B000002	Cubilin-like	Transport/storage	8.66	0.00057	↑	
BN1106_s1444B000095	Dynein	Cytoskeletal	-9.17	0.00271		↑
BN1106_s3227B000227	Enolase	Metabolism. carbohydrate	-10.22	0.00016		↑
tr F2Z4I6 F2Z4I6_BOVIN	Histone H2A	Nuclear regulation	-3.90	0.01352		↑
tr Q17QG8 Q17QG8_BOVIN	Histone H2A	Nuclear regulation	-7.21	0.00003		↑
BN1106_s7612B000030	Legumain	Proteinase	7.57	0.00007	↑	
BN1106_s7612B000031	Legumain	Proteinase	3.12	0.00075	↑	
BN1106_s2087B000065	Legumain-1	Proteinase	3.00	0.00001	↑	
BN1106_s6635B000017	Legumain-1	Proteinase	2.62	0.00009	↑	
BN1106_s10890B000012	Peptidase inhibitor 16	Cysteine-rich proteins	2.72	0.00002	↑	
BN1106_s5591B000098	Peptidase inhibitor 16	Cysteine-rich proteins	1.97	0.00401	↑	
BN1106_s246B000252	Phosphoenolpyruvate carboxykinase	Metabolism. carbohydrate	-24.20	0.01114		↑
BN1106_s1614B000280	Thioredoxin peroxidase	Oxidant metabolism/ detoxification	-10.72	0.00143		↑
BN1106_s5172B000090	Unknown product	Unknown	5.47	0.00238	↑	

Supplementary Table S3. *Fasciola hepatica*-derived proteins identified by LC-MS/MS. Protein functional classification and data generated in Bird's eye view from PatternLab for Proteomics platform (Carvalho et al., 2012a; Carvalho et al., 2012b) are provided in the accompanying spreadsheet (Hyperlinked Excel spreadsheet, zipped). Protein functional classification was manually curated using BLASTP searches against several databases. Accession number of *F. hepatica*-identified proteins, classification based in function and/or protein family, and accession numbers in addition to other parameters of best match identities obtained using BLASTP are provided ("Annotation" sheet). Data generated in the LC-MS/MS analyzes such as unique peptide, peptide count, spectral count, NSAF, and coverage are also provided for all triplicates from all three samples (in separated sheets).

Supplementary Table S4. *Bos taurus*-derived proteins identified by LC-MS/MS. Protein functional classification and data generated in Bird's eye view from PatternLab for Proteomics platform (Carvalho et al., 2012a; Carvalho et al., 2012b) are provided in the accompanying spreadsheet (Hyperlinked Excel spreadsheet, zipped). Protein functional classification was manually curated using BLASTP searches against several databases. Accession number of *F. hepatica*-identified proteins, classification based in function and/or protein family, and accession numbers in addition to other parameters of best match identities obtained using BLASTP are provided ("Annotation" sheet). Data generated in the LC-MS/MS analyzes such as unique peptide, peptide count, spectral count, NSAF, and coverage are also provided for all triplicates from all three samples (in separated sheets).

Supplementary Table S5. Differentially expressed proteins based on t-fold analyses comparing E/S products from NEJ stage with E/S products from the adult stage.

Accession number	Description	Class	Fold Change	pValue
BN1106_s2087B000065	Legumain-1	Secreted proteinase	-9.87	2.20E-05
BN1106_s3008B000074	Cathepsin L3-like	Secreted proteinase	-103.97	0.003495
BN1106_s3173B000376	Alpha-glucosidase	Carbohydrate metabolism	-49.96	0.009465
BN1106_s373B000290	Cathepsin B-like	Secreted proteinase	-34.31	0.003897
BN1106_s4651B000094	Stefin-1	Secreted proteinase inhibitor	35.86	0.003671
BN1106_s5100B000033	Cathepsin B-like	Secreted proteinase	-8.39	0.006446
BN1106_s5163B000012	Cathepsin B-like	Secreted proteinase	-11.88	0.000255
BN1106_s6570B000051	Cathepsin B3-like	Secreted proteinase	-130.49	2.49E-05
BN1106_s6635B000017	Legumain-1	Secreted proteinase	-5.78	0.000183
BN1106_s6720B000015	CD59-like protein	Immunity	-9.66	0.003575
BN1106_s7612B000030	Legumain	Secreted proteinase	-283.67	0.000443
BN1106_s8462B000006	Cathepsin B4 -like	Secreted proteinase	-8.40	0.013572
BN1106_s8881B000009	Cathepsin L-like	Secreted proteinase	-48.74	0.000167
BN1106_s9069B000006	Legumain-1	Secreted proteinase	-7.76	0.013517
tr G3N0V2 G3N0V2_BOVIN	Keratin	Cytoskeletal	-20.71	0.017377
sp P0CH28 UBC_BOVIN	Polyubiquitin-C	Proteasome machinery	7.98	0.021241
tr Q17QG8 Q17QG8_BOVIN	Histone H2A	Nuclear regulation	-10.36	0.024623
BN1106_s8098B000020	Cathepsin L2-like	Secreted proteinase	34.91	0.026001
BN1106_s3227B000227	Enolase	Carbohydrate metabolism	-4.62	0.033486
BN1106_s7353B000023	Niemann-Pick protein	Lipid metabolism	6.84	0.037116
BN1106_s4026B000080	Thioredoxin	Oxidant metabolismo / detoxification	4.40	0.038137
BN1106_s4187B000060	Cathepsin L3-like	Secreted proteinase	-19.85	0.040523
tr M0QVY0 M0QVY0_BOVIN	Keratin	Cytoskeletal	-14.63	0.042002
tr F1MUY2 F1MUY2_BOVIN	Keratin	Cytoskeletal	-14.63	0.042002
BN1106_s6840B000044	Polyubiquitin-A	Proteasome machinery	16.76	0.045865
BN1106_s1110B000106	Cubilin	Transport/Storage	-7.22	0.058307

BN1106_s101B000531	Actin-2	Cytoskeletal	1.32	0.278262
BN1106_s114B000615	Cubilin-like	Transport/Storage	-1.91	0.080549
BN1106_s1444B000095	Dynein	Cytoskeletal	-1.35	0.277081
BN1106_s1614B000280	Thioredoxin peroxidase	Oxidant metabolismo/detoxification	4.13	0.031541
BN1106_s1657B000161	Tetraspanin-CD63 receptor	Signal transduction	-1.35	0.247136
BN1106_s1840B000150	Cathepsin B4-like Ectonucleotide	Secreted proteinase	-3.04	0.042116
BN1106_s1985B000403	pyrophosphatase / phosphodiesterase	Nuclear regulation	-4.62	0.058664
BN1106_s246B000252	Phosphoenolpyruvate carboxykinase (GTP)	Carbohydrate metabolism	-2.40	0.083656
BN1106_s2907B000133	Actin-2	Cytoskeletal	1.32	0.31012
BN1106_s3001B000132	Cubilin-like	Transport/Storage	-1.65	0.071483
BN1106_s3001B000132	Cubilin-like	Transport/Storage	-3.82	0.043215
BN1106_s3009B000044	Carbonic anhydrase 5B	Oxidant metabolismo/detoxification	1.68	0.259563
BN1106_s318B000274	Kunitz-type proteinase inhibitor	Secreted proteinase inhibitor	1.85	0.053469
BN1106_s4223B000091	Legumain-1	Secreted proteinase	1.24	0.301441
BN1106_s455B000331	Actin-2	Cytoskeletal	1.32	0.278262
BN1106_s4986B000028	SAP-1	Lipid metabolism	-2.68	0.053645
BN1106_s5246B000010	CD59-like protein	Immunity	-2.12	0.051046
BN1106_s5602B000082	Cathepsin L-like	Secreted proteinase	3.52	0.028177
BN1106_s5689B000026	Natterin-4	Lipid metabolism	-3.91	0.053573
BN1106_s584B000346	Glucose transporter-2 protein	Transport/Storage	3.02	0.231718
BN1106_s584B000350	Glucose transporter-2 protein	Transport/Storage	4.84	0.119918
BN1106_s617B000566	Leucine amino peptidase 1 C-terminal fragment	Secreted proteinase	1.35	0.217515
BN1106_s63B000399	CD59-like protein	Immunity	-1.06	4.19E-05
BN1106_s6995B000048	Cathepsin L4-like	Secreted proteinase	-2.89	0.117231

BN1106_s6995B000049	Cathepsin L-like	Secreted proteinase	-1.83	0.09822
BN1106_s7443B000031	Unknown product	Unknown	-2.47	0.064674
BN1106_s8038B000016	Unknown product	Unknown	3.04	0.092148
BN1106_s8826B000029	Kunitz-type proteinase inhibitor	Secreted proteinase inhibitor	1.98	0.060199
BN1106_s945B000218	Annexin A11	Cytoskeletal	2.64	0.050399
BN1106_s9797B000034	Leukotriene-A4 hydrolase	Transport/Storage	-2.77	0.015177
sp P00760 TRY1_BOVIN	Cationic trypsin	Secreted proteinase	-2.21	0.037756
BN1106_s3001B000131	Cubilin-like	Transport/Storage	-3.41	0.001893

Each differently expressed protein is mapped according to its fold change and t-test p-value. Proteins are represented by: (blue shading) if had an identification that satisfied both fold and statistical criteria; (yellow shading) had an identifications that was filtered out by the L-stringency; (green shading) had an identification satisfied the fold criteria but, most likely, this happened by chance; and (red shading) had identification did not meet the fold and p-value criteria.

Supplementary Table S6. Differentially expressed proteins based on t-fold analyses comparing E/S products and somatic soluble NEJ.

Accession number	Description	Class	Fold Change	pValue
BN1106_s101B000531	actin-2	Cytoskeletal	-45.76	0.004111344
BN1106_s10890B000012	Cysteine-rich secretory protein family (GLIPR1)	Cysteine-rich proteins	2.73	1.71E-05
BN1106_s14108B000004	Cathepsin B-like	Secreted proteinase	-1.68	0.01209948
BN1106_s1444B000095	dynein	Cytoskeletal	-9.18	0.002711112
BN1106_s1614B000280	Thioredoxin peroxidase	Oxidant		
BN1106_s17622B000002	cubilin-like isoform 1	metabolismo/detoxification	-10.72	0.001428203
BN1106_s2087B000065	Legumain-1	Transport/Storage	8.66	0.000574028
BN1106_s246B000252	Phosphoenolpyruvate carboxykinase (GTP)	Secreted proteinase	3.00	1.17E-05
BN1106_s2907B000133	actin-2	Carbohydrate metabolism	-24.21	0.01114098
BN1106_s2907B000134	actin-2	Cytoskeletal	-33.58	0.010035332
BN1106_s3008B000074	s/protease	Cytoskeletal	-27.63	0.010648377
BN1106_s3227B000227	enolase	Secreted proteinase	8.13	0.000863597
BN1106_s4187B000061	Cathepsin L-like	Carbohydrate metabolism	-10.22	0.000162913
BN1106_s4482B000044	Cathepsin B2-like	Secreted proteinase	9.33	0.00101565
BN1106_s455B000331	actin-2	Secreted proteinase	5.82	1.13E-05
BN1106_s5100B000033	Cathepsin B-like	Cytoskeletal	-51.43	0.000582962
BN1106_s5163B000012	Cathepsin B-like	Secreted proteinase	7.41	0.006798594
BN1106_s5172B000090	Unknown product	Secreted proteinase	7.85	0.000226302
BN1106_s5591B000098	CRISP3: cysteine-rich secretory protein	Unknown	5.48	0.002381086
BN1106_s63B000399	CD59-like protein	Cysteine-rich proteins	1.97	0.004006453
BN1106_s6570B000050	Cathepsin B1-like	Immunity	-10.06	0.004475068
BN1106_s6570B000051	Cathepsin B3-like	Secreted proteinase	4.78	1.00E-05
BN1106_s6635B000017	Legumain-1	Secreted proteinase	6.00	5.19E-05
BN1106_s6720B000015	CD59-like protein	Secreted proteinase	2.63	9.30E-05
		Immunity	4.56	0.006139616

BN1106_s7307B000022	cubilin	Transport/Storage	4.81	1.00E-05
BN1106_s7612B000030	Legumain	Secreted proteinase	7.58	7.01E-05
BN1106_s7612B000031	Legumain	Secreted proteinase	3.12	0.000752774
tr F2Z4I6 F2Z4I6_BOVIN	Histone H2A	Nuclear regulation	-3.90	0.013522408
tr Q17QG8 Q17QG8_BOVIN	Histone H2A	Nuclear regulation	-7.21	3.25E-05

		Oxidant		
BN1106_s4026B000080	Thioredoxin	metabolismo/detoxification	-2.80	0.014941729
BN1106_s9797B000034	Leukotriene-A4 hydrolase - M1	Transport/Storage	3.79	0.016747702
BN1106_s4651B000094	Stefin-1	Secreted proteinase inhibitor	-3.39	0.017454129
BN1106_s26B000447	Collagen alpha-1(XV) chain	Extracellular matrix	-1.80	0.019348208
BN1106_s4187B000060	Cathepsin L3-like	Secreted proteinase	6.09	0.021285821
BN1106_s8462B000006	Cathepsin B4 -like	Secreted proteinase	3.34	0.026458637
sp Q29S21 K2C7_BOVIN	Keratin type II cytoskeletal 7	Cytoskeletal	2.80	0.028125793
BN1106_s1840B000150	Cathepsin B4-like	Secreted proteinase	4.08	0.028955455
BN1106_s9069B000006	legumain-1	Secreted proteinase	1.91	0.029073677
BN1106_s9189B000015	peptidyl-prolyl cis-trans isomerase	Protein modification machinery	-1.58	0.030818119
sp POCH28 UBC_BOVIN	Polyubiquitin-C - cytoplasm - nucleus	Proteasome machinery	-1.65	0.032702869
BN1106_s3173B000376	alpha-glucosidase	Carbohydrate metabolism	11.48	0.035348373
BN1106_s10139B000014	Cathepsin L-like	Secreted proteinase	2.86	0.036243144
BN1106_s5602B000083	Cathepsin L4-like	Secreted proteinase	2.91	0.038707409
BN1106_s1985B000403	Ectonucleotide pyrophosphatase/phosphodiesterase	Nuclear regulation	10.49	0.043132688
BN1106_s114B000615	Cubilin-like	Transport/Storage	2.73	0.0433593
BN1106_s666B000200	mannosidase, alpha, class 2B	Carbohydrate metabolism	2.94	0.043498134
BN1106_s6995B000049	Cathepsin L-like	Secreted proteinase	7.03	0.043554602
BN1106_s6995B000048	Cathepsin L4-like	Secreted proteinase	4.14	0.045332674
BN1106_s373B000290	Cathepsin B-like	Secreted proteinase	1.60	0.056035137
BN1106_s4B000834	calcium-binding protein	Signal transduction	-2.20	0.063554229
BN1106_s4986B000028	SAP-1	Nuclear regulation	2.28	0.067300282
BN1106_s7443B000031	Unknown product	Unknown	2.32	0.071044603

BN1106_s2303B000143	Cathepsin L6-like	Secreted proteinase	4.83	0.098811878
BN1106_s7353B000023	Niemann-Pick protein	Lipid metabolism	-1.66	0.127000635
tr F1MUY2 F1MUY2_BOVIN	keratin	Cytoskeletal	1.69	0.183014303

BN1106_s8038B000016	Unknown product	Unknown	1.38	0.053544143
BN1106_s3001B000132	cubilin-like	Transport/Storage	-1.22	0.069693987
BN1106_s3001B000132	cubilin-like	Transport/Storage	1.38	0.121027116
BN1106_s584B000346	Glucose transporter-2 protein	Transport/Storage	1.46	0.154081202
BN1106_s584B000350	Glucose transporter-2 protein	Transport/Storage	1.46	0.154081202
tr F1MC11 F1MC11_BOVIN	keratin	Cytoskeletal	-1.41	0.163372128
tr G3NOV2 G3NOV2_BOVIN	keratin	Cytoskeletal	1.32	0.167958883
sp P00760 TRY1_BOVIN	Cationic trypsin	Secreted proteinase	1.27	0.172745702
BN1106_s6840B000044	Polyubiquitin-A	Proteasome machinery	-1.19	0.179563896
BN1106_s5689B000026	Natterin-4	Lipid metabolism	1.54	0.193585128
BN1106_s925B000547	Tubulin alpha-3	Cytoskeletal	-1.25	0.199430341
BN1106_s1110B000106	cubilin-like	Transport/Storage	1.39	0.20574462
BN1106_s318B000274	kunitz-type proteinase inhibitor	Secreted proteinase inhibitor	1.58	0.207665857
tr M0QVY0 M0QVY0_BOVIN	keratin	Cytoskeletal	1.32	0.236544944

BN1106_s7273B000042	Major vault protein	Signal transduction	-7.10	8.72E-05
BN1106_s1200B000196	Unknown product	Unknown	2.11	0.000726494
BN1106_s617B000566	Leucine amino peptidase 1 fragment C-terminal - M17	Secreted proteinase	-6.77	0.001202213
BN1106_s1657B000161	Tetraspanin-CD63 receptor	Signal transduction	6.64	0.002766104
tr F1MFW9 F1MFW9_BOVIN	keratin	Cytoskeletal	1.85	0.002858627
BN1106_s945B000218	Annexin A11	Cytoskeletal	-7.65	0.003350674
BN1106_s3001B000131	cubilin-like	Transport/Storage	-2.70	0.003584895
tr E1BJB1 E1BJB1_BOVIN	The tubulin superfamily includes five distinct families	Cytoskeletal	-6.40	0.00531316
sp P06394 K1C10_BOVIN	keratin	Cytoskeletal	-2.06	0.005752445
BN1106_s2275B000114	Uncharacterized protein	Unknown	1.82	0.009403358
BN1106_s114B000614	Cubilin	Transport/Storage	-3.86	0.010447237

Supplementary Table S7. Total protein comparison between Fh E/S products studies. ^aRobinson, M.W., Menon, R., Donnelly, S.M., Dalton, J.P., Ranganathan, S., 2009. An integrated transcriptomics and proteomics analysis of the secretome of the helminth pathogen *Fasciola hepatica*: proteins associated with invasion and infection of the mammalian host. *Molecular & cellular proteomics* : MCP 8, 1891-1907. ^bHernandez-Gonzalez, A., Valero, M.L., del Pino, M.S., Oleaga, A., Siles-Lucas, M., 2010. Proteomic analysis of in vitro newly excysted juveniles from *Fasciola hepatica*. *Molecular and biochemical parasitology* 172, 121-128. ^cWilson, R.A., Wright, J.M., de Castro-Borges, W., Parker-Manuel, S.J., Dowle, A.A., Ashton, P.D., Young, N.D., Gasser, R.B., Spithill, T.W., 2011. Exploring the *Fasciola hepatica* tegument proteome. *International journal for parasitology* 41, 1347-1359. ^dCwiklinski, K., de la Torre Escudero, E., Trelis, M., Bernal, D., Dufresne, P.J., Brennan, G.P., O'Neill, S., Tort, J., Paterson, S., Marcilla, A., Dalton, J.P., Robinson, M.W., 2015b. The extracellular vesicles of the helminth pathogen, *Fasciola hepatica*: biogenesis pathways and cargo molecules involved in parasite pathogenesis. *Molecular & cellular proteomics* : MCP

Accession number	Seq name	Description	Class	This study			Robinson et al. 2008 ^a		Hernández-González et al. 2010 ^b Somatic NEJ	Wilson et al. 2011 ^c Adult E/S products	Cwiklinski et al. 2015 ^d Adult E/S products	Cwiklinski et al. 2015 ^d Adult exosome proteins
				E/S products NEJ	E/S products adult	Somatic soluble NEJ proteins	NEJ E/S products	Adult E/S products				
BN1106_s709B000627	114	ferritin	heme/iron related proteins		*					*	*	
BN1106_s1002B000239	130	ferritin	heme/iron related proteins			*						
BN1106_s2101B000084	342	MF6p/FhH DM-1 protein	heme/iron related proteins		*	*	HAN4019c1 2.q1kT3			*		
BN1106_s284B000287	439	myoglobin 1	heme/iron related proteins		*				FhC00255		*	
BN1106_s284B000288	440	myoglobin 1	heme/iron related proteins			*			FhB00042	*		
BN1106_s3950B000041	564	ferritin	heme/iron related proteins		*	*				*	*	

BN1106_s917B 000270	876	ferritin	heme/iron related proteins			*	
BN1106_s92B0 00564	879	ferritin	heme/iron related proteins		*		
BN1106_s101B 000531	2	Actin-2	Cytoskele tal	*	*	*	gi 1703101
BN1106_s103B 000718	5	Ankyrin 2b	Cytoskele tal			*	
BN1106_s2349 B000188	48	Severin	Cytoskele tal			*	*
BN1106_s2374 B000246	49	PDZ and LIM domain protein	Cytoskele tal			*	
BN1106_s2906 B000293	60	lamin-C	Cytoskele tal			*	
BN1106_s3147 B000076	66	dynein	Cytoskele tal			*	
BN1106_s3353 B000056	69	synaptotagm in	Cytoskele tal		*		
BN1106_s551B 000321	99	myosin	Cytoskele tal		*	*	*
BN1106_s71B0 00363	115	Ankyrin-2	Cytoskele tal			*	
BN1106_s98B0 00745	129	Titin	Cytoskele tal			*	
BN1106_s103B 000723	138	Ankyrin	Cytoskele tal			*	
BN1106_s1037 B000175	144	Na(+)/H(+) exchange regulatory cofactor NHE-RF1- like	Cytoskele tal			*	
BN1106_s1042 B000321	145	thymosin	Cytoskele tal			*	

BN1106_s1081 B000248	156	Actin depolymeriz ing factor- like protein	Cytoskele tal			*			
BN1106_s1096 B000199	160	ankyrin repeat domain- containing protein	Cytoskele tal			*			
BN1106_s1106 B000091	163	Myosin-1	Cytoskele tal			*			
BN1106_s1109 B000181	164	Tubulin polymerizati on- promoting protein	Cytoskele tal			*			
BN1106_s1111 B000208	166	Microtubule -associated protein 1S	Cytoskele tal			*			
BN1106_s1119 B000202	169	Titin	Cytoskele tal			*			
BN1106_s1168 B000108	186	LIM domains protein	Cytoskele tal			*			
BN1106_s1300 B000145	213	moesin/ezri n/radixin homolog 1- like isoform X1	Cytoskele tal		*	*			*
BN1106_s1403 B000129	229	Plastin-2	Cytoskele tal		*	*	Fhep27d03.q 1k	FhB02827	*
BN1106_s1444 B000095	235	dynein	Cytoskele tal	*	*	*			
BN1106_s149B 000360	238	Talin-1	Cytoskele tal			*			
BN1106_s1515 B000336	244	Filamin	Cytoskele tal			*			
BN1106_s1582 B000145	254	Dynein	Cytoskele tal		*	*			

BN1106_s1582 B000149	255	Dynein	Cytoskeletal	*	
BN1106_s19B0 00337	311	Tropomodulin	Cytoskeletal	*	
BN1106_s1922 B000122	315	paramyosin	Cytoskeletal	*	gi 126116628
BN1106_s1972 B000196	321	Tropomyosin	Cytoskeletal	*	
BN1106_s2003 B000172	328	Cofilin	Cytoskeletal	*	
BN1106_s2014 B000189	329	Nascent polypeptide-associated complex subunit alpha	Cytoskeletal	*	
BN1106_s2018 B000301	330	Myosin-2	Cytoskeletal	*	FhC00899
BN1106_s2132 B000163	347	adducin	Cytoskeletal	*	
BN1106_s214B 000743	351	6 kDa tegumental protein	Cytoskeletal	*	
BN1106_s2153 B000115	357	cofilin/tropomyosin type actin binding domain-containing protein	Cytoskeletal	*	
BN1106_s227B 000509	370	Protein human	Cytoskeletal	*	
BN1106_s2291 B000314	376	Dynein	Cytoskeletal	*	
BN1106_s2329 B000134	382	Actin related protein	Cytoskeletal	*	
BN1106_s2333 B000156	384	Troponin I 4	Cytoskeletal	*	

BN1106_s2349 B000191	385	Severin	Cytoskeletal				*	
BN1106_s2434 B000197	397	Actin-interacting protein 1	Cytoskeletal				*	
BN1106_s2590 B000129	412	PDZ and LIM domain protein Zasp	Cytoskeletal				*	
BN1106_s2864 B000144	445	Dynein	Cytoskeletal				*	
BN1106_s2907 B000132	451	actin-2	Cytoskeletal				*	
BN1106_s2907 B000133	452	actin-2	Cytoskeletal	*	*		*	*
BN1106_s2907 B000134	453	actin-2	Cytoskeletal	*			*	
BN1106_s2949 B000195	457	Microtubule-associated protein RP/EB family member 1	Cytoskeletal				*	
BN1106_s296B 000186	458	Filamin	Cytoskeletal				*	*
BN1106_s3045 B000180	470	Troponin T	Cytoskeletal				*	
BN1106_s3182 B000117	488	Myosin motor domain	Cytoskeletal				*	
BN1106_s322B 000089	491	Titin	Cytoskeletal				*	
BN1106_s3225 B000128	492	coronin	Cytoskeletal				*	
BN1106_s323B 000257	495	Myosin motor domain	Cytoskeletal				*	
BN1106_s323B 000258	496	Myosin tail	Cytoskeletal				*	gi 161044/gi 76154815

BN1106_s3266 B000046	499	Annexin	Cytoskeletal	*					*
BN1106_s3478 B000064	523	alpha-actinin	Cytoskeletal					*	
BN1106_s3509 B000140	524	Microtubule-associated protein 1	Cytoskeletal					*	
BN1106_s392B 000871	558	Tubulin beta-2C chain	Cytoskeletal					*	
BN1106_s4069 B000247	578	alpha actinin	Cytoskeletal					*	*
BN1106_s410B 000441	582	Titin	Cytoskeletal					*	
BN1106_s410B 000444	583	Titin	Cytoskeletal					*	
BN1106_s410B 000448	585	Titin	Cytoskeletal					*	
BN1106_s4130 B000080	587	Tropomyosin-2	Cytoskeletal					*	
BN1106_s4255 B000066	600	spectrin alpha	Cytoskeletal					*	
BN1106_s455B 000331	632	actin-2	Cytoskeletal	*	*	*	gi 1703114	FhB00085	
BN1106_s476B 000184	650	adducin	Cytoskeletal					*	
BN1106_s500B 000161	668	Annexin A6	Cytoskeletal		*	*		*	*
BN1106_s502B 000344	671	CG34417 - actin binding	Cytoskeletal					*	
BN1106_s5179 B000059	682	Tubulin-specific chaperone A	Cytoskeletal					*	
BN1106_s527B 000393	689	Myosin	Cytoskeletal				gi 262213552		
BN1106_s5331 B000045	694	LIM and SH3 domain protein	Cytoskeletal					*	

BN1106_s55B000372	701	tubulin	Cytoskeletal			*				*
BN1106_s567B000346	717	Profilin	Cytoskeletal			*				
BN1106_s586B000372	736	Cofilin	Cytoskeletal			*				
BN1106_s602B000099	744	tubulin polymerization-promoting protein family member	Cytoskeletal			*				
BN1106_s647B000405	767	Tropomyosin	Cytoskeletal			*		gi 29337029		
BN1106_s656B000153	771	Laminin	Cytoskeletal			*				
BN1106_s727B000100	798	LIM domains protein 3	Cytoskeletal			*				
BN1106_s819B000364	848	Annexin A13	Cytoskeletal	*		*		FhB01618/ FhB02550	*	*
BN1106_s819B000365	849	Annexin A3	Cytoskeletal			*				
BN1106_s90B000601	868	LIM domains protein 2	Cytoskeletal			*				
BN1106_s925B000539	881	Tubulin	Cytoskeletal			*				
BN1106_s925B000543	882	Tubulin	Cytoskeletal			*		gi 195157178		
BN1106_s925B000547	883	Tubulin alpha-3	Cytoskeletal	*		*				
BN1106_s937B000520	890	Myosin	Cytoskeletal			*				
BN1106_s945B000218	894	Annexin A11	Cytoskeletal	*	*	*		FhB01398	*	*
BN1106_s949B000142	899	dynein light chain	Cytoskeletal		*	*				

BN1106_s949B 000146	900	Dynein light chain LC8	Cytoskeletal		*	*			
BN1106_s10058 B000012	1	Hydroxyglutarate dehydrogenase	Oxidant metabolism/detoxification			*			
BN1106_s3005 B000095	64	Thioredoxin-glutathione reductase	Oxidant metabolism/detoxification		*	*		gi 1578877 71	
BN1106_s638B 000318	106	glutathione dehydrogenase	Oxidant metabolism/detoxification			*			
BN1106_s1029 B000154	137	glutathione S-transferase	Oxidant metabolism/detoxification			*			
BN1106_s10348 B000022	143	Glutathione peroxidase	Oxidant metabolism/detoxification		*				
BN1106_s1061 B000223	151	glutaredoxin	Oxidant metabolism/detoxification			*			
BN1106_s1081 B000242	155	Glutathione S-transferase	Oxidant metabolism/detoxification		*	*		*	*
BN1106_s1459 B000183	236	Malate dehydrogenase	Oxidant metabolism/detoxification		*	*			*
BN1106_s1614 B000280	261	Thioredoxin peroxidase	Oxidant metabolism/detoxification	*	*	*		FhB00158	* *

BN1106_s2277 B000049	374	Retinol dehydrogen ase 12	Oxidant metabolis mo/detoxi fication	*	*			*
BN1106_s2507 B000140	407	Retinol dehydrogen ase 12	Oxidant metabolis mo/detoxi fication	*				
BN1106_s2745 B000189	429	Glyoxalase domain- containing protein	Oxidant metabolis mo/detoxi fication					*
BN1106_s2937 B000224.mRN A-1 transcript_id=B N1106_s2937B0 00224.mRNA-1 gene_id=BN110 6_s2937B00022 4	456	Transketolas e	Oxidant metabolis mo/detoxi fication					*
BN1106_s3009 B000044	465	Carbonic anhydrase 5B	Oxidant metabolis mo/detoxi fication	*	*		FhB00925	*
BN1106_s3189 B000243	489	Superoxide dismutase Cu-Zn	Oxidant metabolis mo/detoxi fication		*			*
BN1106_s3595 B000059	536	Glutathione S- transferase class-mu 26 kDa isozyme 1	Oxidant metabolis mo/detoxi fication					*

BN1106_s3715 B000086	546	carbonyl reductase	Oxidant metabolism/detoxification			*				
BN1106_s3834 B000075	552	isocitrate dehydrogenase 2 (NADP+)	Oxidant metabolism/detoxification			*				
BN1106_s3875 B000041	555	carbonic anhydrase II	Oxidant metabolism/detoxification			*				
BN1106_s4026 B000080	574	Thioredoxin	Oxidant metabolism/detoxification	*	*	*	HAN4018d0 9.q1kT3	Q9U1G7	*	*
BN1106_s4027 B000177	575	alcohol dehydrogenase	Oxidant metabolism/detoxification			*				
BN1106_s4097 B000030	580	Malate dehydrogenase	Oxidant metabolism/detoxification			*				
BN1106_s4370 B000168	613	Glutathione S-transferase	Oxidant metabolism/detoxification		*					
BN1106_s444B 000267	618	Peroxiredoxin 3	Oxidant metabolism/detoxification			*	P91883/ HAN4004e0 1.q1kT3/HAN4005g04.q1kT3	gi 166235906		
BN1106_s4479 B000057	623	Glutathione S-transferase	Oxidant metabolism/detoxification		*	*		FhB00340	*	

BN1106_s5500 B000138	703	Superoxide dismutase	Oxidant metabolis mo/detoxi fication		*		
BN1106_s5504 B000045	704	glutathione S- transferase	Oxidant metabolis mo/detoxi fication		*		
BN1106_s567B 000345	716	L-lactate dehydrogen ase - it is released during tissue damage	Oxidant metabolis mo/detoxi fication		*		
BN1106_s645B 000322	765	Aldehyde dehydrogen ase	Oxidant metabolis mo/detoxi fication		*		
BN1106_s7830 B000018	836	Glutathione S- transferase	Oxidant metabolis mo/detoxi fication	*		gi 452903	*
BN1106_s9130 B000051	872	hydroxyacyl glutathione hydrolase	Oxidant metabolis mo/detoxi fication		*		
BN1106_s9271 B000022	884	Thioredoxin -glutathione reductase	Oxidant metabolis mo/detoxi fication	*	*		*
BN1106_s1191 B000313	12	Von Willebrand factor A domain- containing protein / Vacuolar	Oxidant metabolis mo/detoxi fication	*			*

protein
sorting 26

BN1106_s115B 000510	180	Tenascin	Oxidant metabolis mo/detoxi fication		*	
BN1106_s1246 B000440	201	CRE-LEC-2 protein	Oxidant metabolis mo/detoxi fication		*	
BN1106_s176B 000277	286	Collagen alpha-1(IV) chain	Oxidant metabolis mo/detoxi fication		*	
BN1106_s176B 000279	287	Collagen alpha-1(IV) chain	Oxidant metabolis mo/detoxi fication		*	*
BN1106_s1922 B000120	314	Periostin	Oxidant metabolis mo/detoxi fication	*		*
BN1106_s2057 B000129	336	spectrin	Oxidant metabolis mo/detoxi fication		*	
BN1106_s2351 B000181	386	spectrin beta chain	Oxidant metabolis mo/detoxi fication		*	

BN1106_s2354 B000024	387	Basement membrane-specific heparan sulfate proteoglycan core protein	Oxidant metabolism/detoxification		*		*
BN1106_s25B0 00189	405	Basement membrane-specific heparan sulfate proteoglycan core protein	Oxidant metabolism/detoxification		*		*
BN1106_s26B0 00447	414	Collagen alpha-1(XV) chain	Oxidant metabolism/detoxification	*		*	
BN1106_s392B 000875	559	ARM-1 protein	Oxidant metabolism/detoxification		*		
BN1106_s462B 000766	635	Fibropellin-1	Oxidant metabolism/detoxification		*		*
BN1106_s503B 000225	672	Innexin	Oxidant metabolism/detoxification		*		
BN1106_s6025 B000064	745	Von Willebrand factor A domain-containing protein	Oxidant metabolism/detoxification	*			FhC01779

BN1106_s1442 B000167	234	CD59-like protein	Immunity		*		
BN1106_s243B 000419	395	CD59-like protein	Immunity				*
BN1106_s5246 B000010	688	CD59-like protein	Immunity	*	*		
BN1106_s63B0 00399	760	CD59-like protein	Immunity	*	*		*
BN1106_s6720 B000015	778	CD59-like protein	Immunity	*	*		*
BN1106_s92B0 00559	878	T-cell immunomod ulatory protein	Immunity	*			
BN1106_s2898 B000141	59	Cysteine synthase	Amino acid metabolis m				*
BN1106_s1098 B000219	161	Pyrroline-5- carboxylate reductase	Amino acid metabolis m				*
BN1106_s232B 000326	381	TyrA protein	Amino acid metabolis m				*
BN1106_s2400 B000186	391	Glutamine synthase	Amino acid metabolis m				*
BN1106_s2851 B000085	443	Aspartate aminotransf erase	Amino acid metabolis m		*		
BN1106_s398B 000241	567	Ornithine aminotransf erase	Amino acid metabolis m			*	*

BN1106_s4261 B000116	602	Taurocyami ne kinase	Amino acid metabolis m	*	
BN1106_s436B 000498	610	Fumarate hydratase class I	Amino acid metabolis m	*	
BN1106_s4661 B000179	639	Glutamine synthetase	Amino acid metabolis m	*	
BN1106_s4661 B000180	640	Glutamine synthetase	Amino acid metabolis m	*	
BN1106_s5767 B000030	726	Glutamate dehydrogen ase	Amino acid metabolis m	*	*
BN1106_s771B 000469	828	Alpha- aminoadipic semialdehyd e synthase	Amino acid metabolis m	*	
BN1106_s1241 B000260	17	N-acetyl galactosami nidase	Carbohyd rate metabolis m	*	
BN1106_s1959 B000206	35	Glucose-6- phosphate isomerase	Carbohyd rate metabolis m	*	
BN1106_s2385 B000108	50	Lysosomal alpha- glucosidase	Carbohyd rate metabolis m	*	*

BN1106_s244B 000349	52	UTP-glucose-1-phosphate uridylyltransferase	Carbohydrate metabolism			*	
BN1106_s3173 B000376	67	alpha-glucosidase	Carbohydrate metabolism	*	*	*	*
BN1106_s3375 B000064	70	Fructose-1,6-bisphosphatase 1	Carbohydrate metabolism			*	
BN1106_s531B 000172	97	dihydrolipoamide acetyltransferase component of pyruvate dehydrogenase	Carbohydrate metabolism			*	
BN1106_s7879 B000034	120	Glucose-6-phosphate isomerase	Carbohydrate metabolism			*	
BN1106_s8157 B000032	121	Dihydrolipoamide dehydrogenase	Carbohydrate metabolism			*	*
BN1106_s1026 B000549	135	Aldose reductase	Carbohydrate metabolism			*	
BN1106_s1298 B000178	212	Galactokinase-like protein	Carbohydrate metabolism			*	

BN1106_s1518 B000071	245	Fructose- bisphosphat e aldolase	Carbohyd rate metabolis m				*						
BN1106_s1551 B000468	248	Propionyl- CoA carboxylase beta chain	Carbohyd rate metabolis m				*						*
BN1106_s1672 B000086	271	Pyruvate kinase	Carbohyd rate metabolis m				*						
BN1106_s175B 000200	283	Hexokinase	Carbohyd rate metabolis m			*	*			FhB00376		*	*
BN1106_s219B 000273	363	1,4-alpha- glucan- branching enzyme	Carbohyd rate metabolis m				*						
BN1106_s246B 000252	399	Phosphoenol- pyruvate carboxylase (GTP)	Carbohyd rate metabolis m	*	*	*		Fhep07g02.q 1k	gi 167541044	FhB01525			
BN1106_s269B 000233	422	Phosphoglu comutase-1	Carbohyd rate metabolis m				*						
BN1106_s3213 B000041	490	Triosephosp hate isomerase	Carbohyd rate metabolis m			*	*			FhB00282		*	
BN1106_s3227 B000227	494	enolase	Carbohyd rate metabolis m	*	*	*		Q27655.1/H AN4009g10. q1kT3	gi 3023708	FhB00588		*	*
BN1106_s393B 000274	560	Phosphoglu comutase	Carbohyd rate				*						

			metabolism						
BN1106_s395B000721	563	Phosphoenolpyruvate carboxykinase	Carbohydrate metabolism	*					
BN1106_s4083B000032	579	glycogen debranching enzyme-like isoform X2	Carbohydrate metabolism	*					
BN1106_s4361B000046	611	Pyruvate kinase	Carbohydrate metabolism	*					
BN1106_s4469B000065	622	aldolase A, fructose-bisphosphate	Carbohydrate metabolism	*	HAN4004c01.q1kT3	gi 1703248	FhB00113	*	*
BN1106_s4504B000167	626	Aldose 1-epimerase	Carbohydrate metabolism	*					
BN1106_s561B000223	713	ATP-dependent 6-phosphofruktokinase	Carbohydrate metabolism	*					
BN1106_s580B000238	730	Glycogenin glucosyltransferase	Carbohydrate metabolism	*					
BN1106_s666B000200	777	mannosidase, alpha, class 2B	Carbohydrate metabolism	*	*				*
BN1106_s8460B000014	854	transaldolase 1	Carbohydrate	*					

			metabolism			
BN1106_s85B000787	856	Transaldolase	Carbohydrate metabolism	*		
BN1106_s916B000192	875	Alpha-1,4 glucan phosphorylase	Carbohydrate metabolism	*		
BN1106_s233B000262	47	NADP-dependent malic enzyme	Energy metabolism	*		FhB01995 *
BN1106_s11911B000016	191	Mitochondrial acetate:succinate	Energy metabolism	*		
BN1106_s1501B000239	241	Succinate dehydrogenase ubiquinone flavoprotein subunit	Energy metabolism	*		gi 195436412
BN1106_s1848B000328	302	inorganic pyrophosphatase 1	Energy metabolism	*		
BN1106_s1866B000129	306	ATP synthase	Energy metabolism	*	HAN3004-1a05.q1k	gi 56758584
BN1106_s2001B000142	326	Cytochrome c proximal	Energy metabolism	*		
BN1106_s2574B000116	410	acyl-CoA-binding protein (ACBP)/diazepam	Energy metabolism	*		

binding
inhibitor
(DBI).

BN1106_s2896 B000173	449	NADH- cytochrome b5 reductase	Energy metabolis m					*	
BN1106_s3430 B000064	518	Succinate dehydrogen ase	Energy metabolis m					*	
BN1106_s3452 B000178	520	methylmalo nyl-CoA mutase - involved in key metabolic pathways	Energy metabolis m					*	
BN1106_s4332 B000087	608	FOF1 ATP synthase subunit alpha	Energy metabolis m					*	*
BN1106_s444B 000268	619	Citrate synthase	Energy metabolis m					*	
BN1106_s5004 B000026	669	succinyl- CoA ligase	Energy metabolis m					*	
BN1106_s5174 B000030	681	Glyceraldeh yde-3- phosphate dehydrogen ase - GAIT complex	Energy metabolis m	*			*	Fhep15c10.q 1k	gi 16406594
BN1106_s6083 B000078	753	Succinyl- CoA ligase subunit beta	Energy metabolis m					*	

BN1106_s6797 B000034	781	Malate dehydrogenase	Energy metabolism			*			
BN1106_s2194 B000230	364	Succinyl-CoA synthetase alpha subunit	Intermediate metabolism			*			
BN1106_s1285 B000159	18	Acid sphingomyelinase-like phosphodiesterase	Lipid metabolism		*			*	*
BN1106_s1498 B000257	26	Niemann-Pick C1	Lipid metabolism		*				*
BN1106_s771B 000467	118	Fatty-acid amide hydrolase	Lipid metabolism		*				
BN1106_s10326 B000017.	141	sapoin-like (FhSAP-3)	Lipid metabolism		*			*	*
BN1106_s1228 B000120	196	Fatty acid-binding protein type 2	Lipid metabolism		*	*	Q7M4G1/Fh ep46d02.q1k /Fh ep20f11.q1k	Q7M4G1	*
BN1106_s1252 B000359	203	Propionyl-CoA carboxylase	Lipid metabolism			*			*
BN1106_s1597 B000141	258	LAMA-like protein 2	Lipid metabolism		*			FhB00284	
BN1106_s1639 B000396	267	Prostamide/prostaglandin F synthase	Lipid metabolism			*			
BN1106_s20469 B000004	334	Niemann-Pick type C2	Lipid metabolism		*				*

BN1106_s2223 B000190	366	Threonyl-tRNA synthetase	Lipid metabolism				*		
BN1106_s2258 B000081	369	Niemann-Pick protein	Lipid metabolism	*					
BN1106_s2495 B000112	404	Niemann-Pick type C2	Lipid metabolism			*			
BN1106_s3703 B000103	545	acetate:succinate CoA-transferase	Lipid metabolism					*	
BN1106_s4047 B000060	577	Glycerol-3-phosphate dehydrogenase	Lipid metabolism					*	
BN1106_s4759 B000058	649	Natterin-4	Lipid metabolism					*	
BN1106_s4986 B000028	665	saposin-like protein 1 (FhSAP1)	Lipid metabolism	*		*		*	
BN1106_s4998 B000033	666	Group XV phospholipase A2	Lipid metabolism			*			FhB00083 *
BN1106_s5103 B000076	678	acetyl-CoA acetyltransferase 2	Lipid metabolism					*	
BN1106_s5689 B000026	721	Natterin-4	Lipid metabolism	*		*		*	* *
BN1106_s6908 B000039	786	Niemann-Pick protein	Lipid metabolism			*			
BN1106_s706B 000207	792	methylmalonyl-CoA epimerase	Lipid metabolism					*	

BN1106_s7353 B000023	803	Niemann-Pick protein	Lipid metabolism	*	*	*	*
BN1106_s7521 B000031	821	Saposin-like protein 2 (FhSAP2)	Lipid metabolism		*		
BN1106_s2044 B000106	333	purine nucleoside phosphorylase 5a - transferase	Nuclear metabolism			*	
BN1106_s2970 B000126	460	Deoxyribonuclease	Nuclear metabolism			*	
BN1106_s3026 B000095	466	5'-bisphosphate nucleotidase	Nuclear metabolism			*	
BN1106_s375B 000232	550	Staphylococcal nuclease domain-containing protein 1	Nuclear metabolism			*	
BN1106_s754B 000176	822	Adenosine deaminase - Cat eye syndrome critical region protein 5	Nuclear metabolism			*	
BN1106_s780B 000236	834	adenylate kinase	Nuclear metabolism			*	
BN1106_s992B 000187	905	APEX nuclease	Nuclear metabolism			*	
BN1106_s6B00 0373	741	arginine/serine-rich	ne			*	

		splicing factor						
BN1106_s1454 B000184	22	Histone H2A	Nuclear regulation	*				gi 51701468
BN1106_s1596 B000265	29	Ectonucleotide pyrophosphatase/phosphodiesterase	Nuclear regulation	*				
BN1106_s1789 B000241	31	Barrier-to-autointegration factor	Nuclear regulation			*		
BN1106_s1985 B000403	38	Ectonucleotide pyrophosphatase/phosphodiesterase	Nuclear regulation	*	*	*		*
BN1106_s3725 B000198	76	Histone H2A	Nuclear regulation			*	HAN5021d0 4.q1kT3	
BN1106_s557B 000139	100	AHNAK-like	Nuclear regulation			*		
BN1106_s6466 B000009	107	Histone H3	Nuclear regulation			*		gi 2116601
BN1106_s674B 000165	112	Histone H3	Nuclear regulation			*		
BN1106_s7720 B000056	119	dTMP kinase	Nuclear regulation			*		
BN1106_s1641 B000184	268	DNA-binding protein A	Nuclear regulation			*		
BN1106_s1958 B000299	319	High mobility group protein	Nuclear regulation			*		
BN1106_s1987 B000231	322	Cellular nucleic acid-binding protein	Nuclear regulation			*		

BN1106_s2003 B000165	327	Histone H2A	Nuclear regulation		*	
BN1106_s2127 B000101	346	DEK protein	Nuclear regulation		*	
BN1106_s2195 B000129	365	Zinc finger RNA- binding protein	Nuclear regulation		*	
BN1106_s2761 B000168	433	Uracil-DNA glycosylase	Nuclear regulation		*	
BN1106_s306B 000267	471	Telomerase protein component 1	Nuclear regulation	*		FhC05121
BN1106_s41B0 00298	581	High mobility group protein	Nuclear regulation		*	
BN1106_s5595 B000080	710	chromobox homolog 1 - histone methyltransf erase binding	Nuclear regulation		*	
BN1106_s596B 000431	740	UV excision repair protein RAD23	Nuclear regulation		*	
BN1106_s8B00 0460	843	Histone H1/5	Nuclear regulation		*	
BN1106_s8822 B000019	863	Histone H2B	Nuclear regulation		*	HAN5013f0 6.q1kT3
BN1106_s107B 000175	7	fasciclin-2- like	Protein export machiner y		*	

BN1106_s418B 000293	85	Golgi-associated plant pathogenesis-related protein 1	Protein export machinery	*
BN1106_s103B 000726	139	Synaptic vesicle membrane protein VAT-1	Protein export machinery	*
BN1106_s103B 000727	140	Synaptic vesicle membrane protein VAT-1	Protein export machinery	*
BN1106_s10435 B000022	147	Phosphoglucomutase-1	Protein export machinery	*
BN1106_s1094 B000139	158	Stress-induced-phosphoprotein 1	Protein export machinery	*
BN1106_s10981 B000052	162	NSF attachment protein SNAP	Protein export machinery	*
BN1106_s1142 B000130	176	Syntaxin 1A	Protein export machinery	*
BN1106_s1956 B000118	318	Golgi-associated plant pathogenesis-related protein 1	Protein export machinery	*

BN1106_s1995 B000318	323	Fasciclin I-like protein	Protein export machinery	*				*
BN1106_s2505 B000147	406	phosphoglucuronate dehydrogenase	Protein export machinery				*	
BN1106_s3033 B000087	468	phosphoglycerate kinase	Protein export machinery				*	
BN1106_s3747 B000112	549	ST1 homolog	Protein export machinery		*		*	*
BN1106_s390B 000196	556	Syntenin-1	Protein export machinery		*			
BN1106_s449B 000179	625	clathrin complex	Protein export machinery				*	
BN1106_s5131 B000049	679	coatamer protein complex	Protein export machinery				*	
BN1106_s5333 B000045	695	Lethal(2) giant larvae protein homolog 1	Protein export machinery				*	
BN1106_s5369 B000082	699	Transitional endoplasmic reticulum ATPase	Protein export machinery				*	
BN1106_s7866 B000032	837	phosphoglycerate mutase	Protein export				*	

			machiner y						
BN1106_s11916 B000010	13	DnaJ homolog subfamily	Protein modificati on machiner y		*				
BN1106_s1320 B000236	19	heat shock protein 83 kDa	Protein modificati on machiner y		*			FhB00008	
BN1106_s1679 B000169	30	universal stress protein	Protein modificati on machiner y		*				
BN1106_s2982 B000132	63	peptidylglyc ine alpha- hydroxylatin g monooxyge nase	Protein modificati on machiner y						
BN1106_s309B 000234	65	heat shock 70 kDa protein	Protein modificati on machiner y	*	*	gi 552242		FhB00129	*
BN1106_s3937 B000101.	82	Molecular chaperone HtpG	Protein modificati on machiner y		*				
BN1106_s495B 000230	91	heat shock 70 kDa	Protein modificati on machiner y		*				

BN1106_s9461 B000006	128	heat shock 70 kDa	Protein modificati on machiner y		*	
BN1106_s1057 B000126	149	DnaJ homolog subfamily A member 1	Protein modificati on machiner y	*	*	
BN1106_s1147 B000259	179	heat shock protein 70	Protein modificati on machiner y		*	
BN1106_s1242 B000159	200	DNAJ homolog subfamily C member 11	Protein modificati on machiner y		*	*
BN1106_s1396 B000332	224	Methyltrans ferase	Protein modificati on machiner y		*	
BN1106_s14B0 00365	227	Protein archease - extracellular vesicular exosome	Protein modificati on machiner y	*		
BN1106_s1793 B000159	293	chaperonin containing t- complex	Protein modificati on machiner y		*	
BN1106_s2018 B000302	331	chaperonin containing Tcp1	Protein modificati on		*	

			machinery		
BN1106_s2179 B000235	362	heat shock factor-binding protein 1-like	Protein modification machinery	*	
BN1106_s2415 B000155	393	Acidic leucine-rich nuclear phosphoprotein 32 family member B	Protein modification machinery	*	
BN1106_s2487 B000188	403	DnaK-type molecular chaperone	Protein modification machinery	*	
BN1106_s2641 B000139	417	Aconitate hydratase 1	Protein modification machinery	*	
BN1106_s2740 B000079	427	HSP90	Protein modification machinery	*	
BN1106_s2763 B000063	434	Protein disulfide-isomerase	Protein modification machinery	*	*
BN1106_s2909 B000085	454	10 kDa heat shock protein	Protein modification	*	

			machinery	
BN1106_s332B000232	505	Adenosylhomocysteine	Protein modification machinery	*
BN1106_s3324B000219	507	chaperonin family - cpn60	Protein modification machinery	*
BN1106_s3592B000072	535	DnaJ (Hsp40) homolog	Protein modification machinery	*
BN1106_s369B000200	543	heat shock protein	Protein modification machinery	*
BN1106_s3867B000081	553	T-complex protein 1 subunit zeta - chaperonin containing Tcp1	Protein modification machinery	*
BN1106_s4119B000141	586	T-complex protein 1 subunit alpha	Protein modification machinery	*
BN1106_s470B000292	643	heat shock protein p36-like	Protein modification machinery	*

BN1106_s4703 B000071	644	Chaperonin GroEL	Protein modificati on machiner y	*
BN1106_s4999 B000041	667	protein disulfide- isomerase A3-like	Protein modificati on machiner y	*
BN1106_s5284 B000043	691	Peptidyl- prolyl cis- trans isomerase B - therefore function as protein folding chaperones	Protein modificati on machiner y	*
BN1106_s5514 B000140	705	Chaperonin containing TCP1	Protein modificati on machiner y	*
BN1106_s553B 000158	706	Calnexin	Protein modificati on machiner y	*
BN1106_s5618 B000057	714	protein disulfide- isomerase A6-like	Protein modificati on machiner y	*
BN1106_s58B0 00487	729	Degradation arginine- rich protein for mis- folding	Protein modificati on machiner y	*

BN1106_s6031 B000032	746	Alpha crystallin- containing small heat shock protein variant	Protein modificati on machiner y		*	
BN1106_s6241 B000014	757	Peptidyl- prolyl cis- trans isomerase	Protein modificati on machiner y		*	
BN1106_s639B 000754	764	isochorismat ase domain containing 1	Protein modificati on machiner y		*	
BN1106_s6573 B000067	773	Peptidyl- prolyl cis- trans isomerase FKBP5	Protein modificati on machiner y		*	
BN1106_s746B 000284	819	Chaperonin containing TCP1, subunit 3	Protein modificati on machiner y		*	
BN1106_s7787 B000022	833	T-complex protein 1 subunit delta	Protein modificati on machiner y		*	
BN1106_s9189 B000015	877	peptidyl- prolyl cis- trans isomerase	Protein modificati on machiner y	*	*	FhB03741

BN1106_s208B 000185	39	ubiquitin- protein ligase BRE1	Proteoso me machiner y		*	
BN1106_s2242 B000188	43	Proteasome subunit beta 2	Proteoso me machiner y		*	*
BN1106_s1043 B000210	146	ubiquitin- protein ligase UBR4 20S	Proteoso me machiner y	*		
BN1106_s1639 B000395	266	proteasome subunit alpha 3 20S	Proteoso me machiner y		*	*
BN1106_s325B 000622	498	proteasome subunit alpha 3	Proteoso me machiner y			
BN1106_s4335 B000092	609	UDP-N- acteylglucos amine pyrophosph orylase 1	Proteoso me machiner y		*	
BN1106_s452B 000151	629	UDP- glucose 4- epimerase	Proteoso me machiner y		*	
BN1106_s452B 000152	630	UDP- glucose 4- epimerase	Proteoso me machiner y		*	

BN1106_s5073 B000167	675	26S proteasome regulatory complex component - Posttranslational modification	Proteosome machinery				*		
BN1106_s510B 000501	676	26S proteasome non-ATPase regulatory subunit 11	Proteosome machinery				*		
BN1106_s5276 B000036	690	ubiquitin- activating enzyme E1	Proteosome machinery				*		
BN1106_s5855 B000168	735	Proteasome beta 1 subunit	Proteosome machinery				*		*
BN1106_s6576 B000103	774	Ubiquitin	Proteosome machinery		*		*		*
BN1106_s6840 B000044	784	Polyubiquitin-A	Proteosome machinery	*	*		*		
BN1106_s6922 B000040	788	Proteasome subunit beta type	Proteosome machinery				*		
BN1106_s79B0 00381	840	Ubiquitin carboxyl- terminal hydrolase	Proteosome machinery				*		

BN1106_s945B 000221	895	ubiquitin- related modifier	Proteoso me machiner y	*
BN1106_s1026 B000539	3	Ribosomal protein S10	Protein synthesis machiner y	*
BN1106_s1079 B000440	8	Eukaryotic translation initiation factor 5A	Protein synthesis machiner y	*
BN1106_s11983 B000006	15	Ribosomal protein S14	Protein synthesis machiner y	*
BN1106_s3754 B000092	77	Large subunit ribosomal protein L21e	Protein synthesis machiner y	*
BN1106_s11425 B000010	177	60S ribosomal protein L3	Protein synthesis machiner y	*
BN1106_s116B 000323	182	40S ribosomal protein S12	Protein synthesis machiner y	*
BN1106_s1164 B000121	184	Elongation factor 1- gamma	Protein synthesis machiner y	*
BN1106_s12813 B000012	209	Small subunit ribosomal protein S6e	Protein synthesis machiner y	*

BN1106_s1385 B000133	223	Small subunit ribosomal protein S18e	Protein synthesis machinery	*
BN1106_s1628 B000104	264	60s ribosomal protein L27e	Protein synthesis machinery	*
BN1106_s1661 B000090	270	ribosomal protein S2	Protein synthesis machinery	*
BN1106_s1739 B000159	282	elongation factor 2	Protein synthesis machinery	*
BN1106_s1888 B000145	309	Ribosomal protein L19	Protein synthesis machinery	*
BN1106_s1935 B000255	316	60S ribosomal protein L8	Protein synthesis machinery	*
BN1106_s2104 B000158	343	60S ribosomal protein L18	Protein synthesis machinery	*
BN1106_s2398 B000171	390	40S ribosomal protein S21	Protein synthesis machinery	*
BN1106_s2474 B000182	401	ATP-dependent RNA helicase DDX23	Protein synthesis machinery	*

BN1106_s2662 B000418	419	60S ribosomal protein L18a	Protein synthesis machiner y	*
BN1106_s2741 B000351	428	ribosomal protein L24e Large subunit	Protein synthesis machiner y	*
BN1106_s2798 B000065	435	Putative 60S ribosomal protein L23a	Protein synthesis machiner y	*
BN1106_s285B 000836	441	Ribosomal protein l7ae	Protein synthesis machiner y	*
BN1106_s3036 B000185	469	Asparagine- -tRNA ligase	Protein synthesis machiner y	*
BN1106_s338B 000296	512	Ribosomal protein L26	Protein synthesis machiner y	*
BN1106_s346B 000282	521	Ribosomal protein L11	Protein synthesis machiner y	*
BN1106_s3540 B000083	528	Ribosomal protein	Protein synthesis machiner y	*
BN1106_s3580 B000148	532	ATP- dependent RNA helicase DDX5/DBP 2	Protein synthesis machiner y	*

BN1106_s3607 B000071	538	40S ribosomal protein SA	Protein synthesis machiner y	*	
BN1106_s401B 000237	573	40s ribosomal protein S5	Protein synthesis machiner y	*	
BN1106_s410B 000447	584	Large subunit ribosomal protein L14e	Protein synthesis machiner y	*	
BN1106_s4248 B000039	597	Ribosomal protein L7a	Protein synthesis machiner y	*	
BN1106_s4252 B000085	599	elongation factor 1- alpha	Protein synthesis machiner y	*	gi 46410394
BN1106_s446B 000198	621	40S ribosomal protein S8	Protein synthesis machiner y	*	
BN1106_s4543 B000079	631	Elongation factor 1-beta	Protein synthesis machiner y	*	
BN1106_s48B0 00386	653	Small subunit ribosomal protein S27e	Protein synthesis machiner y	*	
BN1106_s498B 000146	663	60S ribosomal protein L13	Protein synthesis machiner y	*	

BN1106_s507B 000153	674	40S ribosomal protein S4	Protein synthesis machiner y	*
BN1106_s5230 B000038	687	60S ribosomal protein L12	Protein synthesis machiner y	*
BN1106_s554B 000504	707	Small subunit ribosomal protein S30e	Protein synthesis machiner y	*
BN1106_s5854 B000082	734	60S ribosomal protein L4	Protein synthesis machiner y	*
BN1106_s6136 B000050	754	Ribosomal protein	Protein synthesis machiner y	*
BN1106_s6277 B000067	759	Large subunit ribosomal protein L6e	Protein synthesis machiner y	*
BN1106_s714B 000190	796	Ribosomal protein L30	Protein synthesis machiner y	*
BN1106_s725B 000470	797	Eukaryotic translation initiation factor 3	Protein synthesis machiner y	*
BN1106_s73B0 00493	801	60s ribosomal protein L13a	Protein synthesis machiner y	*
BN1106_s801B 000129	844	60S ribosomal protein L5	Protein synthesis	*

			machiner y						
BN1106_s886B 000188	865	Elongation factor 1-beta	Protein synthesis machiner y			*			
BN1106_s914B 000124	873	40S ribosomal protein S20	Protein synthesis machiner y			*			
BN1106_s9429 B000021	893	Large subunit ribosomal protein LP1	Protein synthesis machiner y			*			
BN1106_s5825 B000038	731	lipocalin	s/lipocali n			*			
BN1106_s10332 B000010	6	Cathepsin L1-like	Secreted proteinase			*			
BN1106_s13444 B000002	20	Cathepsin B-like	Secreted proteinase			*		*	*
BN1106_s1861 B000097	32	Legumain-2	Secreted proteinase			*	gi 40643267	*	*
BN1106_s3518 B000132	71	Lysosomal Pro-X carboxypept idase - s28	Secreted proteinase			*		*	*
BN1106_s468B 000343	88	Xaa-Pro dipeptidase- M24	Secreted proteinase			*			FhB02186
BN1106_s5163 B000012	95	Cathepsin B-like	Secreted proteinase	*	*	*			
BN1106_s5602 B000082	101	Cathepsin L-like	Secreted proteinase	*	*				
BN1106_s6570 B000050	109	Cathepsin B1-like	Secreted proteinase	*		*	gi 27526823		
BN1106_s6570 B000051	110	Cathepsin B3-like	Secreted proteinase	*	*	*	gi 107921798		

BN1106_s7079 B000034	113	Leucine aminopeptidase 2 - M17	Secreted proteinase		*				*
BN1106_s8177 B000010	122	Cathepsin L-like	Secreted proteinase						
BN1106_s8490 B000026	124	Cathepsin L1-like	Secreted proteinase		*			FhB03790/ FhB03882/ FhB03882/ FhB03693/ FhC11819	* *
BN1106_s10139 B000014	133	Cathepsin L-like	Secreted proteinase	*		*	A5Z1V3		
BN1106_s10332 B000011	142	Cathepsin L1-like	Secreted proteinase		*				*
BN1106_s10947 B000008	159	Legumain-1	Secreted proteinase						
BN1106_s1241 B000264	199	serine carboxypeptidase A - S10	Secreted proteinase		*			FhB02190	* *
BN1106_s1252 B000363	204	Leishmanolysin-like peptidase - M8	Secreted proteinase						
BN1106_s13034 B000002	215	Dipeptidyl- peptidase III - M49	Secreted proteinase			*			*
BN1106_s1407 B000292	230	Prolyl oligopeptidase - S9	Secreted proteinase			*			
BN1106_s14108 B000004	231	Cathepsin B-like	Secreted proteinase	*		*			
BN1106_s1620 B000120	262	Lysosomal Pro-X carboxypeptidase - s28	Secreted proteinase		*			FhB00297	* *
BN1106_s16222 B000004	263	Legumain-1	Secreted proteinase			*			

BN1106_s1772 B000188	290	Cathepsin B-like	Secreted proteinase		*					*
BN1106_s1840 B000150	301	Cathepsin B4-like	Secreted proteinase	*	*	*				
BN1106_s19975 B000004	325	Cathepsin L3-like	Secreted proteinase	*						
BN1106_s2087 B000065	337	Legumain-1	Secreted proteinase	*	*	*	Fhep29h09.q 1k			
BN1106_s2303 B000143	378	Cathepsin L6-like	Secreted proteinase	*		*				
BN1106_s2684 B000094	421	calpain	Secreted proteinase			*				
BN1106_s2882 B000074	447	Legumain-1	Secreted proteinase							
BN1106_s2882 B000077	448	Legumain-1	Secreted proteinase							
BN1106_s3008 B000074	464	Cathepsin L3-like	Secreted proteinase	*	*	*	Q9GRW4/Q 9GRW6/Q9 5VA7	A5X483	gi 161347489/ gi 222820543/ gi 10798509	
BN1106_s3536 B000078	527	Cathepsin L-like	Secreted proteinase		*					*
BN1106_s373B 000290	547	Cathepsin B-like	Secreted proteinase	*	*	*				
BN1106_s4000 B000155	572	Cathepsin L-like	Secreted proteinase		*					
BN1106_s4187 B000060	591	Cathepsin L3-like	Secreted proteinase	*	*	*				
BN1106_s4187 B000061	592	Cathepsin L-like	Secreted proteinase	*		*				
BN1106_s4223 B000091	594	Legumain 3	Secreted proteinase	*	*				FhB00106	*
BN1106_s4276 B000065	603	Metalloprot ease ARX1 - without EC number associated	Secreted proteinase			*				
BN1106_s4482 B000044	624	Cathepsin B2-like	Secreted proteinase	*		*				

BN1106_s4511 B000075	627	cytosol alanyl aminopeptid ase - M1	Secreted proteinase			*		
BN1106_s4636 B000039	636	Cathepsin L-like	Secreted proteinase		*		A8W7J0	
BN1106_s5100 B000033	677	Cathepsin B-like	Secreted proteinase	*	*	*		
BN1106_s5602 B000083	711	Cathepsin L4-like	Secreted proteinase	*		*		
BN1106_s5701 B000008	722	cathepsin L- like	Secreted proteinase			*		
BN1106_s5702 B000055	723	Cathepsin L-like	Secreted proteinase		*			
BN1106_s5880 B000098	738	Mastin - S1	Secreted proteinase			*		
BN1106_s617B 000566	755	Leucine amino peptidase 1 fragment C- terminal - M17	Secreted proteinase	*	*	*		*
BN1106_s617B 000567	756	Leucine amino peptidase 1 fragment N- terminal - M17	Secreted proteinase			*		
BN1106_s6354 B000017	762	Cathepsin L1-like	Secreted proteinase		*		FhB03910	
BN1106_s6635 B000017	775	Legumain-1	Secreted proteinase	*	*	*		
BN1106_s6995 B000048	790	Cathepsin L4-like	Secreted proteinase	*	*	*		
BN1106_s6995 B000049	791	Cathepsin L-like	Secreted proteinase	*	*	*		
BN1106_s7289 B000014	800	Cathepsin L1-like	Secreted proteinase		*		Q7JNQ9/ Q9NB30/ Q9GRW	FhB03688 *

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BN1106_s7456 B000012	818	Cathepsin L1-like	Secreted proteinase		*				
BN1106_s7612 B000030	824	Legumain	Secreted proteinase	*	*	*	P80527.1		
BN1106_s7612 B000031	825	Legumain	Secreted proteinase	*		*	Fhep29h09.q 1k		
BN1106_s7612 B000032	826	Legumain	Secreted proteinase			*			
BN1106_s793B 000177	841	Cathepsin B-like	Secreted proteinase		*			*	*
BN1106_s8098 B000020	846	Cathepsin L2-like	Secreted proteinase	*	*			*	
BN1106_s8462 B000006	855	Cathepsin B4-like	Secreted proteinase	*	*	*			*
BN1106_s8881 B000009	866	Cathepsin L-like	Secreted proteinase	*	*				
BN1106_s9069 B000006	870	legumain-1	Secreted proteinase	*	*	*			
BN1106_s9304 B000006	887	Cathepsin B-like	Secreted proteinase		*		HAN4015b0 5.p1kT7		FhB03844
BN1106_s98B0 00759	902	cytosol alanyl aminopeptid ase - M1	Secreted proteinase			*			
BN1106_s9961 B000006	907	Puromycin- sensitive aminopeptid ase	Secreted proteinase			*			
BN1106_s3864 B000104	79	Serpin	Secreted proteinase inhibitor		*	*	Fhep20a08.q 1k		
BN1106_s122B 000261	195	Serpin B6	Secreted proteinase inhibitor		*	*			*

BN1106_s1612 B000138	259	Multi-domain cystatin	Secreted proteinase inhibitor		*	*			*
BN1106_s1727 B000096	279	Serpin	Secreted proteinase inhibitor		*	*			
BN1106_s2757 B000215	431	Cystatin	Secreted proteinase inhibitor		*	*			
BN1106_s318B 000274	487	kunitz-type proteinase inhibitor (Fh-KTM)	Secreted proteinase inhibitor	*	*	*		FhC02704	*
BN1106_s3226 B000049	493	serpin	Secreted proteinase inhibitor		*	*			
BN1106_s3911 B000104	557	kunitz-type proteinase inhibitor (Fh-KTM2)	Secreted proteinase inhibitor						
BN1106_s4618 B000050	634	Serpin B	Secreted proteinase inhibitor		*	*			
BN1106_s4651 B000094	638	Stefin-1	Secreted proteinase inhibitor	*	*	*			*
BN1106_s5476 B000058	700	inhibidor proteases	Secreted proteinase inhibitor	*					
BN1106_s8826 B000029	864	kunitz-type proteinase inhibitor	Secreted proteinase inhibitor	*	*			FhC02704	
BN1106_s1026 B000543	4	Universal stress protein UspA	Signal transduction			*			

BN1106_s1551 B000464	27	KH domain- containing, RNA- binding, signal transduction -associated protein 1	Signal transducti on		*		
BN1106_s1971 B000297	37	Protein DJ-1	Signal transducti on		*	*	
BN1106_s2316 B000078	46	cAMP- dependent protein kinase type II-alpha regulatory subunit	Signal transducti on			*	
BN1106_s2848 B000228	56	SLIT and NTRK-like protein	Signal transducti on			*	*
BN1106_s3261 B000048	68	otoferlin a	Signal transducti on		*		*
BN1106_s366B 000435	74	calumenin- B	Signal transducti on			*	
BN1106_s3904 B000042	81	14-3-3 protein	Signal transducti on		*	*	gi 58263527 * *
BN1106_s397B 000170	83	Tensin	Signal transducti on			*	
BN1106_s4074 B000042	84	14-3-3 protein	Signal transducti on			*	
BN1106_s4999 B000040	92	Integrin- linked	Signal transducti on			*	

		protein kinase		
BN1106_s5073 B000165	93	major vault protein	Signal transduction	*
BN1106_s538B 000488	98	Galectin domain protein	Signal transduction	*
BN1106_s596B 000423	105	Universal stress protein UspA	Signal transduction	*
BN1106_s828B 000244	123	Sarcoplasmic calcium-binding protein	Signal transduction	*
BN1106_s101B 000544	132	Dickkopf-related protein 3	Signal transduction	*
BN1106_s1139 B000359	170	cell division cycle and apoptosis regulator protein 1-like	Signal transduction	*
BN1106_s11465 B000018	178	Ras-related protein Rab-14	Signal transduction	*
BN1106_s1277 B000102	208	Calcium binding protein	Signal transduction	*
BN1106_s1419 B000169	232	Serine/threonine-protein phosphatase	Signal transduction	*
BN1106_s1441 B000250	233	Guanine nucleotide-binding protein	Signal transduction	*

		subunit beta-1 (G-prot)						
BN1106_s1506 B000116	243	Guanine nucleotide-binding protein	Signal transduction			*		
BN1106_s1560 B000153	250	Calmodulin-like protein 3 (CaM3)	Signal transduction			*		
BN1106_s1657 B000161	269	Tetraspanin-CD63 receptor	Signal transduction	*	*	*	FhB00703	*
BN1106_s168B 000273	272	Rab11 family-interacting protein	Signal transduction			*		
BN1106_s17035 B000006	276	Translationally controlled tumor protein	Signal transduction		*	*		
BN1106_s1806 B000287	295	Calcium-binding protein	Signal transduction			*		
BN1106_s1806 B000294	296	Calcium binding protein	Signal transduction		*	*	FhB02185	
BN1106_s1819 B000120	297	serine/threonine protein kinase	Signal transduction		*			
BN1106_s1823 B000148	298	Lysosome-associated membrane glycoprotein	Signal transduction		*	*		*
BN1106_s1855 B000093	305	adenylate kinase	Signal transduction			*		

BN1106_s1908 B000177	313	RAS-like GTP- binding protein	Signal transducti on	*	*		*
BN1106_s204B 000249	332	Calpain-B	Signal transducti on	*	*		
BN1106_s2053 B000154	335	mucin	Signal transducti on		*		
BN1106_s2096 B000232	339	14-3-3 family	Signal transducti on		*		
BN1106_s210B 000998	340	Calmodulin- like protein 1 (CaM1)	Signal transducti on	*	*		
BN1106_s2124 B000372	345	Ras-related protein Ral- A	Signal transducti on	*			
BN1106_s214B 000741	349	Calcium- binding protein	Signal transducti on		*	gi 2764758	
BN1106_s214B 000742	350	Calcium- binding protein CaBP4	Signal transducti on	*	*		FhB01383
BN1106_s214B 000744	352	(calcium- binding EF- hand protein 4)	Signal transducti on		*		
BN1106_s214B 000747	354	CaBP3 (calcium- binding EF- hand protein 3)	Signal transducti on		*		
BN1106_s2140 B000163	356	Calponin	Signal transducti on		*		

BN1106_s2277 B000048	373	Calmodulin-like protein 2 (CaM2)	Signal transduction	*	*	FhB00790
BN1106_s2409 B000122	392	Calbindin-32	Signal transduction		*	
BN1106_s2438 B000175	398	guanine nucleotide-binding protein subunit beta-2-like	Signal transduction		*	
BN1106_s2487 B000187	402	Protein NDRG1	Signal transduction		*	
BN1106_s258B 000276	411	ras-related protein Rab-8A,	Signal transduction	*		*
BN1106_s2615 B000090	415	Myoferlin or Dysferlin	Signal transduction	*	*	
BN1106_s2673 B000071	420	Calreticulin	Signal transduction		*	
BN1106_s2716 B000103	424	dehydrogenase/reductase SDR family member 1-li	Signal transduction		*	
BN1106_s280B 000159	436	Calcium-binding protein	Signal transduction		*	
BN1106_s2898 B000145	450	Cystathionine beta-synthase	Signal transduction		*	
BN1106_s3172 B000053	477	14-3-3	Signal transduction	*	*	

BN1106_s318B 000272	480	Calcium-binding EF-hand	Signal transduction			*	
BN1106_s344B 000191	519	Nucleoside diphosphate kinase - functions of the NDP kinases in the processes of signal transduction in various organisms	Signal transduction		*	*	
BN1106_s3585 B000136	533	Myoferlin or Dysferlin	Signal transduction		*	*	*
BN1106_s3590 B000078	534	FERM domain-containing protein	Signal transduction			*	
BN1106_s4B00 0834	569	calcium-binding protein	Signal transduction	*		*	
BN1106_s4B00 0836	570	calcium-binding protein	Signal transduction		*	*	
BN1106_s417B 000229	590	cAMP-dependent protein kinase type II regulatory subunit	Signal transduction			*	
BN1106_s4290 B000110	604	Adenylyl cyclase-associated protein 1	Signal transduction			*	

BN1106_s4512 B000085	628	ADP- ribosylation factor	Signal transducti on		*		
BN1106_s4560 B000072	633	Tetraspanin	Signal transducti on	*		*	*
BN1106_s4672 B000098	641	Rho GDP- dissociation inhibitor	Signal transducti on	*	*		
BN1106_s468B 000347	642	SPARC protein	Signal transducti on		*		
BN1106_s483B 000264	657	Receptor expression- enhancing protein	Signal transducti on		*		
BN1106_s4840 B000058	658	Otoferlin	Signal transducti on	*		*	
BN1106_s519B 000125	684	SWI/SNF- related matrix- associated actin- dependent regulator of chromatin subfamily A-like protein 1	Signal transducti on		*		
BN1106_s605B 000204	749	Rab GDP dissociation inhibitor alpha	Signal transducti on		*		
BN1106_s6059 B000016	750	Calcium- binding protein	Signal transducti on	*			

BN1106_s652B 000433	768	Zinc binding protein	Signal transduction	*		
BN1106_s678B 000118	780	Calmodulin-like protein 4 (CaM4)	Signal transduction	*	*	*
BN1106_s686B 000273	785	14-3-3 protein gamma	Signal transduction		*	FhB00240
BN1106_s7273 B000042	799	Major vault protein	Signal transduction	*	*	*
BN1106_s736B 000233	804	Dihydropyrimidinase-like 2	Signal transduction		*	
BN1106_s773B 000382	832	Calponin	Signal transduction		*	
BN1106_s7814 B000036	835	Integrin-linked protein kinase	Signal transduction		*	
BN1106_s844B 000259	853	Rab-protein 11	Signal transduction	*	*	*
BN1106_s8501 B000034	857	Ras-related protein Rab-5B	Signal transduction		*	
BN1106_s915B 000136	874	Tetraspanin-1	Signal transduction	*	*	*
BN1106_s995B 000144	906	protein MEMO1	Signal transduction		*	
BN1106_s1871 B000313	307	Programmed cell death 6-interacting protein	Signal transduction apoptosis	*		FhC01381 *

BN1106_s347B 000346	522	programmed cell death- involved protein	Signal transducti on apoptosis		*
BN1106_s3654 B000233	540	programmed cell death protein 6- like isoform X1	Signal transducti on apoptosis	*	
BN1106_s1922 B000117.	34	Small nuclear ribonucleopr oteins G	Transcript ion machiner y		*
BN1106_s2871 B000068	57	poly(A) binding protein	Transcript ion machiner y		*
BN1106_s2945 B000112	61	seryl- aminoacyl- tRNA synthetase	Transcript ion machiner y		*
BN1106_s3553 B000143	72	Heterogeneo us nuclear ribonucleopr oteins A2/B1	Transcript ion machiner y		*
BN1106_s4644 B000085	87	Heterogeneo us nuclear ribonucleopr oteins F/H	Transcript ion machiner y		*
BN1106_s1270 B000089	207	Heterogeneo us nuclear ribonucleopr oteins	Transcript ion machiner y		*
BN1106_s135B 000521	220	Template- activating factor I	Transcript ion machiner y		*

BN1106_s1521 B000163	246	Tar DNA-binding protein	Transcription machinery	*
BN1106_s1560 B000152	249	RNA-binding region RNP-1 (RNA recognition motif)	Transcription machinery	*
BN1106_s1575 B000264	251	Transcriptional coactivator	Transcription machinery	*
BN1106_s1714 B000259	278	SAFB Scaffold attachment factor B2	Transcription machinery	*
BN1106_s1945 B000138	317	Splicing factor, arginine/serine-rich 7	Transcription machinery	*
BN1106_s1960 B000081	320	RNA-binding protein 4.1	Transcription machinery	*
BN1106_s2169 B000110	361	Splicing factor arginine/serine-rich 1/9	Transcription machinery	*
BN1106_s2968 B000206	459	serine/arginine-rich splicing factor 7-like	Transcription machinery	*
BN1106_s303B 000438	467	Regulator of differentiation 1	Transcription machinery	*

BN1106_s3074 B000155	473	transformer-2 protein homolog beta-like	Transcription machinery		*
BN1106_s310B 000140	474	Heterogeneous nuclear ribonucleoprotein U-like	Transcription machinery		*
BN1106_s3171 B000156	476	Heterogeneous nuclear ribonucleoprotein K	Transcription machinery		*
BN1106_s3948 B000057	562	splicing regulatory protein (FUSE binding protein 2)	Transcription machinery		*
BN1106_s397B 000172	566	Heterogeneous nuclear ribonucleoprotein K	Transcription machinery		*
BN1106_s5603 B000136	712	Activated RNA polymerase II transcriptional coactivator p15	Transcription machinery		*
BN1106_s607B 000421	752	Transcription elongation factor B polypeptide 1	Transcription machinery	*	*
BN1106_s698B 000162	789	small nuclear ribonucleoprotein D1	Transcription machinery		*

BN1106_s947B 000845	896	RNA-binding protein	Transcription machinery			*		
BN1106_s986B 000164	903	RNA polymerase II transcription elongation factor,	Transcription machinery		*	*		
BN1106_s1437 B000141	21	vacuolar protein sorting 4b	Transport /Storage		*			*
BN1106_s1966 B000132	36	Calponin/Tr ansgelin	Transport /Storage			*		
BN1106_s2298 B000195	44	Vesicle-associated membrane protein-associated protein A	Transport /Storage			*		
BN1106_s2471 B000098	53	ATP binding cassette	Transport /Storage		*		*	*
BN1106_s274B 000296	55	ATP-binding cassette	Transport /Storage		*		*	*
BN1106_s584B 000346	102	Glucose transporter-2 protein	Transport /Storage	*	*	*		
BN1106_s584B 000348	103	Solute carrier family 2 facilitated glucose transporter member 3	Transport /Storage			*		

BN1106_s1061 B000222	150	Alpha/beta hydrolase domain- containing protein	Transport /Storage			*		
BN1106_s1110 B000106	165	cubilin-like	Transport /Storage	*	*	*		*
BN1106_s114B 000614	171	Cubilin	Transport /Storage	*		*		
BN1106_s114B 000615	172	Cubilin-like	Transport /Storage	*	*	*		*
BN1106_s1326 B000426	216	retinitis pigmentosa 1-like 1 protein-like - function not known, probably transport sodium- coupled	Transport /Storage			*		
BN1106_s1326 B000429	217	monocarbox ylate transporter 1-like	Transport /Storage		*			
BN1106_s1581 B000120	253	Anoctamin	Transport /Storage		*			
BN1106_s1633 B000182	265	H ⁺ -ATPase subunit B	Transport /Storage			*		
BN1106_s168B 000275	273	GPI- anchored surface glycoprotein	Transport /Storage			*		
BN1106_s168B 000276	274	GPI- anchored surface glycoprotein	Transport /Storage					

BN1106_s171B 000376	277	Vesicle-associated membrane protein 7	Transport /Storage	*		
BN1106_s17622 B000002	288	cubilin-like isoform 1	Transport /Storage	*		*
BN1106_s18772 B000008	308	Vacuolar H ⁺ + ATPase 100kD subunit 1	Transport /Storage		*	*
BN1106_s1902 B000116	312	DRP1, density-regulated protein	Transport /Storage			*
BN1106_s2110 B000156	344	V-type H ⁺ -transporting ATPase subunit A	Transport /Storage			*
BN1106_s223B 000273	367	Calcium-transporting ATPase	Transport /Storage			*
BN1106_s2318 B000216	380	Alpha-tocopherol transfer protein-like	Transport /Storage			
BN1106_s2431 B000094	396	DNA damage-inducible protein 1	Transport /Storage			*
BN1106_s2566 B000129	408	vacuolar protein sorting 26 or von Willebrand factor A	Transport /Storage			*
BN1106_s2597 B000195	413	Charged multivesicular body protein 4	Transport /Storage		*	

BN1106_s2655 B000264	418	Charged multivesicular body protein	Transport /Storage		*					*
BN1106_s2858 B000111	444	Vacuolar protein sorting-associated protein VTA1	Transport /Storage		*					*
BN1106_s2916 B000225	455	Transmembrane protein C2orf18	Transport /Storage		*					
BN1106_s3001 B000131	461	cubilin-like	Transport /Storage	*	*	*			*	
BN1106_s3001 B000132	462	cubilin-like	Transport /Storage	*	*	*	HAN4005a0 7.q1kT3			*
BN1106_s3001 B000132	463	cubilin-like	Transport /Storage	*	*	*				
BN1106_s3067 B000141	472	transporter SVOPL	Transport /Storage			*				
BN1106_s3313 B000078	504	ATP:ADP antiporter	Transport /Storage			*				
BN1106_s3321 B000106	506	ATPase, H+ transporting, lysosomal accessory protein 1	Transport /Storage		*					
BN1106_s335B 000427	511	Endophilin-B1	Transport /Storage			*				
BN1106_s3396 B000086	515	ATP-binding cassette subfamily D (ALD) - ABC transporter	Transport /Storage		*			FhC06858		

BN1106_s3396 B000087	516	ATP-binding cassette subfamily D (ALD) - ABC transporter sodium/potassium-transporting ATPase subunit beta-3	Transport /Storage	*	
BN1106_s3547 B000116	529	Voltage-dependent anion channel protein 2	Transport /Storage		*
BN1106_s3549 B000112	530	calponin/transgelin	Transport /Storage	*	gi 29841466
BN1106_s3747 B000111	548	importin-beta 3	Transport /Storage	*	
BN1106_s420B 000182	593	Mitochondrial import receptor subunit TOM34 - cytosolic cochaperone of the Hsp90/Hsp70 protein complex	Transport /Storage		*
BN1106_s4802 B000087	654	V-type proton ATPase 116 kDa subunit a isoform 1	Transport /Storage	*	

BN1106_s521B 000167	686	SNaK1	Transport /Storage				*		*
BN1106_s5340 B000050	696	GTP- binding nuclear protein Ran	Transport /Storage				*		
BN1106_s5369 B000081	698	Transitional endoplasmic reticulum ATPase	Transport /Storage				*		
BN1106_s577B 000267	727	Calcium- transporting ATPase	Transport /Storage				*		
BN1106_s577B 000269	728	Calcium- transporting ATPase	Transport /Storage				*		
BN1106_s584B 000350	733	Glucose transporter- 2 protein	Transport /Storage	*	*		*		*
BN1106_s6006 B000040	743	cubilin-like	Transport /Storage			*			
BN1106_s605B 000203	748	Putative rab GDP- dissociation inhibitor	Transport /Storage			*	*		*
BN1106_s7307 B000022	802	cubilin	Transport /Storage	*			*		*
BN1106_s795B 000311	842	Nuclear transport factor-2	Transport /Storage				*		
BN1106_s823B 000216	851	CRAL- TRIO domain- containing protein - sec14 cytosolic factor family	Transport /Storage			*			

BN1106_s871B 000120	862	B-cell receptor- associated protein	Transport /Storage			*
BN1106_s912B 000169	871	Charged multivesicul ar body protein 2a	Transport /Storage		*	
BN1106_s9797 B000034	901	cubilin-like protein	Transport /Storage	*	*	*
BN1106_s2196 B000154	40	hypothetical protein T265_12952 , partial	Unknown conserved			*
BN1106_s4413 B000122	86	hypothetical protein	Unknown conserved		*	*
BN1106_s487B 000135	90	uncharacteri zed protein	Unknown conserved		*	*
BN1106_s1251 B000326	202	tr-G7YKJ4- G7YKJ4_C LOSI OS=Clonorc his sinensis GN=CLF_1 10325 PE=4 SV=1 - probable fragment	Unknown conserved			*
BN1106_s1287 B000157	210	Uncharacter ized protein	Unknown conserved		*	
BN1106_s173B 000867	280	Protein FAM79A - uk function	Unknown conserved			*
BN1106_s214B 000745	353	Tegument antigen	Unknown conserved			*

BN1106_s214B 000748	355	Tegument antigen	Unknown conserved			*		
BN1106_s37B0 00343	544	conserved hypothetical protein	Unknown conserved			*		
BN1106_s426B 000263	601	Tegumental protein	Unknown conserved			*		
BN1106_s574B 000139	724	Unknown product	Unknown conserved	*				
BN1106_s586B 000374	737	Fasciola/Schistosoma cross-reactive protein	Unknown conserved		*	*		
BN1106_s606B 000244	751	hypothetical protein T265_05756	Unknown conserved		*			
BN1106_s739B 000131	805	Tegumental protein	Unknown conserved			*		
BN1106_s739B 000132	806	hypothetical protein T265_08040	Unknown conserved		*	*	FhC01433	*
BN1106_s789B 000472	838	hypothetical protein T265_14322, partial protein	Unknown conserved			*		
BN1106_s789B 000473	839	F37C4.5-like - no known function	Unknown conserved			*		
BN1106_s1074 B000200	153	Uncharacterized protein	Unknown			*		
BN1106_s1076 B000677	154	Unknown product	Unknown			*		

BN1106_s1200 B000196	193	Unknown product	Unknown	*	*
BN1106_s1200 B000197	194	Unknown product	Unknown		*
BN1106_s1233 B000314	197	Unknown product	Unknown		*
BN1106_s1349 B000189	219	Unknown product	Unknown	*	
BN1106_s136B 000270	221	Unknown product	Unknown		*
BN1106_s13980 B000012	225	Unknown product	Unknown	*	
BN1106_s1536 B000294	247	Unknown product	Unknown		*
BN1106_s1579 B000120	252	Unknown product	Unknown		*
BN1106_s18B0 00411	294	Unknown product	Unknown		*
BN1106_s1830 B000391	299	Unknown product	Unknown		*
BN1106_s19966 B000004	324	Unknown product	Unknown	*	
BN1106_s216B 000184	358	Unknown product	Unknown	*	*
BN1106_s2275 B000114	371	Uncharacter ized protein	Unknown	*	*
BN1106_s263B 000603	416	uncharacteri zed protein	Unknown		*
BN1106_s2751 B000093	430	Unknown product	Unknown		
BN1106_s3270 B000103	500	Unknown product	Unknown		*
BN1106_s3381 B000139.	513	Unknown product	Unknown	*	
BN1106_s3381 B000140	514	Unknown product	Unknown		*
BN1106_s4307 B000027	606	Unknown product	Unknown		

BN1106_s440B000223.	616	Unknown product	Unknown		*			
BN1106_s440B000226.	617	Unknown product	Unknown		*			*
BN1106_s4767B000027	651	Unknown product	Unknown		*			*
BN1106_s4767B000028	652	Unknown product	Unknown		*			*
BN1106_s4811B000069.	656	Unknown product	Unknown		*			
BN1106_s5172B000090.	680	Unknown product	Unknown	*		*		
BN1106_s6032B000034	747	Unknown product	Unknown			*		
BN1106_s6800B000066	782	Unknown product	Unknown			*		
BN1106_s6821B000024	783	Unknown product	Unknown		*		*	*
BN1106_s709B000651	794	unknown	Unknown		*			
BN1106_s7443B000031	808	Unknown product	Unknown	*	*	*		
BN1106_s7704B000009	827	Unknown product	Unknown		*	*		
BN1106_s8038B000016	845	Unknown product	Unknown	*	*	*	*	*
BN1106_s8194B000020	850	Unknown product	Unknown			*		
BN1106_s8592B000014	858	Unknown product	Unknown		*			
BN1106_s8629B000023	859	Unknown product	Unknown			*		
BN1106_s928B000210	885	Unknown product	Unknown			*		
BN1106_s986B000166	904	Unknown product	Unknown			*		
BN1106_s999B000190	908	Unknown product	Unknown			*		

BN1106_s1062 B000110	152	CRIP	Cysteine rich proteins		*							
BN1106_s10890 B000012	157	Peptidase inhibitor 16	Cysteine rich proteins	*		*						
BN1106_s2878 B000056	446	GLIPR1-like protein 1	Cysteine rich proteins			*						
BN1106_s4131 B000138	588	GLIPR1-like protein 1	Cysteine rich proteins			*						
BN1106_s5591 B000098.	708	Peptidase inhibitor 16	Cysteine rich proteins	*		*						
BN1106_s5591 B000098	709	Peptidase inhibitor 16	Cysteine rich proteins	*								
BN1106_s9331 B000024	888	Peptidase inhibitor 16	Cysteine rich proteins	*								
Not founded in this study or retrieve no hit in the <i>F. hepatica</i> genomic database												
							FABP3 (Q9U1G6)	FABP1 (Q9UAS2)	Ubiquitin (gi 66818311)	FABP1 (gi 47115698)	LDL receptor (BN1106_s60B000536)	20S proteasome subunit alpha 6 (BN1106_s1579B000119)
							FABP Fh15 (Q7M4G0)	FABP3 (Q9U1G6)	UCE E2 (gi 34719464)	Peptidyl-prolyl cis-trans isomerase (FhB03741)	Beta-galactosidase (BN1106_s5248B000014)	Proteasome subunit beta type-5 (BN1106_s6770B000051)

Cathepsin L (A8W638)	FABP Fh15 (Q7M4G0)	Histone H4 (gi 194772468)	Thioredoxin peroxidase (FhB00158)	Acid phosphatase-like protein (BN1106_s1079B000448)	Otoferlin (BN1106_s92B000560)
Histone H4 (Fhep10a01.q1k)	Cathepsin L (Q8T5Z9)	HSP-90 (gi 226479066)	Retinal dehydrogenase (FhB03623)	Branched-chain amino acid aminotransferase (BN1106_s676B000138)	Inositol transporter (BN1106_s3611B000052)
FABP (HAN3004-1f09.q1k)	Fg SAP-3 (HAN5007d12.q1kaT3)		Ferritin (FhB00163)	Aspartate aminotransferase (BN1106_s4453B000140)	Beta-1,4- galactosyltransferase 2 (BN1106_s741B000214)
SjCHGC001 76 protein (HAN5016d06.q1kT3)			NPC-2 (FhB03724)	Glutamate dehydrogenase NAD(P)+ (BN1106_s8641B000016)	ALIX (BN1106_s2963B000136)
peptidyl- prolyl cis- trans isomerase (HAN5005h03.q1kaT3)			Ubiquitin L40 precursor (FhB01298)	EH domain- containing protein 1 (BN1106_s2100B000128)	Proteasome subunit alpha 7 (BN1106_s7720B000057)

ATP sintase alpha subunit mitochondr ial (FhB00596)	Oestrogen- regulated protein EP45 (BN1106_ s4565B00 0032)	Proteasome subunit alpha type (BN1106_s4 981B000066)
Serine proteinase inhibitor (FhB01959)		Proteasome subunit alpha type (BN1106_s3 658B000104)
Haemo globin (FhB003 23)		Proteasome subunit alpha 6 (BN1106_s1 259B000205)
Glutath ione dehydr ogenas e (FhB01 082)		20S proteasome subunit beta 2 (BN1106_s2 284B000154)
Calpon in (FhB01 516)		Proteasome subunit alpha type (BN1106_s9 050B000016)
GST (FhB00 203)		Phospholipid -translocating ATPase IIB (BN1106_s4 35B000242)
Amino acylase		Vacuolar assembly protein

(Irc449 28)	(BN1106_s2 316B000077)
Programmed cell death protein (FhC00663)	Syntenin-1 (BN1106_s4740 B000062)
	Charged multivesicular body protein 5 (BN1106_s6543 B000070)
	Ras-related protein (BN1106_s637 B000246)
	Alpha- galactosidase (BN1106_s124 1B000260)
	Uncharacterise d (BN1106_s263 B000609)

Anexo C

Tabelas com as anotações funcionais de proteínas e valores de NSAF feitos com a base de dados de *F. hepatica* do capítulo I

Adult PES NSAF

Accession number	Hyperlink	Annotation	Class	Run #1 (UniquePeptideCount)	Run #1 (PeptideCount)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePeptideCount)	Run #2 (PeptideCount)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePeptideCount)	Run #3 (PeptideCount)	Run #3 (SpecCount)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	NSAF/Total	Sum total NSAF	NSAF/Total	x10000
BN1106_s101B000531.mRNA-1	2	Actin-2	cs	0	6	13	0.000511976	0.1197	0	7	8	0.000315408	0.1144	*	*	*	*	*	0.000827384	0.000282003	2.9339546	0.000282003	2.8
BN1106_s1032B000017.mRNA-1	141	Saposin-3 (FHSAP-3)	met/lipid	7	7	18	0.003028892	0.4886	10	10	19	0.003200678	0.5909	1	1	2	0.00046	0.125	0.00689333	0.002279972		0.002279972	22.8
BN1106_s10332B000010.mRNA-1	6	Cathepsin-L1D-like	s/protease	3	47	804	0.045615196	3.4215	2	49	714	0.040553542	4.215	3	23	612	0.047435	0.3448	0.13360355	0.045537021		0.045537021	455.4
BN1106_s10332B000011.mRNA-1	142	Cathepsin L1D-like	s/protease	9	51	1069	0.02590798	0.2324	7	52	1038	0.025184146	0.2324	4	26	527	0.017448	0.1915	0.068540346	0.02336108		0.02336108	233.6
BN1106_s10348B000022.mRNA-2	143	Glutathione peroxidase	detox/ox	3	3	4	0.000501963	0.2966	3	3	6	0.000753773	0.2966	1	1	1	0.000171	0.161	0.001427173	0.000486433		0.000486433	43.9
BN1106_s1057B000126.mRNA-1	149	DnaI homolog subfamily A member 1	pm	1	1	1	3.68E-05	0.0622	1	1	1	3.69E-05	0.0622	*	*	*	*	*	7.37117E-05	2.51237E-05		2.51237E-05	0.3
BN1106_s1081B0000242.mRNA-1	155	Glutathione S-transferase	detox/ox	18	18	36	0.002278141	0.5	20	20	37	0.002233996	0.5	5	5	7	0.000605	0.2949	0.005227295	0.001781655		0.001781655	17.8
BN1106_s1110B000106.mRNA-2	165	Cubilin-like	tr	0	3	4	0.000228694	0.1158	0	4	5	0.000286181	0.1158	*	*	*	*	*	0.000514875	0.000175488		0.000175488	1.8
BN1106_s1142B000130.mRNA-1	176	Syntaxin 1A	pe	1	1	1	3.90E-05	0.0421	2	2	2	7.80E-05	0.0868	*	*	*	*	*	0.00011699	3.98746E-05		3.98746E-05	0.4
BN1106_s1140B00015.mRNA-1	172	Cubilin-like	tr	0	5	10	0.000919746	0.2484	0	2	8	0.000736606	0.1242	*	*	*	*	*	0.0001907651	0.000650198		0.000650198	6.5
BN1106_s1191B000313.mRNA-1	12	Von Willebrand factor A domain-containing protein	extrmat	2	2	2	4.57E-05	0.0324	1	1	1	2.29E-05	0.017	*	*	*	*	*	6.85803E-05	2.33747E-05		2.33747E-05	0.2
BN1106_s1228B000120.mRNA-1	196	Fatty acid-binding protein type 2	met/lipid	31	32	193	0.015041727	0.3789	28	28	223	0.017398922	0.4316	16	16	81	0.008624	0.3526	0.041064827	0.013996409		0.013996409	140.0
BN1106_s122B000261.mRNA-1	195	Serpin B6	s/prothn	7	19	30	0.001965653	0.5885	7	17	21	0.001377469	0.5664	1	3	3	0.000269	0.1239	0.003611656	0.001230986		0.001230986	12.3
BN1106_s1241B000264.mRNA-1	199	Carboxypeptidase	s/protease	5	5	9	0.000322691	0.0557	2	2	7	0.000521258	0.0363	*	*	*	*	*	0.000573948	0.000195623		0.000195623	2.0
BN1106_s1285B000159.mRNA-1	18	Acid sphingomyelinase-like phosphodiesterase	met/lipid	6	6	11	0.000473509	0.1512	6	6	12	0.000517123	0.1657	3	3	3	0.000176	0.0756	0.001167053	0.00039775		0.00039775	4.0
BN1106_s1287B000157.mRNA-1	210	Uncharacterized protein	met/lipid	2	2	10	0.000299755	0.0324	3	3	5	0.000150042	0.0324	*	*	*	*	*	0.000449798	0.000153308		0.000153308	1.5
BN1106_s1300B000145.mRNA-1	213	Moesin/raxin/radixin homolog 1-like isoform X1	cs	17	18	32	0.000863121	0.224	14	14	23	0.00062105	0.2295	3	3	5	0.000184	0.0546	0.001668411	0.000568656		0.000568656	5.7
BN1106_s1326B000429.mRNA-1	217	Sodium-coupled monocarboxylate transporter 1-like	tr	1	1	1	7.37E-05	0.0547	1	1	2	0.000147504	0.0547	*	*	*	*	*	0.000221176	7.53848E-05		7.53848E-05	0.8
BN1106_s1344B000002.mRNA-1	20	Cathepsin B-like	s/protease	9	12	53	0.007848197	0.58	7	11	49	0.007263855	0.43	3	6	22	0.004451	0.37	0.019562553	0.00666764		0.00666764	66.7
BN1106_s1349B000189.mRNA-1	219	Unknown product	uk	*	*	*	*	*	1	1	1	0.000308837	0.3542	1	1	1	0.000421	0.3542	0.000320286	0.000248909		0.000248909	2.5
BN1106_s1403B000129.mRNA-1	229	Plastin-2	s/protease	2	2	2	5.11E-05	0.0345	2	2	2	5.12E-05	0.0345	*	*	*	*	*	0.000102356	3.48868E-05		3.48868E-05	0.3
BN1106_s1437B000141.mRNA-1	21	Vacuolar protein sorting 4b	tr	5	5	6	0.000214608	0.1039	2	2	2	7.16E-05	0.0249	1	1	1	4.89E-05	0.0435	0.000335086	0.00011421		0.00011421	1.1
BN1106_s1442B000167.mRNA-1	234	CD59-like protein	imm	0	3	6	0.000728258	0.2295	0	4	8	0.000972078	0.2295	0	2	3	0.000497	0.1066	0.002197785	0.000749086		0.000749086	7.5
BN1106_s1444B000095.mRNA-1	235	Dynein	cs	5	5	6	0.000998287	0.5281	5	5	6	0.000999384	0.5281	*	*	*	*	*	0.00199767	0.00068088		0.00068088	6.8
BN1106_s1459B000183.mRNA-1	236	Malate dehydrogenase	detox/ox	2	2	2	9.03E-05	0.0366	2	2	2	9.04E-05	0.0367	*	*	*	*	*	0.000180684	6.15836E-05		6.15836E-05	0.6
BN1106_s1498B000257.mRNA-1	26	Niemann-Pick C1	met/lipid	4	4	5	7.90E-05	0.0288	2	2	2	3.16E-05	0.0271	*	*	*	*	*	0.00011066	3.77169E-05		3.77169E-05	0.4
BN1106_s1480B000365.mRNA-2	227	Protein arceuthae	pm	1	1	2	0.000519576	0.1754	2	2	3	0.000780221	0.1754	*	*	*	*	*	0.001299797	0.000443019		0.000443019	4.4
BN1106_s1581B000120.mRNA-1	253	Anoectamin	tr	4	4	6	0.000212542	0.052	4	4	7	0.000411955	0.0534	1	1	1	2.77E-05	0.0219	0.000291172	9.9242E-05		9.9242E-05	1.0
BN1106_s1582B000145.mRNA-3	254	Dynein	cs	1	1	1	0.000155873	0.1053	1	1	1	0.000156044	0.1053	*	*	*	*	*	0.000311917	0.000106313		0.000106313	1.1
BN1106_s1597B000141.mRNA-1	258	LAMA-like protein 2	met/lipid	13	13	21	0.000209405	0.0687	2	2	3	8.98E-05	0.0242	*	*	*	*	*	0.000299249	0.000101995		0.000101995	1.0
BN1106_s1612B000138.mRNA-1	259	Multi-domain cystatin	s/prothn	13	13	1	0.000204088	0.0778	9	9	12	0.000117265	0.0541	1	1	1	1.33E-05	0.0099	0.000335587	0.00014381		0.00014381	1.1
BN1106_s1614B000280.mRNA-1	261	Thioredoxin peroxidase	detox/ox	23	23	87	0.0008258262	0.5962	24	24	61	0.00579664	0.5897	14	14	20	0.002594	0.5833	0.016684834	0.005674401		0.005674401	56.7
BN1106_s1620B000120.mRNA-1	262	Pro-X carboxypeptidase	s/protease	19	19	36	0.001083506	0.2459	18	18	34	0.001022436	0.2622	4	4	4	0.000164	0.0447	0.000272421	0.000774521		0.000774521	7.7
BN1106_s1657B000161.mRNA-1	269	Tetraspanin-CD63 receptor	st	5	5	16	0.000784525	0.1689	9	9	22	0.001079908	0.1689	2	2	2	0.000134	0.0596	0.001998044	0.00068113		0.00068113	6.8
BN1106_s1703B000006.mRNA-1	276	Translocation-coupled tumor protein	st	3	3	4	0.000377272	0.2102	3	3	4	0.000377686	0.1274	*	*	*	*	*	0.000754988	0.000257318		0.000257318	2.6
BN1106_s1727B000096.mRNA-1	279	Serpin	s/prothn	6	22	36	0.001692333	0.4667	5	19	24	0.001129462	0.4159	1	4	4	0.000257	0.1587	0.000378679	0.001049327		0.001049327	10.5
BN1106_s175B000200.mRNA-1	283	Hexokinase	met/carb	6	6	8	0.000493937	0.04	4	4	6	0.000187253	0.0611	*	*	*	*	*	0.000436649	0.000148826		0.000148826	1.5
BN1106_s1772B000188.mRNA-1	290	Cathepsin B-like	s/protease	19	19	51	0.001469268	0.2938	22	22	45	0.001297838	0.284	6	6	7	0.000275	0.0856	0.000426606	0.001073032		0.001073032	10.4
BN1106_s1806B000294.mRNA-1	296	Calcium binding protein	st	3	3	7	0.001328916	0.4231	5	5	7	0.001330376	0.4231	*	*	*	*	*	0.002659292	0.000906385		0.000906385	9.1
BN1106_s1819B000120.mRNA-1	297	Serine/threonine protein kinase	st	2	2	3	0.000176987	0.0797	3	3	3	0.000177182	0.1594	*	*	*	*	*	0.000354169	0.000120714		0.000120714	1.2
BN1106_s1823B000148.mRNA-1	298	Lysosome-associated membrane glycoprotein	st	0	1	1	0.000170206	0.1379	0	1	1	0.000170393	0.1594	*	*	*	*	*	0.000340599	0.000116089		0.000116089	1.2
BN1106_s1840B000150.mRNA-1	301	Cathepsin B4-like	s/protease	13	26	92	0.00549326	0.4637	11	24	73	0.004363573	0.4637	6	14	32	0.00261	0.4597	0.012467098	0.004294247		0.004294247	42.5
BN1106_s1861B000097.mRNA-1	32	Legumain-2	tr	18	20	37	0.00128916	0.2588	17	19	41	0.001430099	0.2637	7	7	8	0.000381	0.0635	0.001030059	0.001056612		0.001056612	10.6
BN1106_s1871B000313.mRNA-1	307	Programmed cell death 6-interacting protein	st/apoptosis	7	7	9	0.000168485	0.0923	9	9	10	0.000187411	0.0936	*	*	*	*	*	0.000355895	0.000121302		0.000121302	1.2
BN1106_s1877B000008.mRNA-1	308	Vacuolar H + ATPase 100kD subunit 1	tr	2	2	3	0.000212554	0.1579	2	2	3	0.000212787	0.1579	*	*	*	*	*	0.000425341	0.000144972		0.000144972	1.4
BN1106_s1908B000177.mRNA-1	313	RAS-like GTP-binding protein	st	0	4	4	0.000308498	0.1927	4	4	4	0.000308837	0.2031	*	*	*	*	*	0.000617336	0.000210411		0.000210411	2.1
BN1106_s1971B000297.mRNA-1	37	Protein DJ-1	st	2	2	5	0.000404588	0.1366	4	4	4	0.000567046	0.2022	*	*	*	*	*	0.000971634	0.000331169		0.000331169	3.3
BN1106_s1985B000403.mRNA-1	38	Ectonucleotide pyrophosphatase/phosphodiesterase	nr	4	5	6	0.000223797	0.0705	5	5	5	0.000186703	0.1033	*	*	*	*	*	0.000410475	0.000139914		0.000139914	1.4
BN1106_s1996B000004.mRNA-2	324	Unknown product	uk	1	1	1	0.000296158	0.38	1	1	1	0.000296484	0.38	*	*	*	*	*	0.000529542	0.000201994		0.000201994	2.0
BN1106_s2046B000004.mRNA-1	334	Niemann-Pick type C2	met/lipid	0	5	14	0.002012727	0.4175	0	5	14	0.002014939	0.4175	0	3	5	0.000982	0.1845	0.000509683	0.001707885		0.001707885	17.1
BN1106_s204B000249.mRNA-1	332	Calpain-B	cs	3	3	5	9.79E-05	0.0701	6	6	9	0.000176478	0.1085										

BN1106_s3008B000074.mRNA-1	464	Cathepsin L3-like	s/protease	9	17	23	0.001131502	0.3721	7	14	17	0.000837247	0.4086	*	*	*	*	*	0.001968749	0.000671022	0.000671022	6.7
BN1106_s3009B000044.mRNA-1	465	Carbonic anhydrase SB	detox/ox	7	7	14	0.000558789	0.1617	8	8	14	0.000559404	0.1887	1	1	1	5.45E-05	0.0323	0.00117272	0.000399706	0.000399706	4.0
BN1106_s306B000267.mRNA-1	471	Telomerase protein component 1	nr	3	3	3	8.86E-05	0.0936	2	2	3	0.000559404	0.1887	1	1	1	5.45E-05	0.0323	0.00117272	0.000399706	0.000399706	4.0
BN1106_s309B000234.mRNA-1	65	Heat shock 70 kDa protein	pm	4	4	6	0.000137748	0.062	6	6	9	0.000206849	0.093	*	*	*	*	*	0.00034597	0.000117451	0.000117451	1.2
BN1106_s3172B000053.mRNA-1	477	14-3-3	st	4	4	5	0.000302202	0.1061	3	3	6	0.000363044	0.151	*	*	*	*	*	0.00065244	0.00022674	0.00022674	2.3
BN1106_s3173B0000376.mRNA-1	67	Alpha-glucosidase	met/carb	7	7	9	0.000215649	0.1553	6	6	8	0.000191899	0.123	1	1	1	3.27E-05	0.0227	0.000440282	0.000150645	0.000150645	1.5
BN1106_s3189B000243.mRNA-1	489	Superoxide dismutase Cu-Zn	detox/ox	6	6	10	0.00025495	0.4188	4	4	7	0.000648558	0.1325	*	*	*	*	*	0.001574053	0.000356495	0.000356495	5.4
BN1106_s318B000274.mRNA-1	487	Kunitz-type proteinase inhibitor (Fh-KTM)	s/protein	19	20	83	0.0168364	0.7671	21	23	93	0.01888617	0.7671	9	10	57	0.015796	0.6438	0.005117695	0.001759132	0.001759132	175.6
BN1106_s3213B000041.mRNA-1	490	Triosephosphate isomerase	met/carb	5	5	10	0.000585293	0.1581	2	2	4	0.000234375	0.0949	*	*	*	*	*	0.000819668	0.000279373	0.000279373	2.8
BN1106_s3226B000049.mRNA-1	493	Serin	s/protein	9	12	20	0.01583735	0.1877	9	12	21	0.001664749	0.5134	5	7	7	0.000757	0.5294	0.000400574	0.001365304	0.001365304	13.7
BN1106_s3227B0000227.mRNA-1	494	Enolase	met/carb	3	3	8	0.00021578	0.0273	3	3	6	0.000162013	0.0273	1	1	1	3.68E-05	0.0237	0.000414641	0.000141325	0.000141325	1.4
BN1106_s326B0000048.mRNA-1	68	Otoferlin a	st	7	7	8	0.000107304	0.0779	6	6	7	9.40E-05	0.0399	*	*	*	*	*	0.000210298	6.86097E-05	6.86097E-05	0.7
BN1106_s326B0000046.mRNA-1	499	Annexin	cs	5	5	6	0.00017387	0.1057	7	7	8	0.000232081	0.1761	*	*	*	*	*	0.000400951	0.000138363	0.000138363	1.4
BN1106_s3321B000106.mRNA-1	506	ATPase, H+ transporting, lysosomal accessory protein 1	tr	1	1	1	8.00E-05	0.0703	1	1	1	8.01E-05	0.0703	*	*	*	*	*	0.000160174	5.45931E-05	5.45931E-05	0.5
BN1106_s3353B000056.mRNA-1	69	Synaptotagmin	cs	3	3	3	0.000115989	0.1018	3	3	3	0.000116116	0.0548	*	*	*	*	*	0.000232105	7.91101E-05	7.91101E-05	0.8
BN1106_s3381B0001139.mRNA-1	513	Unknown product	uk	1	1	2	0.000290351	0.1176	1	1	1	0.000145335	0.1176	*	*	*	*	*	0.000453687	0.000148498	0.000148498	1.5
BN1106_s3396B000086.mRNA-1	515	ATP-binding cassette subfamily D (ALD) - ABC transporter	tr	4	4	5	0.000278344	0.1955	5	5	5	0.00044584	0.1955	1	1	1	7.61E-05	0.0602	0.000800236	0.000202725	0.000202725	2.7
BN1106_s3396B000087.mRNA-1	516	ATP-binding cassette subfamily D (ALD) - ABC transporter	tr	5	5	7	0.000209405	0.1111	5	5	5	0.000149739	0.1232	*	*	*	*	*	0.000359144	0.00012241	0.00012241	1.2
BN1106_s344B000191.mRNA-1	519	Nucleoside diphosphate kinase	st	3	3	6	0.000584523	0.1776	2	2	7	0.000682693	0.1842	*	*	*	*	*	0.001267216	0.000431914	0.000431914	4.3
BN1106_s3518B000132.mRNA-1	71	Pro-X carboxypeptidase	s/protease	23	23	72	0.00213234	0.238	26	26	113	0.00350268	0.338	8	8	9	0.000364	0.154	0.00584674	0.001992785	0.001992785	19.9
BN1106_s3536B000078.mRNA-1	527	Cathepsin L-like	s/protease	9	15	37	0.001602026	0.2193	8	14	38	0.001647133	0.231	2	5	6	0.000355	0.1374	0.003604063	0.001228398	0.001228398	12.3
BN1106_s3585B000136.mRNA-1	533	Myoferlin or Dysferlin	st	21	21	32	0.000431168	0.2129	22	22	31	0.000418153	0.1793	1	1	1	1.84E-05	0.0136	0.000867728	0.000295754	0.000295754	3.0
BN1106_s3654B000233.mRNA-1	540	Programmed cell death protein 6-like isoform X1	st/apoptosis	2	2	3	0.000235046	0.1111	2	2	3	0.000235305	0.1111	*	*	*	*	*	0.000470351	0.000160313	0.000160313	1.6
BN1106_s373B000290.mRNA-1	547	Cathepsin B-like	s/protease	2	2	2	8.58E-05	0.0406	3	3	3	0.000128906	0.0899	*	*	*	*	*	0.000214749	7.31944E-05	7.31944E-05	0.7
BN1106_s374B000112.mRNA-1	549	ST1 homolog	pe	4	4	6	0.000308498	0.1736	3	3	4	0.000205892	0.0868	*	*	*	*	*	0.00051439	0.000175323	0.000175323	1.8
BN1106_s3864B000104.mRNA-1	79	Serin	tr	18	21	43	0.001824471	0.4527	15	17	35	0.01486667	0.5072	3	5	5	0.00029	0.1347	0.00360096	0.00122734	0.00122734	12.3
BN1106_s3904B000042.mRNA-1	81	14-3-3 protein	uk	4	8	12	0.000485506	0.1421	6	6	14	0.000567046	0.1257	*	*	*	*	*	0.001052551	0.000358748	0.000358748	3.6
BN1106_s390B000196.mRNA-1	556	Syntenin-1	pe	5	5	7	0.000371525	0.0681	6	6	9	0.0004972	0.172	*	*	*	*	*	0.000849725	0.000289618	0.000289618	2.9
BN1106_s390B000041.mRNA-1	564	Ferritin	hsp	4	4	5	0.00043298	0.2456	3	3	3	0.000260074	0.2456	*	*	*	*	*	0.000693054	0.000236218	0.000236218	2.4
BN1106_s400B000155.mRNA-1	572	Cathepsin L-like	s/protease	2	2	2	8.16E-05	0.0744	4	4	5	0.000209149	0.1019	*	*	*	*	*	0.000285776	9.74031E-05	9.74031E-05	1.0
BN1106_s402B000080.mRNA-1	574	Thioredoxin	detox/ox	22	22	181	0.025771473	0.7692	20	20	155	0.022093751	0.6442	16	16	34	0.006614	0.5192	0.001878731	0.018568362	0.018568362	185.7
BN1106_s4131B0001138.mRNA-1	588	GLP1R-like protein 1	crp	3	3	8	0.0005659	0.1774	3	3	7	0.0005579	0.1774	1	1	1	0.000109	0.0968	0.001305561	0.000444302	0.000444302	4.4
BN1106_s4187B000060.mRNA-1	591	Cathepsin L-like	s/protease	1	16	27	0.0010439	0.1645	1	12	26	0.00106342	0.1567	*	*	*	*	*	0.002050242	0.000698798	0.000698798	7.0
BN1106_s4223B000091.mRNA-1	594	Legumain	s/protease	32	41	181	0.007303088	0.5095	37	46	174	0.00720364	0.5232	18	22	40	0.002205	0.376	0.016536308	0.00563184	0.00563184	56.4
BN1106_s4370B000168.mRNA-1	613	Glutathione S-transferase	detox/ox	1	3	5	0.000390789	0.0921	1	4	7	0.000434181	0.1046	0	1	1	8.46E-05	0.0335	0.000828613	0.000282422	0.000282422	2.8
BN1106_s440B000223.mRNA-1	616	Unknown product	uk	6	6	10	0.000860925	0.343	7	7	9	0.000775685	0.2733	3	3	3	0.000353	0.2035	0.001898451	0.000687078	0.000687078	6.8
BN1106_s440B000226.mRNA-1	617	Unknown product	uk	5	5	8	0.00068874	0.3372	5	5	7	0.00060331	0.343	*	*	*	*	*	0.001292051	0.000439079	0.000439079	4.4
BN1106_s4413B000122.mRNA-1	86	Hypothetical protein	uc	4	4	6	0.000203779	0.0826	2	2	4	0.000136002	0.0573	*	*	*	*	*	0.00033978	0.00011581	0.00011581	1.2
BN1106_s4479B000057.mRNA-1	623	Glutathione S-transferase	detox/ox	3	8	16	0.000471966	0.0996	3	8	14	0.000413424	0.0797	0	1	1	4.03E-05	0.0159	0.00025687	0.000315508	0.000315508	3.2
BN1106_s455B000331.mRNA-1	632	Actin-2	cs	0	6	13	0.000511976	0.1197	0	7	8	0.000315408	0.1144	*	*	*	*	*	0.000827384	0.000282003	0.000282003	2.8
BN1106_s4560B000072.mRNA-1	633	Tetraspanin	st	2	2	2	0.000336544	0.0727	2	2	6	0.000404296	0.1127	1	1	1	9.20E-05	0.0727	0.000832792	0.000283846	0.000283846	2.8
BN1106_s461B000050.mRNA-1	634	Serin B	s/protein	5	15	24	0.001255795	0.2968	7	15	23	0.001204793	0.311	2	3	4	0.000286	0.1095	0.002746518	0.000936115	0.000936115	9.4
BN1106_s463B000039.mRNA-1	636	Cathepsin L-like	s/protease	36	55	172	0.006833363	0.4461	33	49	184	0.00683622	0.4612	15	20	26	0.0001318	0.3459	0.014537799	0.0004955019	0.0004955019	49.6
BN1106_s4651B000094.mRNA-1	638	Stefin-1	s/protein	17	17	522	0.007807113	0.899	24	24	538	0.080559761	0.899	15	15	268	0.054763	0.7879	0.213400702	0.072734835	0.072734835	727.3
BN1106_s4672B000098.mRNA-1	641	Rho GDP-dissociation inhibitor	st	0	2	2	0.000174211	0.0941	0	1	1	8.72E-05	0.0765	*	*	*	*	*	0.000261412	8.90988E-05	8.90988E-05	0.9
BN1106_s468B000343.mRNA-1	88	Xaa-Pro dipeptidase	s/protease	5	5	9	0.000264427	0.1012	6	6	8	0.000235305	0.1012	*	*	*	*	*	0.000499732	0.000170327	0.000170327	1.7
BN1106_s4767B000027.mRNA-1	651	Unknown product	uk	0	2	3	0.000279395	0.1321	1	3	4	0.000372936	0.1321	*	*	*	*	*	0.00065233	0.000223338	0.000223338	2.2
BN1106_s4767B000028.mRNA-2	652	Unknown product	uk	9	9	23	0.000254168	0.3582	11	11	26	0.002876336	0.3881	5	5	20	0.003019	0.306	0.00843733	0.002875753	0.002875753	28.8
BN1106_s4811B000069.mRNA-1	656	Unknown product	uk	3	3	4	0.000199433	0.0572	2	2	2	9.98E-05	0.0943	*	*	*	*	*	0.000292529	0.000101999	0.000101999	1.0
BN1106_s4840B000058.mRNA-1	658	Otoferlin	st	4	4	6	0.000246799	0.0889	2	2	2	8.24E-05	0.0944	*	*	*	*	*	0.000329155	0.00012188	0.00012188	1.1
BN1106_s4862B000066.mRNA-1	659	V-type proton ATPase 116 kDa subunit a isoform 1	tr	2	2	2	4.78E-05	0.0435	2	2	2	4.78E-05	0.0435	*	*	*	*	*	9.5873E-05	3.25797E-05	3.25797E-05	0.3
BN1106_s487B0001135.mRNA-1	90	Uncloned protein	uc	4	4	5	0.000152032	0.0739	3	3	3	9.13E-05	0.0431	*	*	*	*	*	0.000243351	8.29432E-05	8.29432E-05	0.8
BN1106_s4986B000028.mRNA-1	665	saposin-1 (FHSAP1)	met/lipid	2	2	3	0.000435527	0.1961	2	2	2	0.00029067	0.1961	*	*	*	*	*	0.000726197	0.000247515	0.000247515	2.5
BN1106_s4998B000033.mRNA-1	666	Group XV phospholipase A2	met/lipid	0																		

BN1106_s6995B000048.mRNA-1	790	Cathepsin L4-like	s/protease	1	8	19	0.001069774	0.1103	1	6	14	0.000789121	0.0798	*	*	*	*	0.001858894	0.00063358	0.00063358	6.3	
BN1106_s6995B000049.mRNA-1	791	Cathepsin L-like	s/protease	2	15	94	0.004282906	0.1508	1	12	76	0.003466581	0.1262	1	4	29	0.001805	0.0892	0.009554585	0.00326555	0.00326555	32.6
BN1106_s709B000627.mRNA-1	114	Ferritin	hrp	5	5	8	0.000709361	0.2156	4	4	7	0.000621373	0.2096	*	*	*	*	0.001330735	0.000453564	0.000453564	4.5	
BN1106_s709B000651.mRNA-2	794	Unknown product	uk	1	1	1	0.000227814	0.1846	2	2	3	0.000684194	0.1846	*	*	*	*	0.000912008	0.000310846	0.000310846	3.1	
BN1106_s7289B000014.mRNA-1	800	Cathepsin L-like	s/protease	31	86	1469	0.066726477	0.6227	23	79	1289	0.058614681	0.6442	7	31	1310	0.081291	0.4417	0.20663169	0.070427706	0.070427706	704.3
BN1106_s7353B000023.mRNA-1	803	Niemann-Pick protein	met/lipid	13	14	52	0.005167864	0.4966	0	14	47	0.004676088	0.4564	0	11	15	0.002037	0.3691	0.011880484	0.004049307	0.004049307	40.5
BN1106_s739B000132.mRNA-1	806	Hypothetical protein T265_08040	uc	8	8	18	0.001206075	0.2896	6	6	11	0.000737856	0.2308	*	*	*	*	0.001943931	0.000662563	0.000662563	6.6	
BN1106_s7443B000031.mRNA-1	808	Unknown product	uk	0	3	7	0.00172759	0.3167	0	3	9	0.002223629	0.1833	0	2	3	0.001011	0.1833	0.004962697	0.00169147	0.00169147	16.9
BN1106_s7456B000012.mRNA-1	818	Cathepsin L1-like	s/protease	4	30	1818	0.119118561	0.3982	4	29	1647	0.108032953	0.3717	1	16	1210	0.108309	0.3717	0.335460179	0.11433721	0.11433721	1143.4
BN1106_s7521B000031.mRNA-1	821	Saposin-2 (FhSAP2)	met/lipid	16	16	57	0.008356944	0.6337	17	17	52	0.007632258	0.6337	12	12	16	0.003205	0.3366	0.019193884	0.006541984	0.006541984	65.4
BN1106_s7612B000030.mRNA-1	824	Legumain	s/protease	4	5	8	0.000558789	0.3066	1	2	6	0.000419553	0.1274	*	*	*	*	0.000978342	0.000334545	0.000334545	3.3	
BN1106_s7704B000009.mRNA-1	827	Unknown product	uk	2	2	2	0.000180584	0.1341	2	2	2	0.000180783	0.1341	1	1	1	0.000123	0.0793	0.000484718	0.00016521	0.00016521	1.7
BN1106_s771B000467.mRNA-1	118	Fatty-acid amide hydrolase	met/lipid	2	2	2	5.11E-05	0.0379	2	2	2	5.11E-05	0.0379	*	*	*	*	0.00010218	3.48266E-05	3.48266E-05	0.3	
BN1106_s7830B000018.mRNA-1	836	Glutathione S-transferase	detox/ox	2	7	12	0.000541753	0.1433	2	7	11	0.000497153	0.1372	0	1	1	6.17E-05	0.0244	0.001100581	0.000375119	0.000375119	3.8
BN1106_s793B000177.mRNA-1	841	Cathepsin B-like	s/protease	17	17	42	0.001813214	0.3207	18	18	34	0.001469454	0.3149	3	3	3	0.000177	0.0671	0.003459603	0.00117916	0.00117916	11.8
BN1106_s8038B000016.mRNA-1	845	Unknown product	uk	21	23	64	0.004249806	0.4126	21	23	62	0.004121525	0.4529	11	13	14	0.00127	0.3498	0.009641348	0.003286127	0.003286127	32.9
BN1106_s8098B000020.mRNA-1	846	Cathepsin L2-like	s/protease	88	123	3986	0.147560903	0.655	86	117	4173	0.154653404	0.6925	38	51	5819	0.294289	0.49	0.596503716	0.203310481	0.203310481	2033.1
BN1106_s819B000364.mRNA-1	848	Annexin A13	cs	18	18	31	0.001289454	0.4073	17	17	26	0.001082666	0.3258	1	1	1	5.68E-05	0.0309	0.002428944	0.000827874	0.000827874	8.3
BN1106_s823B000216.mRNA-1	851	AL-TRIO domain-containing protein - sec14 cytosolic factor fur	tr	*	*	*	*	*	1	1	2	8.15E-05	0.0412	1	1	1	5.56E-05	0.0412	0.000137027	4.6704E-05	4.6704E-05	0.5
BN1106_s842B000259.mRNA-1	853	Rab-protein 11	st	2	2	4	0.000275496	0.1023	2	2	3	0.000206849	0.1023	*	*	*	*	0.000482345	0.000164401	0.000164401	1.6	
BN1106_s8462B000006.mRNA-1	855	Cathepsin B4-like	s/protease	6	9	28	0.003316974	0.192	6	9	26	0.003083432	0.192	3	5	5	0.000809	0.192	0.007209588	0.002457294	0.002457294	24.6
BN1106_s8490B000026.mRNA-1	124	Cathepsin L1-like	s/protease	41	82	3748	0.119355003	0.4	41	84	3773	0.120283191	0.3806	24	46	4291	0.186677	0.314	0.426315631	0.145304101	0.145304101	1453.0
BN1106_s8592B000014.mRNA-2	858	Unknown product	uk	*	*	*	*	*	1	1	1	0.000251258	0.1525	1	1	10	0.003429	0.1525	0.003679995	0.001254278	0.001254278	12.5
BN1106_s8826B000029.mRNA-1	864	Kunitz-type proteinase inhibitor (Fh-KTM2)	s/protein	7	8	26	0.00561851	0.5588	7	9	27	0.005886077	0.6029	4	5	9	0.002677	0.4853	0.014225369	0.004848531	0.004848531	48.5
BN1106_s8881B000009.mRNA-1	866	Cathepsin L-like	s/protease	5	9	13	0.000482463	0.1153	4	7	9	0.000334338	0.1003	1	3	3	0.000152	0.0376	0.000968946	0.000330252	0.000330252	3.3
BN1106_s9069B000006.mRNA-1	870	Legumain-1	s/protease	0	5	7	0.00080353	0.155	0	4	6	0.000689497	0.186	*	*	*	*	0.001493028	0.000508879	0.000508879	5.1	
BN1106_s912B000169.mRNA-1	871	Charged multivesicular body protein 2a	tr	2	2	8	0.000497745	0.0966	1	1	2	0.000124573	0.0588	*	*	*	*	0.000622318	0.000212109	0.000212109	2.1	
BN1106_s915B000136.mRNA-1	874	Tetraspanin-1	st	0	3	4	0.000199433	0.1448	0	3	3	0.000149739	0.165	*	*	*	*	0.000349173	0.000119011	0.000119011	1.2	
BN1106_s9271B000022.mRNA-1	884	Thioredoxin-glutathione reductase	detox/ox	1	1	1	0.000112181	0.1364	2	2	2	0.000224609	0.1364	*	*	*	*	0.00033679	0.000114791	0.000114791	1.1	
BN1106_s928B000564.mRNA-1	879	Ferritin	hrp	1	1	1	0.000109688	0.0889	1	1	1	0.000109809	0.0889	*	*	*	*	0.000219497	7.48127E-05	7.48127E-05	0.7	
BN1106_s9304B000006.mRNA-1	887	Cathepsin B-like	s/protease	9	10	27	0.004299073	0.5914	11	12	28	0.004463198	0.5054	3	4	4	0.00087	0.3548	0.009632359	0.003283064	0.003283064	32.8
BN1106_s945B000218.mRNA-1	894	Annexin A11	cs	9	9	17	0.000513744	0.1755	6	6	11	0.000332788	0.1429	*	*	*	*	0.000846532	0.000288529	0.000288529	2.9	
BN1106_s949B000142.mRNA-1	899	Dynein light chain	cs	1	1	2	0.000266809	0.0991	2	2	2	0.000267103	0.0991	*	*	*	*	0.00053912	0.000181977	0.000181977	1.8	
BN1106_s949B000146.mRNA-1	900	Dynein light chain LC8	cs	3	3	4	0.000580703	0.2843	3	3	4	0.000581341	0.2059	*	*	*	*	0.001162044	0.000396067	0.000396067	4.0	
BN1106_s9797B000034.mRNA-1	901	Cubilin-like protein	tr	5	6	13	0.000631157	0.1836	5	7	14	0.000680455	0.1836	2	2	2	0.000133	0.0852	0.001444265	0.000492259	0.000492259	4.9
BN1106_s986B000164.mRNA-1	903	RNA polymerase II transcription elongation factor,	tm	2	2	2	0.000236927	0.184	1	1	1	0.000118594	0.088	*	*	*	*	0.00035552	0.000121174	0.000121174	1.2	

PES NEJ NSAF

Accession number	Hyperlink	Annotation	Class	Run #1 (UniquePc ptideCount)	Run #1 (PeptideCou nt)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePc ptideCount)	Run #2 (PeptideCo unt)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePcpt ideCount)	Run #3 (PeptideCou nt)	Run #3 (SpecCo unt)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	Contig/Total	Sum total NSAF	Contig/Total	x10000
BN1106_s10139B000014.mRNA-1	133	Cathepsin L-like	s/protease	5	19	79	0.02139814	0.3034	7	21	84	0.022750076	0.2966	4	14	284	0.045963384	0.2552	0.090111601	0.030785284	2.9270998	0.030785284	307.9
BN1106_s101B000531.mRNA-1	2	Actin-2	cs	0	1	1	0.00020891	0.0426	0	2	2	0.000417776	0.0691	*	*	*	*	*	0.000626686	0.000214098	0.000214098	0.000214098	2.1
BN1106_s1043B000210.mRNA-1	146	Ubiquitin-protein ligase UBR4	prot	1	1	3	3.93472E-05	0.0025	1	1	2	2.62287E-05	0.0025	1	1	1	7.83677E-06	0.0025	7.34127E-05	2.50804E-05	2.50804E-05	2.50804E-05	0.3
BN1106_s10890B00012.mRNA-1	157	Peptidase inhibitor 16	crp	5	10	19	0.007244915	0.3835	6	10	20	0.00762543	0.3544	5	12	35	0.007974298	0.4223	0.022846444	0.007804532	0.007804532	0.007804532	78.0
BN1106_s1110B000106.mRNA-2	165	Cubilin-like	tr	4	6	8	0.002426006	0.2703	4	5	8	0.002426006	0.2046	2	2	4	0.000724856	0.0811	0.005577121	0.00190534	0.00190534	0.00190534	19.1
BN1106_s114B000614.mRNA-1	171	Cubilin-like	tr	1	1	1	0.000279538	0.0961	1	1	1	0.000279509	0.0961	1	1	1	0.000167026	0.0961	0.000726073	0.000248052	0.000248052	0.000248052	2.5
BN1106_s114B000615.mRNA-1	172	Cubilin-like	tr	0	2	3	0.001463667	0.1242	0	2	2	0.000975676	0.1242	*	*	*	*	*	0.002439343	0.000833365	0.000833365	0.000833365	8.3
BN1106_s1200B000196.mRNA-1	193	Unknown product	uk	2	2	2	0.000887572	0.1525	2	2	2	0.000887479	0.1525	2	2	3	0.000795499	0.1525	0.002570551	0.00087819	0.00087819	0.00087819	8.8
BN1106_s13980B000012.mRNA-1	225	Unknown product	uk	0	1	1	0.001061488	0.2162	0	1	1	0.001061377	0.2162	*	*	*	*	*	0.002122866	0.000725245	0.000725245	0.000725245	7.3
BN1106_s14108B000004.mRNA-1	231	Cathepsin B4-like	s/protease	1	4	5	0.002600998	0.2053	2	4	6	0.003120871	0.2053	*	*	*	*	*	0.005721869	0.001954791	0.001954791	0.001954791	19.5
BN1106_s1444B000095.mRNA-1	235	Dynein	cs	1	1	2	0.001765172	0.236	1	1	2	0.001764987	0.236	1	1	1	0.000527353	0.236	0.004057512	0.001386188	0.001386188	0.001386188	13.9
BN1106_s1454B0000184.mRNA-1	22	Histone H2A	nr	1	2	3	0.001885203	0.304	0	1	2	0.001256671	0.152	*	*	*	*	*	0.003141874	0.001073374	0.001073374	0.001073374	10.7
BN1106_s1596B0000265.mRNA-1	29	Ectonucleotide pyrophosphatase	nr	1	2	2	0.000458018	0.0496	1	1	1	0.000228985	0.0496	*	*	*	*	*	0.000687004	0.000234705	0.000234705	0.000234705	2.3
BN1106_s1614B0000280.mRNA-1	261	Thioredoxin	detox/ox	2	2	2	0.001007053	0.141	1	1	3	0.001510422	0.141	1	1	5	0.001504309	0.141	0.004021784	0.001373982	0.001373982	0.001373982	13.7
BN1106_s1657B000161.mRNA-1	269	Tetraspanin-CD63 receptor	st	3	3	4	0.001040399	0.106	2	2	4	0.00104029	0.106	2	2	4	0.000621648	0.106	0.002702338	0.000923213	0.000923213	0.000923213	9.2
BN1106_s171B000376.mRNA-1	277	Vesicle-associated membrane	tr	2	2	2	0.000717353	0.1461	4	4	4	0.002151834	0.2785	*	*	*	*	*	0.002869187	0.000980215	0.000980215	0.000980215	9.8
BN1106_s17622B000092.mRNA-1	288	Cubilin-like	tr	2	7	69	0.017540322	0.1845	2	9	76	0.019317756	0.246	6	6	10	0.015948597	0.2168	0.052806674	0.018040613	0.018040613	0.018040613	180.4
BN1106_s184B0000150.mRNA-1	308	Cathepsin B4-like	s/protease	1	10	29	0.009185298	0.1774	1	8	28	0.008867637	0.1774	1	10	105	0.019871437	0.1694	0.037924372	0.012956296	0.012956296	0.012956296	129.6
BN1106_s1922B000120.mRNA-1	314	Peroxisin	extrmat	1	1	1	0.000122927	0.0188	1	1	1	0.000122914	0.0188	*	*	*	*	*	0.000245884	8.39877E-05	8.39877E-05	8.39877E-05	0.8
BN1106_s1985B000403.mRNA-1	38	Ectonucleotide pyrophosphatase	nr	3	3	5	0.000989296	0.1285	4	4	7	0.001348487	0.1788	2	2	4	0.000472891	0.0856	0.002847058	0.000972655	0.000972655	0.000972655	9.7
BN1106_s1995B000318.mRNA-1	323	Fasciclin I-like protein	pc	2	2	2	0.000236597	0.0422	2	2	2	0.000236572	0.0422	*	*	*	*	*	0.000473169	0.00161651	0.00161651	0.00161651	1.6
BN1106_s19975B000004.mRNA-1	325	Cathepsin L3-like	s/protease	4	39	161	0.027261447	0.7874	3	41	146	0.065902998	0.7816	5	37	235	0.06338847	0.7701	0.201972916	0.069001034	0.069001034	0.069001034	690.0
BN1106_s2087B000065.mRNA-1	337	Legumin-1	s/protease	20	24	90	0.017284871	0.3178	22	26	92	0.017667133	0.335	18	21	143	0.016409841	0.2983	0.051361846	0.017547009	0.017547009	0.017547009	175.5
BN1106_s225B000081.mRNA-1	369	Niemann-Pick protein	met/lipid	1	1	1	0.00045139	0.0747	1	1	1	0.00045139	0.0747	1	1	2	0.000539476	0.0747	0.001442304	0.000492742	0.000492742	0.000492742	4.9
BN1106_s2275B000114.mRNA-1	371	Uncharacterized protein	uk	*	*	*	*	*	1	1	2	0.000717278	0.0457	1	1	3	0.000642938	0.0457	0.001360215	0.00044697	0.00044697	0.00044697	4.6
BN1106_s230B000143.mRNA-1	378	Cathepsin L6-like	s/protease	4	12	49	0.021502551	0.3352	3	11	44	0.019306396	0.3525	8	8	216	0.097444921	0.33290604	0.097444921	0.033290604	0.033290604	0.033290604	332.9
BN1106_s2385B000108.mRNA-1	50	Lysosomal alpha-glucosidase	met/carb	6	9	9	0.003073701	0.2087	6	6	9	0.00307338	0.2087	3	3	3	0.000612188	0.1261	0.006795269	0.002309204	0.002309204	0.002309204	23.1
BN1106_s246B000252.mRNA-1	399	Phosphoenolpyruvate carboxyl	met/carb	2	2	2	0.000253797	0.0404	3	3	3	0.000380656	0.0856	*	*	*	*	*	0.00634452	0.000216751	0.000216751	0.000216751	2.2
BN1106_s26B0000447.mRNA-1	414	Collagen alpha-1(XV) chain	extrmat	2	2	2	8.26844E-05	0.0179	3	3	3	0.000124014	0.0232	*	*	*	*	*	0.000260698	7.06153E-05	7.06153E-05	7.06153E-05	0.7
BN1106_s2907B000133.mRNA-1	452	Actin-2	cs	0	1	1	0.000317024	0.0381	0	2	2	0.000374009	0.0619	*	*	*	*	*	0.000561033	0.000191669	0.000191669	0.000191669	1.9
BN1106_s2907B000134.mRNA-1	453	Actin-2	cs	0	1	1	0.000174169	0.0355	0	2	2	0.000348301	0.0576	*	*	*	*	*	0.00052247	0.000178494	0.000178494	0.000178494	1.8
BN1106_s3001B000131.mRNA-1	461	Cubilin-like	tr	2	2	2	0.000498731	0.0349	1	1	1	0.000498731	0.0349	2	2	3	0.000446995	0.0413	0.001444405	0.000493459	0.000493459	0.000493459	4.9
BN1106_s3001B000132.mRNA-1	463	Cubilin-like	tr	1	3	6	0.002276816	0.1981	1	3	5	0.001897148	0.1401	3	3	8	0.001813891	0.1981	0.005987855	0.002045661	0.002045661	0.002045661	20.5
BN1106_s3001B000132.mRNA-2	462	Cubilin-like	tr	1	3	5	0.001685625	0.1373	1	3	5	0.002696719	0.1202	*	*	*	*	*	0.004382344	0.001497162	0.001497162	0.001497162	15.0
BN1106_s3008B000074.mRNA-1	464	Cathepsin L3-like	s/protease	14	80	373	0.097339537	0.7043	14	80	325	0.084004090	0.6977	12	66	801	0.12489863	0.6645	0.307042576	0.104896517	0.104896517	0.104896517	1049.0
BN1106_s3009B000045.mRNA-1	465	Carbonic anhydrase 5B	detox/ox	2	2	2	0.000311725	0.0315	6	6	6	0.000453016	0.0335	1	1	2	0.000464744	0.0335	0.002585953	0.001581722	0.001581722	0.001581722	1.6
BN1106_s3172B000376.mRNA-1	67	Alpha-glucosidase	met/carb	3	24	74	0.00940568	0.4666	25	85	71	0.009023426	0.466	15	15	47	0.003569448	0.2718	0.021998553	0.007515478	0.007515478	0.007515478	75.2
BN1106_s318B000274.mRNA-1	487	Kunitz-type proteinase inhibitor	s/protein	7	7	11	0.011836322	0.6438	6	6	13	0.013986919	0.6438	1	1	3	0.001928813	0.2055	0.02752053	0.009481075	0.009481075	0.009481075	94.8
BN1106_s3227B000227.mRNA-1	494	Enolase	met/carb	3	3	4	0.00101445	0.1585	3	3	4	0.00101445	0.1585	3	3	4	0.000341963	0.0729	0.001915723	0.000654478	0.000654478	0.000654478	6.5
BN1106_s373B000290.mRNA-1	547	Cathepsin B-like	s/protease	4	4	4	0.003870586	0.0986	4	4	7	0.004325498	0.0986	3	3	21	0.002856879	0.0986	0.011052963	0.00377608	0.00377608	0.00377608	37.8
BN1106_s4026B000080.mRNA-1	574	Thioredoxin	detox/ox	3	3	4	0.003021159	0.2692	4	4	7	0.003264676	0.3846	4	4	9	0.004061634	0.3654	0.012369269	0.004225776	0.004225776	0.004225776	42.3
BN1106_s4187B000060.mRNA-1	591	Cathepsin L-like	s/protease	8	20	80	0.016407339	0.3368	5	18	63	0.01291943	0.3081	1	11	259	0.031738956	0.141	0.061065725	0.020862194	0.020862194	0.020862194	208.6
BN1106_s4187B000061.mRNA-1	592	Cathepsin L3-like	s/protease	2	67	346	0.113716933	0.682	2	69	301	0.098916823	0.6736	2	57	761	0.149443975	0.682	0.362077731	0.123698457	0.123698457	0.123698457	1237.0
BN1106_s4223B000091.mRNA-1	594	Legumin-1	s/protease	1	5	17	0.003638562	0.0845	0	5	30	0.006420321	0.079	0	4	25	0.003197169	0.079	0.013256052	0.004528733	0.004528733	0.004528733	45.3
BN1106_s4482B000044.mRNA-1	624	Cathepsin B2-like	s/protease	31	37	130	0.022150798	0.4252	30	35	132	0.022449229	0.4252	22	28	243	0.024739847	0.3948	0.069379873	0.023702599	0.023702599	0.023702599	237.0
BN1106_s455B000331.mRNA-1	632	Actin-2	cs	0	1	1	0.00020891	0.0426	0	2	2	0.000417776	0.0691	*	*	*	*	*	0.000626686	0.000214098	0.000214098	0.000214098	2.1
BN1106_s4651B000094.mRNA-1	638	Stefin-1	s/protein	3	3	3	0.002380307	0.2626	2	2	2	0.001586706	0.1515	*	*	*	*	*	0.003967013	0.001355271	0.001355271	0.001355271	13.6

BN1106_s8098B000020.mRNA-1	846	Cathepsin L2-like	s/	0	8	33	0.006480386	0.095	0	8	25	0.004908871	0.0925	*	*	*	*	*	0.011389257	0.00389097	0.00389097	38.9
BN1106_s8462B000006.mRNA-1	855	Cathepsin B4 -like	s/	4	6	22	0.013824824	0.192	5	6	26	0.016336721	0.192	3	6	81	0.030413518	0.168	0.060575063	0.020694567	0.020694567	206.9
BN1106_s8826B000029.mRNA-1	864	Kunitz-type proteinase inhibitor	s/	2	2	3	0.003465447	0.2206	2	2	2	0.002310057	0.2206	1	1	2	0.001380425	0.2206	0.007155929	0.002444716	0.002444716	24.4
BN1106_s8881B000009.mRNA-1	866	Cathepsin L-like	s/	12	20	90	0.017718076	0.1278	12	19	83	0.016338296	0.1278	13	17	112	0.01317458	0.1053	0.047230952	0.01613575	0.01613575	161.4
BN1106_s9069B000006.mRNA-1	870	Legumain-1	s/	3	4	10	0.006089158	0.1783	2	3	12	0.007306226	0.1783	4	4	11	0.004002162	0.2171	0.017397545	0.005943612	0.005943612	59.4
BN1106_s9189B000015.mRNA-1	877	Peptidyl-prolyl cis-trans isomer	pm	1	1	1	0.001540199	0.2745	1	1	1	0.001540038	0.2745	1	1	1	0.000920283	0.2745	0.00400052	0.001366718	0.001366718	13.7
BN1106_s925B000547.mRNA-1	883	Tubulin alpha-3	cs	1	1	2	0.001114186	0.1064	1	1	1	0.000557035	0.1064	*	*	*	*	*	0.001671221	0.000570948	0.000570948	5.7
BN1106_s92B000559.mRNA-1	878	T-cell immunomodulatory pro	imm	1	1	1	0.000168563	0.0429	1	1	2	0.00033709	0.0429	*	*	*	*	*	0.000505652	0.000172749	0.000172749	1.7
BN1106_s9331B000024.mRNA-7	888	Peptidase inhibitor 16	crp	7	16	28	0.039275068	0.9107	8	18	27	0.03786843	0.9107	4	7	11	0.009219265	0.8214	0.086362764	0.02950455	0.02950455	295.0
BN1106_s945B000218.mRNA-1	894	Annexin A11	cs	1	1	1	0.000160306	0.0449	1	1	1	0.00016029	0.0449	*	*	*	*	*	0.000320596	0.000109527	0.000109527	1.1
BN1106_s9797B000034.mRNA-1	901	Cubilin-like	tr	2	3	4	0.001030166	0.0787	3	4	5	0.001287573	0.1279	1	1	11	0.001692718	0.0525	0.004010456	0.001370112	0.001370112	13.7

SSP NEJ NSAF

Accession number	Hyperlink	Annotation	Class	Run #1 (UniquePeptideCount)	Run #1 (PeptideCount)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePeptideCount)	Run #2 (PeptideCount)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePeptideCount)	Run #3 (PeptideCount)	Run #3 (SpecCount)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	NSAF/Total	Sum total NSAF	NSAF/Total	x10000
BN1106_s10028000239.mRNA-1	130	Ferritin	hrp	3	3	3	0.000470464	0.2237	2	2	2	0.0004483	0.1009	3	3	3	0.0004743	0.2456	0.001393053	0.000516802	2.6955262	0.000516802	51.68017368
BN1106_s10058000012.mRNA-1	1	Hydroxyglutamate dehydrogenase	deto/ox	6	6	7	0.000551292	0.1256	2	2	2	0.0002251	0.0573	3	3	3	0.0002382	0.1013	0.001014619	0.000376408	3.674084403	0.000376408	37.64084403
BN1106_s10139000044.mRNA-1	133	Cathepsin L-related	s/protease	10	22	104	0.012822567	0.3655	11	17	54	0.0095159	0.3069	9	20	74	0.0091983	0.3103	0.031536791	0.011699679	0.011699679	11.69967906	11.69967906
BN1106_s10139000531.mRNA-1	2	Adin-2	cs	4	132	4	0.017434577	0.7367	1	38	131	0.017434577	0.5027	1	40	132	0.017434577	0.5027	0.015958566	0.015958566	15.95856666	0.015958566	159.58566666
BN1106_s10160000544.mRNA-1	132	Dickkopf-related protein 3	cs	2	2	2	0.0049257	0.2771	2	2	2	0.0049257	0.2771	2	2	2	0.0049257	0.2771	0.011016232	0.003752971	0.003752971	3.752971219	3.752971219
BN1106_s10260000539.mRNA-1	3	Ribosomal protein S10	ps	3	3	3	0.001207947	0.223	2	2	2	0.0006906	0.1689	2	2	2	0.0004871	0.1216	0.002385668	0.000885407	0.000885407	8.854073702	8.854073702
BN1106_s10260000543.mRNA-1	4	Universal stress protein UspA	st	18	18	36	0.0071655	0.6746	13	13	25	0.0075252	0.4734	17	17	34	0.0075252	0.4734	0.022428466	0.008320604	0.008320604	83.20604144	83.20604144
BN1106_s10260000549.mRNA-1	135	Aldose reductase	met/carb	2	2	2	0.000229937	0.0804	1	1	1	0.0001643	0.0611	2	2	2	0.0002318	0.0997	0.000260275	0.000232264	0.000232264	2.322645629	2.322645629
BN1106_s10298000154.mRNA-1	137	Glutathione S-transferase	deto/ox	4	4	6	0.000717496	0.1538	3	3	4	0.0006628	0.107	4	4	5	0.0006028	0.1405	0.002003961	0.000234265	0.000234265	2.342651444	2.342651444
BN1106_s10378000175.mRNA-1	144	Na(+)/H(+) exchange regulatory cofa	cs	1	1	2	0.000376371	0.0895	2	2	2	0.00059379	0.0789	2	2	3	0.0005692	0.1684	0.001483478	0.000550348	0.000550348	5.503480895	5.503480895
BN1106_s1038000718.mRNA-1	5	Ankyrin 2b	cs	2	2	3	0.000168657	0.0865	2	2	2	0.000168657	0.0865	2	2	3	0.00017	0.0503	0.00038692	0.00012565	0.00012565	1.256498214	1.256498214
BN1106_s1038000723.mRNA-1	138	Ankyrin	cs	11	11	15	0.00045298	0.1647	9	9	14	0.0006043	0.1157	13	13	18	0.000548	0.1867	0.001602569	0.000595531	0.000595531	5.95530666	5.95530666
BN1106_s1038000726.mRNA-1	139	Synaptic vesicle membrane protein V	pe	1	1	1	0.000152456	0.0901	1	1	1	0.000152456	0.0901	1	1	1	0.000152456	0.0901	0.000398166	0.000114325	0.000114325	1.143251594	1.143251594
BN1106_s1039000727.mRNA-1	140	Unknown product	uk	5	5	5	0.00067645	0.1838	3	3	5	0.0004871	0.0865	3	3	3	0.0004871	0.0865	0.001834172	0.00068787	0.00068787	6.87870007	6.87870007
BN1106_s10428000321.mRNA-1	145	Thyrosin	cs	7	7	7	0.006540592	0.5976	12	12	25	0.0155804	0.7561	14	14	26	0.0114297	0.7561	0.03550736	0.012446822	0.012446822	12.4468224	12.4468224
BN1106_s10435800022.mRNA-1	147	Phosphoglucomutase-1	pe	*	*	*	*	*	1	1	1	0.00021616	0.0717	1	1	1	0.00021616	0.0717	0.000390813	0.000144986	0.000144986	1.449859101	1.449859101
BN1106_s10578000126.mRNA-1	149	DnaI homolog subfamily A member	pm	5	5	6	0.00053366	0.1841	2	2	3	0.0003814	0.0597	6	6	6	0.00053366	0.1841	0.001453055	0.000539062	0.000539062	5.39061784	5.39061784
BN1106_s10611000222.mRNA-1	150	Alpha-beta hydrolase domain-contain	r	1	1	1	8.18E-05	0.0435	1	1	2	0.0002339	0.0435	2	2	3	0.0002475	0.0435	0.000561371	0.000208928	0.000208928	2.08928673	2.08928673
BN1106_s10618000223.mRNA-1	151	Glutaredoxin	deto/ox	1	1	1	0.000131453	0.0846	*	*	*	*	*	2	2	2	0.0002651	0.0625	0.000396509	0.000147099	0.000147099	1.470987694	1.470987694
BN1106_s10628000110.mRNA-1	152	CRIP	crp	7	7	19	0.00363116	0.2822	7	7	17	0.0043008	0.2822	8	18	18	0.0032122	0.2822	0.010876091	0.004034867	0.004034867	40.34867371	40.34867371
BN1106_s10748000200.mRNA-1	153	Uncharacterized protein	uk	1	1	1	0.000337314	0.1226	2	2	2	0.0009624	0.2453	2	2	2	0.0006801	0.2453	0.001981679	0.000735173	0.000735173	7.351733499	7.351733499
BN1106_s10748000067.mRNA-1	154	Unknown product	uk	3	3	4	0.00230789	0.3226	3	3	4	0.003297	0.3226	3	3	3	0.00230789	0.3226	0.00560381	0.00207893	0.00207893	20.78929921	20.78929921
BN1106_s10798000440.mRNA-1	4	Eukaryotic translation initiation facto	ps	5	5	7	0.001345627	0.3118	6	6	9	0.0027478	0.3763	4	6	6	0.0011628	0.2688	0.004981217	0.001847957	0.001847957	18.47957123	18.47957123
BN1106_s1078000175.mRNA-1	7	Fasciclin-2-like	pe	2	2	3	9.04E-05	0.0253	2	2	2	0.00011628	0.2688	2	2	2	6.08E-05	0.0253	0.000515232	0.0016407E-05	0.0016407E-05	5.61047E-05	5.61047E-05
BN1106_s10818000242.mRNA-1	155	Glutathione S-transferase	deto/ox	10	10	17	0.002597603	0.3376	10	10	15	0.0032759	0.359	11	11	17	0.0026188	0.4073	0.008492328	0.0003150527	0.0003150527	3.150526813	3.150526813
BN1106_s10818000248.mRNA-1	156	Actin depolymerizing factor-like prot	cs	3	3	4	0.00100719	0.1268	3	3	3	0.00022614	0.0597	3	3	4	0.0010154	0.1268	0.002022614	0.000750359	0.000750359	7.503594966	7.503594966
BN1106_s108908000102.mRNA-1	157	Peptidase inhibitor 16	crp	3	3	15	0.002603537	0.3107	6	6	12	0.0029769	0.1893	3	3	4	0.0010154	0.1268	0.003802628	0.000108954	0.000108954	1.08954333	1.08954333
BN1106_s10948000139.mRNA-1	158	Stress-induced-phosphoprotein 1	pe	2	2	2	0.000224171	0.1223	2	2	2	0.0003204	0.0752	3	3	3	0.000339	0.1818	0.000883576	0.000327994	0.000327994	3.27993529	3.27993529
BN1106_s10968000199.mRNA-1	160	Ankyrin repeat domain-containing pr	cs	7	7	10	0.000508609	0.1408	6	6	7	0.000508609	0.1408	7	7	7	0.0004102	0.1166	0.001427681	0.000429648	0.000429648	4.296482199	4.296482199
BN1106_s109818000052.mRNA-1	162	NSF attachment protein SNAP	pe	3	3	4	0.000563075	0.1732	2	2	2	0.0002562	0.0777	2	2	3	0.0004258	0.1012	0.000988833	0.000366842	0.000366842	3.668423046	3.668423046
BN1106_s1098000219.mRNA-1	161	Pyruvate-5-carboxylate reductase	met/ua	1	1	1	8.96E-05	0.0401	2	2	2	0.0001807	0.0777	2	2	2	0.0001807	0.0777	0.000526461	0.000195309	0.000195309	1.953092102	1.953092102
BN1106_s11068000091.mRNA-1	163	Myyosin-1	cs	5	5	5	2.45E-05	0.0095	5	5	5	3.00E-05	0.0074	5	5	5	2.47E-05	0.0071	8.42634E-05	0.000605603	0.000605603	6.05603642	6.05603642
BN1106_s11098000181.mRNA-1	164	Tubulin polymerization-promoting pr	cs	2	2	2	0.0004584	0.2179	2	2	2	0.0006552	0.2115	1	1	1	0.0002311	0.1282	0.001346652	0.000498846	0.000498846	4.988485706	4.988485706
BN1106_s11108000106.mRNA-2	165	Cubilin-like	tr	6	6	10	0.001380511	0.2394	0	4	7	0.0013812	0.1622	5	5	9	0.0012526	0.2046	0.004014313	0.00148925	0.00148925	14.892502	14.892502
BN1106_s11118000208.mRNA-1	166	Microtubule-associated protein 1S	cs	13	13	19	0.000891535	0.2126	8	8	10	0.0006707	0.0906	11	11	1	1.60E-05	0.0098	3.87857E-05	0.000143898	0.000143898	1.43898994	1.43898994
BN1106_s11198000202.mRNA-1	169	Titin	cs	19	19	32	0.000891535	0.2126	18	18	30	0.0006623	0.0906	11	11	14	0.0006623	0.2021	0.002224479	0.000825249	0.000825249	8.252487043	8.252487043
BN1106_s11398000359.mRNA-1	170	Cell division cycle and apoptosis reg	st	24	24	32	0.001304638	0.3273	18	18	30	0.0017481	0.2258	26	26	42	0.0017791	0.2258	0.00477911	0.001772978	0.001772978	17.72978408	17.72978408
BN1106_s11425800010.mRNA-1	177	60S ribosomal protein L3	ps	4	4	8	0.000681052	0.1333	4	4	6	0.0007301	0.1405	6	6	7	0.0006008	0.1643	0.00201899	0.000746385	0.000746385	7.463854778	7.463854778
BN1106_s11465800018.mRNA-1	178	Ras-related protein Rab-14	st	1	1	1	0.000164015	0.0642	1	1	1	0.0002344	0.0642	1	1	1	0.0001654	0.0642	0.000563792	0.000209158	0.000209158	2.091583345	2.091583345
BN1106_s11478000259.mRNA-1	179	Heat shock protein 70	pm	11	11	19	0.003881997	0.4457	7	7	15	0.0043803	0.3943	10	10	14	0.0042878	0.4457	0.0115581	0.004287883	0.004287883	42.87882817	42.87882817
BN1106_s1148000614.mRNA-1	171	Cubilin-like	tr	4	4	4	0.0008907	0.2491	4	4	7	0.0012733	0.2491	4	4	5	0.002805164	0.2491	0.002805164	0.001040674	0.001040674	10.40674065	10.40674065</

BN1106_s1551B000468.mRNA-1	248	Propionyl-CoA carboxylase beta chain met/carb
BN1106_s1560B000152.mRNA-1	249	RNA-binding region RNP-1 tm
BN1106_s1560B000153.mRNA-1	250	Calmodulin st
BN1106_s1575B000264.mRNA-1	251	Transcriptional coactivator tm
BN1106_s1579B000120.mRNA-1	252	Unknown product uk
BN1106_s1582B000145.mRNA-1	254	Dynein cs
BN1106_s1582B000149.mRNA-1	255	Dynein cs
BN1106_s1612B0000138.mRNA-1	259	Multi-domain cystatin sp/protinh
BN1106_s1614B0000280.mRNA-1	261	Thioredoxin peroxidase detox/ox
BN1106_s16222B0000004.mRNA-1	263	Legumin-1 sp/protase
BN1106_s1628B000104.mRNA-1	264	60s ribosomal protein L27c ps
BN1106_s1633B000182.mRNA-1	265	H+-ATPase subunit B tr
BN1106_s1639B0000395.mRNA-1	266	20S proteasome subunit alpha 3 prot
BN1106_s1639B0000396.mRNA-1	267	Prostaglandin-prostaglandin synthase met/lipid
BN1106_s1641B0001380.mRNA-1	268	DNA-binding protein A nr
BN1106_s1657B0001601.mRNA-1	269	Tetraspanin-CD63 receptor st
BN1106_s1661B0000090.mRNA-1	270	Ribosomal protein S2 ps
BN1106_s1672B0000086.mRNA-1	271	Pyruvate kinase met/carb
BN1106_s1679B0000169.mRNA-1	30	Universal surface protein pm
BN1106_s1680B000273.mRNA-1	272	Rab11 family-interacting protein st
BN1106_s1680B000275.mRNA-1	273	GPI-anchored surface glycoprotein tr
BN1106_s17035B0000006.mRNA-1	276	Transcriptionally controlled tumor prot
BN1106_s1714B0000259.mRNA-1	278	SFAF5 Scaffold attachment factor B2 tm
BN1106_s1727B0000094.mRNA-1	279	Serpins sp/protinh
BN1106_s1739B000159.mRNA-1	282	Elongation factor 2 ps
BN1106_s173B0000867.mRNA-1	280	Protein FAM79A - uk function uc
BN1106_s175B000200.mRNA-1	283	Hexokinase met/carb
BN1106_s17622B0000002.mRNA-1	288	Cubilin-like tr
BN1106_s176B0000277.mRNA-1	286	Collagen alpha-1(IV) chain extmat
BN1106_s176B000279.mRNA-1	287	Collagen alpha-1(IV) chain extmat
BN1106_s1789B0000241.mRNA-1	31	Barrier-to-autointegration factor nr
BN1106_s1793B0000159.mRNA-1	293	Chaperonin containing I-complex pm
BN1106_s1806B0000287.mRNA-1	295	Calcium-binding protein st
BN1106_s1806B0000294.mRNA-1	296	Calcium binding protein st
BN1106_s18123B0000148.mRNA-1	298	Lyxosome-associated membrane zlyv st
BN1106_s1830B0000391.mRNA-1	299	Unknown product uk
BN1106_s1840B000150.mRNA-1	301	Cathepsin B4-like sp/protase
BN1106_s1848B0000328.mRNA-1	302	Inorganic pyrophosphatase 1 met/energy
BN1106_s1855B0000993.mRNA-1	305	Adenylyl kinase ps
BN1106_s1866B0000129.mRNA-1	306	ATP synthase met/energy
BN1106_s1888B0000145.mRNA-1	309	Ribosomal protein L19 ps
BN1106_s18B000411.mRNA-1	294	Unknown product uk
BN1106_s1902B000116.mRNA-1	312	DRP1, density-regulated protein st
BN1106_s1908B000177.mRNA-1	313	RAS-like GTP-binding protein tr
BN1106_s1922B0000117.mRNA-1	34	Small nuclear ribonucleoprotein G tm
BN1106_s1922B000122.mRNA-1	315	Paranymin cs
BN1106_s1935B0000255.mRNA-1	316	60S ribosomal protein L8 ps
BN1106_s1945B0000138.mRNA-1	317	Splicing factor, arginine/serine-rich 7 tm
BN1106_s1956B0000118.mRNA-1	318	Golgi-associated plant pathogenesis-pe
BN1106_s1958B0000299.mRNA-1	319	High mobility group protein nr
BN1106_s1959B0000206.mRNA-1	325	Gluconate-6-phosphate isomerase met/carb
BN1106_s1960B0000081.mRNA-1	320	RNA-binding protein 4.1 tm
BN1106_s1966B0000132.mRNA-1	326	Calponin/Transgelin tr
BN1106_s1971B0000297.mRNA-1	37	Protein DJ-1 st
BN1106_s1974B0000196.mRNA-1	321	Tropomyosin cs
BN1106_s1985B0000403.mRNA-1	38	Ectonucleotide diphosphohydrolase/pho nr
BN1106_s1987B0000213.mRNA-1	322	Cellular nucleic acid-binding protein nr
BN1106_s1980B000337.mRNA-1	311	Tropomodulin cs
BN1106_s2001B0001442.mRNA-1	326	Cytochrome c proximal met/energy
BN1106_s2003B0000165.mRNA-1	327	Histone H2A nr
BN1106_s2003B0000172.mRNA-1	328	Cofilin cs
BN1106_s2014B0000189.mRNA-1	329	Nascent polypeptide-associated comp cs
BN1106_s2018B0000301.mRNA-1	330	Myosin-2 cs
BN1106_s2018B0000302.mRNA-1	331	chaperonin containing Tcp1 pm
BN1106_s2044B0000106.mRNA-1	333	purine nucleotide phosphorylase 5a - met/uc
BN1106_s204B0000249.mRNA-1	332	Calpain-B st
BN1106_s2053B0000154.mRNA-1	335	Mucin st
BN1106_s2057B0000129.mRNA-1	336	Spectrin extmat
BN1106_s2087B0000065.mRNA-1	337	Legumin-1 sp/protase
BN1106_s208B000185.mRNA-1	39	Ubiquitin-protein ligase BRE1 prot
BN1106_s2096B0000232.mRNA-1	339	14-3-3 family tr
BN1106_s2101B0000084.mRNA-1	342	MF0p protein hrp
BN1106_s2104B0000158.mRNA-1	343	60S ribosomal protein L18 ps
BN1106_s210B0000998.mRNA-1	340	Calmodulin st
BN1106_s2110B0000156.mRNA-1	344	V-type H+-transporting ATPase subu tr
BN1106_s2127B0000101.mRNA-1	346	DEK protein nr
BN1106_s2132B0000163.mRNA-1	347	Adducin cs
BN1106_s2169B0000110.mRNA-1	361	Calponin 2 uc
BN1106_s214B0000741.mRNA-1	349	Calcium-binding protein st
BN1106_s214B0000742.mRNA-1	350	Calcium-binding protein st
BN1106_s214B0000743.mRNA-1	351	6 kDa tegumental protein cs
BN1106_s214B0000744.mRNA-1	352	CaBP4 (calcium-binding EF-hand p) st
BN1106_s214B0000745.mRNA-1	353	Tegument antigen uc
BN1106_s214B0000747.mRNA-1	354	CaBP3 (calcium-binding EF-hand p) st
BN1106_s214B0000748.mRNA-1	355	Tegument antigen uc
BN1106_s2153B0000115.mRNA-1	357	Unknown protein type actin bindin cs
BN1106_s2169B0000110.mRNA-1	361	Splicing factor arginine/serine-rich 1 tm
BN1106_s2179B0000235.mRNA-1	362	Heat shock factor-binding protein 1-pm
BN1106_s2194B0000230.mRNA-1	364	Succinyl-CoA synthetase alpha subu met/int
BN1106_s2195B0000129.mRNA-1	365	Zinc finger RNA-binding protein nr
BN1106_s2196B0000154.mRNA-1	40	Hypothetical protein T265_12952_p uc
BN1106_s219B0000273.mRNA-1	363	1,4-alpha-glucan-branching enzyme met/carb

8	8	13	0.001023828	0.2489	4	4	7	0.0007879	0.0947	7	7	12	0.0009528	0.1916	0.002764571	0.001025615	0.001025615	102.5614732
5	5	5	0.000244899	0.0808	3	3	3	0.00021	0.0466	4	4	4	0.0001975	0.0685	0.000652435	0.000242044	0.000242044	24.20437971
2	2	2	0.000572084	0.208	*	*	*	*	*	1	1	1	0.0002884	0.208	0.00060464	0.000319219	0.000319219	31.92193689
2	2	2	0.000340526	0.1762	1	1	1	0.0002434	0.081	2	2	3	0.000515	0.1762	0.001098843	0.000407654	0.000407654	40.7654201
1	1	1	0.000295076	0.1148	*	*	*	*	*	1	1	2	0.0002955	0.1148	0.000588547	0.000218342	0.000218342	21.8343125
4	4	4	0.001504544	0.2842	4	4	6	0.0032276	0.3895	3	3	4	0.000278	0.3158	0.000238985	0.002318985	0.002318985	23.1898524
5	5	5	0.002357488	0.3407	1	1	1	0.0005616	0.1429	3	3	9	0.0035651	0.4176	0.006484211	0.002405545	0.002405545	240.5545462
27	27	36	0.000298494	0.2472	18	18	25	0.0008317	0.1562	25	25	35	0.0008317	0.2406	0.002948909	0.000297801	0.000297801	92.7020794
20	20	80	0.018336018	0.609	14	14	39	0.012776	0.4872	17	17	17	0.0210158	0.5962	0.043127823	0.015999779	0.015999779	1599.977897
15	15	14	0.003208803	0.2949	1	1	3	0.0023235	0.1859	4	4	12	0.003235	0.2949	0.003992137	0.003484343	0.003484343	348.4342712
2	2	3	0.00059925	0.1341	1	1	1	0.0002855	0.0559	2	2	2	0.0004028	0.1341	0.001287512	0.000477648	0.000477648	47.76476985
8	8	8	0.0004992	0.2112	5	5	5	0.0004459	0.0995	8	8	8	0.001448414	0.1867	0.000503033	0.00053734	0.00053734	53.73400891
1	1	1	0.000133415	0.0485	2	2	2	0.0003814	0.0896	*	*	*	0.000514787	0.000190978	0.000514787	0.000190978	19.09782409	
1	1	1	0.000177887	0.0697	*	*	*	0.000027	0.1257	1	1	1	0.0001793	0.0697	0.000537228	0.000312526	0.000312526	13.25261798
2	2	2	0.0003744	0.0838	3	3	3	0.0008207	0.1257	2	2	2	0.0003775	0.0838	0.001545539	0.000576711	0.000576711	57.67109354
1	1	1	0.000118395	0.0331	1	1	1	0.0001692	0.0331	1	1	1	0.0001194	0.0728	0.000406976	0.000159882	0.000159882	15.98818441
2	2	2	0.000240776	0.0909	3	3	3	0.0002427	0.0909	2	2	2	0.0002427	0.0909	0.000999721	0.000370881	0.000370881	37.08814433
1	1	1	0.0001625238	0.2879	1	1	1	0.0007743	0.2879	1	1	1	0.0005462	0.2879	0.002945713	0.001092816	0.001092816	109.281568
*	*	*	*	*	3	3	3	0.0002387	0.1788	1	1	1	0.0002387	0.0861	0.001254033	0.000465228	0.000465228	46.52275996
1	1	1	7.04E-05	0.0217	1	1	1	0.0001006	0.0217	1	1	1	7.10E-05	0.0217	0.000241942	8.97569E-05	8.97569E-05	8.975692309
10	10	14	0.000391685	0.1056	8	8	13	0.0005198	0.0798	10	10	12	0.00043995	0.0923	0.001249995	0.000366437	0.000366437	46.37294804
3	3	3	0.000683221	0.172	*	*	*	*	*	3	3	3	0.0006888	0.172	0.001370288	0.000509002	0.000509002	50.90018242
1	1	1	4.47E-05	0.0248	*	*	*	*	*	2	2	2	9.41E-05	0.0352	0.000140797	5.22335E-05	5.22335E-05	5.223350559
1	1	3	0.000567543	0.1111	2	2	5	0.0008112	0.1206	3	3	4	0.0008011	0.1937	0.000808663	0.000808663	80.86232804	
23	23	36	0.001660888	0.4323	23	23	33	0.002176	0.3626	27	27	38	0.0017675	0.4529	0.005604415	0.002079514	0.002079514	207.951426
2	2	4	0.000674627	0.0943	*	*	*	*	*	2	2	5	0.0008502	0.0943	0.001524805	0.00056568	0.00056568	56.56799607
7	7	8	0.000602193	0.1642	4	4	4	0.0004303	0.0737	6	6	7	0.0005312	0.1495	0.001563768	0.000580135	0.000580135	58.13476464
2	2	5	0.002198542	0.123	*	*	*	*	*	5	5	16	0.0018665	0.123	0.004650882	0.001580805	0.001580805	15.80804696
2	2	3	7.31E-05	0.0279	1	1	2	6.97E-05	0.0102	3	3	6	0.0001474	0.0389	0.000290224	0.000107669	0.000107669	10.76687835
5	5	5	5.02E-05	0.0196	5	5	5	7.17E-05	0.0171	6	6	8	8.09E-05	0.0222	0.000202828	7.52461E-05	7.52461E-05	75.24611117
1	1	2	0.000794561	0.1333	*	*	*	*	*	2	2	3	0.0012016	0.2556	0.001996146	0.00074054	0.00074054	74.05403046
8	8	8	0.00053366	0.1567	4	4	4	0.0003814	0.0821	4	4	5	0.0003363	0.0933	0.001251296	0.000464212	0.000464212	46.42123261
*	*	*	*	*	2	2	2	0.0004806	0.1467	2	2	7	0.0004806	0.14	0.001162018	0.000431091	0.000431091	43.10914293
1	1	1	0.0004584	0.1923	1	1	1	0.0006552	0.1923	2	2	2	0.0009243	0.4359	0.002037874	0.000576021	0.000576021	57.60207702
0	0	1	0.00041098	0.1379	*	*	*	*	*	1	1	1	0.0004143	0.1379	0.00025319	0.000306181	0.000306181	30.61811739
3	3	4	0.001765991	0.3704	1	1	2	0.0012618	0.1481	2	2	2	0.0008901	0.1481	0.003917576	0.001453362	0.001453362	145.3362368
8	8	21	0.003276691	0.1694	6	6	17	0.0027617	0.1694	11	11	19	0.00292453	0.1694	0.009247361	0.003447361	0.003447361	344.7361411
3	3	2	0.0005653	0.1897	2	2	2	0.000404	0.1462	4	4	5	0.0007124	0.1897	0.001681685	0.00062388	0.00062388	62.38800841
10	10	15	0.002695118	0.5829	5	5	8	0.0020544	0.3417	6	6	9	0.0016303	0.402	0.006379834	0.002366823	0.002366823	

BN1106_s2223B000190.mRNA-1	366	Threonyl-tRNA synthetase	met/lipid	1	1	1	5.50E-05	0.0246	*	*	*	*	*	1	1	1	5.55E-05	0.0246	0.000110466	4.09812E-05	4.09812E-05	4.098117251
BN1106_s2224B000273.mRNA-1	367	Calcium-translocating ATPase	tr	9	9	10	0.00033632	0.1063	11	11	11	0.0005288	0.1148	10	10	10	0.0003391	0.1016	0.001204299	0.000446777	0.000446777	44.67769747
BN1106_s2242B000188.mRNA-1	43	Proteasome-subunit beta	prot	2	2	3	0.00054490	0.1624	2	1	1	0.0002594	0.0609	2	2	3	0.0005284	0.1624	0.00051889	0.00051889	0.00051889	50.1888534
BN1106_s2277B0000114.mRNA-1	371	Uncharacterized protein	uk	2	2	2	0.000326532	0.0913	2	2	2	0.0004667	0.0913	2	2	2	0.0003292	0.0913	0.000164607	0.000164607	0.000164607	41.64065473
BN1106_s2277B000048.mRNA-1	373	Calmodulin-like protein 2 (CaM2)	st	5	5	10	0.002517974	0.5563	5	5	5	0.0028791	0.3944	5	5	8	0.0023058	0.3099	0.007427911	0.002755644	0.002755644	275.5644038
BN1106_s2277B000049.mRNA-1	374	Ratino1 dehydrogenase 12	deto/ox	1	2	1	0.00014569	0.0385	4	4	5	0.0007556	0.1668	2	3	3	0.0003794	0.0902	0.000477604	0.000477604	0.000477604	47.6040248
BN1106_s227B000509.mRNA-1	370	Protein hsi-fai	cs	6	6	8	0.000377862	0.1162	6	6	6	0.0004051	0.0713	5	5	5	0.000381	0.0898	0.00163864	0.000431776	0.000431776	43.1776256
BN1106_s2291B0000314.mRNA-1	376	Dynein	cs	3	3	3	0.001205233	0.2472	0	2	3	0.0012151	0.2472	0	2	3	0.0012151	0.2472	0.001493691	0.001536961	0.001536961	153.6961245
BN1106_s2298B0000195.mRNA-1	44	Vesicle-associated membrane protein tr		7	7	8	0.000874746	0.2966	3	3	3	0.0004688	0.1223	3	4	4	0.0004409	0.1223	0.001784537	0.000662037	0.000662037	66.20365408
BN1106_s2303B0000143.mRNA-1	378	Cathepsin L-like	s/ptotase	1	9	31	0.006192248	0.3352	5	*	*	*	*	1	9	36	0.0072498	0.3352	0.013442034	0.004986794	0.004986794	498.6794088
BN1106_s2316B0000078.mRNA-1	46	cAMP-dependent protein kinase type st		1	10	10	0.001539690	0.2967	5	5	9	0.0011003	0.1531	13	23	0.0019835	0.4139	0.004623498	0.001715249	0.001715249	17.15248869	
BN1106_s2329B0000134.mRNA-1	382	Actin related protein	cs	1	1	1	0.000319243	0.125	*	*	*	*	*	1	1	1	0.0003219	0.125	0.000641096	0.000237837	0.000237837	23.78371619
BN1106_s232B0000326.mRNA-1	384	TyrA	met/aa	8	8	14	0.001286821	0.2571	15	5	6	0.0007882	0.1851	10	10	10	0.0012973	0.3188	0.003372936	0.001251108	0.001251108	125.110848
BN1106_s2333B0000156.mRNA-1	381	Tropinin I 4	cs	9	9	17	0.002218391	0.2518	15	15	23	0.0042897	0.3504	13	13	30	0.0039468	0.2774	0.010454939	0.003878626	0.003878626	387.8626487
BN1106_s233B0000262.mRNA-1	47	NADP-dependent malic enzyme	met/energy	12	23	46	0.002709622	0.5453	13	23	22	0.0018522	0.2273	24	24	44	0.002613	0.603	0.007174822	0.00261752	0.00261752	266.1571989
BN1106_s2349B0000188.mRNA-1	48	Severin	cs	12	12	21	0.002607153	0.4167	7	7	10	0.0017744	0.2153	13	13	18	0.002253	0.4236	0.006634563	0.002461324	0.002461324	246.1323761
BN1106_s2349B0000191.mRNA-1	385	Severin	cs	10	15	0.001289251	0.25	9	9	13	0.0015597	0.1875	12	12	18	0.0015597	0.2716	0.00445995	0.001649398	0.001649398	164.9397966	
BN1106_s2351B0000181.mRNA-1	386	Spectrin beta chain	extmat	43	45	61	0.000971523	0.2686	33	34	41	0.0009333	0.1884	40	42	54	0.0008671	0.2668	0.00277189	0.00102833	0.00102833	103.232994
BN1106_s2354B0000024.mRNA-1	387	Basement membrane-specific heparan extmat		16	16	29	0.00148286	0.2824	12	22	0.0012451	0.165	19	19	30	0.0011976	0.3378	0.003590973	0.003321823	0.003321823	10.23182514	
BN1106_s2374B0000046.mRNA-1	49	PDZ and LIM domain protein	cs	1	1	1	0.0001146	0.0417	1	1	1	0.0001638	0.0353	*	*	*	*	*	0.000278394	0.00010328	0.00010328	10.32801724
BN1106_s2398B0000171.mRNA-1	390	40S ribosomal protein S21	ps	3	6	6	0.002648536	0.3704	4	4	8	0.0005073	0.4691	4	4	8	0.0035603	0.4691	0.011256079	0.0001387	0.0001387	417.5837253
BN1106_s2400B0000186.mRNA-1	391	Glutamine synthase	met/aa	7	7	9	0.000656729	0.2327	7	1	1	0.0001043	0.0388	7	7	7	0.0007357	0.2204	0.001496687	0.000555248	0.000555248	55.5248023
BN1106_s2409B000122.mRNA-1	392	Calbindin-D28	st	1	1	1	0.00012287	0.0481	1	1	1	*	*	1	1	1	0.0001239	0.0481	0.000246745	9.153876105	9.153876105	91.53870148
BN1106_s2415B0000155.mRNA-1	393	Acidic leucine-rich nuclear phosphop	pn	6	5	6	0.000734697	0.1815	7	8	16	0.0009776	0.3801	10	10	8	0.0008376	0.3801	0.0024274	0.00083373	0.00083373	83.3796037
BN1106_s2431B0000094.mRNA-1	396	DNA damage-inducible protein 1	cs	1	1	1	8.53E-05	0.031	*	*	*	*	*	1	1	1	8.60E-05	0.031	0.00017367	6.35746E-05	6.35746E-05	63.5746E-05
BN1106_s2434B0000197.mRNA-1	397	Actin-interacting protein 1	cs	3	3	3	0.000462851	0.068	5	5	9	0.0005422	0.11	4	6	6	0.00055	0.0841	0.001557058	0.000576045	0.000576045	57.66451196
BN1106_s2438B0000175.mRNA-1	398	Guanine nucleotide-binding protein s	st	3	3	3	0.000612947	0.24	2	2	2	0.000584	0.12	3	3	3	0.000618	0.24	0.001814949	0.000673319	0.000673319	67.33188342
BN1106_s2438B0000419.mRNA-1	395	CD59-like protein	imm	1	1	2	0.000428206	0.1018	1	1	4	0.001284	0.1018	1	1	3	0.00229811	0.1018	0.001814949	0.000673319	0.000673319	67.33188342
BN1106_s2440B0000349.mRNA-1	52	UTP-glucose-1-phosphate uridylyltra	met/carb	8	8	10	0.000887527	0.2333	6	6	6	0.0007609	0.1886	6	6	6	0.0007156	0.1861	0.002363662	0.000876883	0.000876883	87.68832352
BN1106_s2460B000252.mRNA-1	399	Phosphoenolpyruvate carboxylase	met/carb	62	63	163	0.009415233	0.7254	25	25	62	0.0051186	0.3231	60	61	146	0.0085023	0.7754	0.023036321	0.0085023	0.0085023	854.6131294
BN1106_s2487B0000187.mRNA-1	402	Protein NDRG1	st	4	4	6	0.000623638	0.1221	4	4	6	*	*	2	2	4	0.0004192	0.0436	0.001042795	0.00038662	0.00038662	38.68615305
BN1106_s2487B0000188.mRNA-1	403	DnaK-type molecular chaperone	pn	9	9	12	0.000645207	0.2075	8	8	11	0.0008453	0.1459	12	12	14	0.0007589	0.2451	0.002249429	0.000834505	0.000834505	83.4504738
BN1106_s2505B0000147.mRNA-1	406	Phosphoglucomate dehydrogenase	pe	10	10	19	0.001232731	0.2528	8	8	16	0.0015198	0.2063	10	10	8	0.0012731	0.2695	0.00405602	0.001504568	0.001504568	150.456795
BN1106_s2566B0000129.mRNA-1	408	Vacuolar protein sorting 26 / Von Wt ir	cs	2	2	2	0.000101722	0.0455	*	*	*	*	*	3	3	3	0.0001538	0.074	0.000255552	9.4806E-05	9.4806E-05	94.80601339
BN1106_s2574B0000116.mRNA-1	410	Acy-CoA-binding protein (ACBP)	met/energy	3	3	3	0.001324268	0.4938	2	2	2	0.0012618	0.3086	4	4	5	0.0022252	0.6049	0.004811248	0.001784901	0.001784901	178.4901263
BN1106_s2590B0000129.mRNA-1	412	PDZ and LIM domain protein Zap	cs	5	5	9	0.001393061	0.2035	7	7	10	0.0022123	0.2554	8	12	0.0018726	0.342	0.00547948	0.002032337	0.002032337	203.2236868	
BN1106_s2590B000189.mRNA-1	405	Basement membrane-specific heparan extmat		96	96	133	0.000747829	0.2063	75	75	103	0.0008278	0.1455	107	107	139	0.000788	0.2263	0.00236354	0.000876838	0.000876838	87.68379818
BN1106_s2615B0000090.mRNA-1	415	Myoferlin / Dysferlin	st	2	2	2	8.76E-05	0.0159	2	3	3	0.0001879	0.0319	2	2	3	0.0001325	0.0159	0.000408045	0.000151379	0.000151379	15.13785439
BN1106_s263B0000603.mRNA-1	416	Uncharacterized protein	uk	4	4	7	0.002121073	0.4339	4	4	6	0.0025985	0.339	4	4	7	0.0021384	0.339	0.006857987	0.002544211	0.002544211	254.4210709
BN1106_s2641B0000139.mRNA-1	417	Acetate hydratase 1	pn	8	8	11	0.000483773	0.1562	4	4	5	0.0003143	0.0812	6	6	8	0.0003547	0.1119	0.00152776	0.000427663	0.000427663	42.76627896
BN1106_s2662B0000418.mRNA-1	419	60S ribosomal protein L18a	cs	4	4	4	0.000723328	0.1768	3	2	4	0.0005162	0.1162	3	3	3	0.0003562	0.1667	0.001784703	0.000662998	0.000662998	66.20982574
BN1106_s2673B0000071.mRNA-1	420	Calretinin	st	6	6	9	0.00084278	0.2441	4	4	9	0.0013321	0.3697	12	12	17	0.0034522	0.4479	0.003631523	0.001347241	0.001347241	134.7240868
BN1106_s2684B0000099.mRNA-1	421	Calpain	s/ptotase	6	6	8	0.000363921	0.1285	6	6	6	*	*	6	6	6	0.000321	0.1183	0.000684955	0.000254108	0.000254108	25.41081347
BN1106_s269B0000233.mRNA-1	422	Phosphoglucomutase-1	met/carb	11	11	14	0.001153395	0.2845	4	4	4	0.0005591	0.1554	8	10	10	0.0010571	0.2962	0.002809966	0.001024558	0.001024558	10.2455424
BN1106_s269B0000447.mRNA-1	414	Collagen alpha-1(XV) chain	extmat	8	8	10	0.000188185	0.0537	4	4	6	0.0001614	0.0258	7	7	11	0.0002087	0.0463	0.00058262	0.000207107	0.000207107	20.71069754
BN1106_s2716B0000103.mRNA-1	424	Dehydrogenase/reductase SDR fami	st	4	4	4	0.000590996	0.1983	1	1	1	0.0001408	0.0358	2	2	2	0.0001986	0.0882	0.000930387	0.00034516	0.00034516	34.51595454
BN1106_s2740B0000079.mRNA-1	427	HSP90	pn	3	3	3	0.000541746	0.0707	3	3	*	*	*	3	3	3	0.0005462	0.1313	0.001087921	0.000403602	0.000403602	40.36024565
BN1106_s2741B0000351.mRNA-1	428	Ribosomal protein L24e Large subu	ps	2	3	3	0.000612947	0.0743	*	*	*	*	*	3	3	5	0.0010299	0.1257	0.001642877	0.000609483	0.000609483	60.94828154
BN1106_s2745B0000189.mRNA-1	429	Glyoxalase domain-containing	deto/ox	1	1	1	0.000133915	0.0375	1	1	1	0.0001914	0.0375	1	1	2	0.00027	0.0375	0.000595234	0.00022086	0.00022086	22.08660003
BN1106_s2757B0000215.mRNA-1	431	Cystatin A	s/prothrin	2	2	4	0.001857415	0.2727	2	*	*	*	*	2	2	3	0.0014044	0.2727	0.003261865	0.0012101		

BN1106_s3182B000117.mRNA-1	488	Myosin motor domain	cs	5	5	6	0.000117745	0.034	5	5	6	0.0001683	0.0318	6	6	7	0.0001385	0.0313	0.000424526	0.000157493	0.000157493	15.74929773
BN1106_s3189B000243.mRNA-1	489	Superoxide dismutase Cu-Zn	detox/ox	3	3	5	0.001117351	0.2438	4	4	7	0.0022358	0.2875	3	3	8	0.0018024	0.2438	0.000155521	0.000191261	0.000191261	19.12621273
BN1106_s318B000272.mRNA-1	480	Calcium-binding EF-hand	st	2	2	2	0.00030301	0.1271	1	1	4	*	*	1	1	1	0.0001527	0.0551	0.000455754	0.000169078	0.000169078	16.90780556
BN1106_s318B000274.mRNA-1	487	Kunitz-type proteinase inhibitor (Fh)-s/protinh	cs	4	4	11	0.005387775	0.7397	5	5	9	0.0063005	0.5342	6	6	12	0.0059256	0.7397	0.017613871	0.006543387	0.006543387	65.34483284
BN1106_s3213B000044.mRNA-1	490	Triosephosphate isomerase	met/carb	24	24	51	0.007207577	0.7391	15	15	25	0.0050498	0.4664	21	21	38	0.0054143	0.7391	0.017671618	0.006555907	0.006555907	65.5590671
BN1106_s3225B000128.mRNA-1	492	Cecropin	cs	4	4	3	0.0002268	0.0647	3	3	3	0.0002268	0.0647	2	2	3	0.0002268	0.0647	0.000262334	0.000262334	0.000262334	26.23253345
BN1106_s3226B000049.mRNA-1	493	Serpin	s/protinh	4	4	5	0.002103249	0.3583	5	5	10	0.0027328	0.3102	5	5	10	0.0019277	0.3102	0.00676753	0.002590225	0.002590225	25.92504818
BN1106_s3226B000227.mRNA-1	494	Enolase	met/carb	39	39	106	0.006903561	0.6011	21	21	60	0.0055851	0.3105	39	39	108	0.0070913	0.6066	0.019579999	0.007265888	0.007265888	72.63887577
BN1106_s322B000089.mRNA-1	491	Titin	cs	5	5	7	0.000916801	0.2821	5	5	8	0.0014975	0.1538	8	8	13	0.0017165	0.3187	0.004130899	0.001532502	0.001532502	15.32501803
BN1106_s323B000257.mRNA-1	495	Myosin motor domain	cs	28	28	38	0.001091969	0.3502	11	11	23	0.0016531	0.1927	23	24	49	0.0024843	0.3187	0.006044806	0.002243868	0.002243868	22.43868433
BN1106_s323B000258.mRNA-1	496	Myosin tail	cs	80	192	192	0.005384318	0.5576	72	72	144	0.0057717	0.4886	91	91	184	0.0052022	0.5733	0.0163582	0.006068648	0.006068648	60.6647996
BN1106_s327B000103.mRNA-1	500	Unknown product	uk	2	2	12	0.006600967	0.5385	2	2	7	0.0055703	0.4923	3	3	12	0.0066549	0.7385	0.018759387	0.006695945	0.006695945	69.59452756
BN1106_s3313B000078.mRNA-1	504	ATP-ADP antiporter	tr	1801	5	5	0.000689812	0.1801	2	2	2	0.0003286	0.0675	3	3	5	0.0005795	0.1061	0.001597996	0.000592833	0.000592833	59.28327306
BN1106_s3324B000219.mRNA-1	507	Chaperonin family - cpn60	pm	4	4	6	0.000391481	0.0931	4	4	6	0.0005595	0.0912	5	5	12	0.0007894	0.1223	0.001740374	0.000645653	0.000645653	64.56527706
BN1106_s3325B000232.mRNA-1	505	Adenosylhomocysteinase	pm	3	3	3	0.000287576	0.0965	3	3	5	0.0006885	0.1206	4	4	4	0.0003866	0.126	0.001359182	0.000504236	0.000504236	50.42363633
BN1106_s335B000427.mRNA-1	511	Endophilin-B1	cs	6	6	19	0.005434796	0.3238	6	6	8	0.0081766	0.424	7	7	21	0.006056	0.496	0.019667395	0.00729631	0.00729631	72.96310262
BN1106_s3375B000064.mRNA-1	70	Fructose-1,6-bisphosphatase 1	met/carb	4	4	4	0.0005653	0.2767	*	*	*	*	*	2	2	2	0.000285	0.0751	0.000850261	0.000315434	0.000315434	31.5434159
BN1106_s338B000296.mRNA-1	512	Ribosomal protein L26	ps	1	1	1	0.000251797	0.0986	2	2	2	0.0007198	0.162	2	2	2	0.0005077	0.162	0.001479282	0.000548791	0.000548791	54.87913724
BN1106_s3430B000064.mRNA-1	518	Succinate dehydrogenase	met/energy	3	3	3	0.000417376	0.1751	3	3	3	0.0005965	0.144	3	3	3	0.0004208	0.1751	0.000532255	0.000532255	0.000532255	5.32250614
BN1106_s344B000191.mRNA-1	519	Nucleoside diphosphate kinase - func st	cs	6	26	6	0.006116027	0.4276	8	8	20	0.0067242	0.4013	10	10	28	0.0066403	0.5263	0.019480552	0.007226994	0.007226994	72.26994199
BN1106_s3452B000178.mRNA-1	520	Methylmalonyl-CoA mutase - involv met/energy	cs	9	9	9	0.000442029	0.1745	7	7	8	0.0005616	0.143	10	11	11	0.0005447	0.1497	0.000548284	0.00057439	0.00057439	57.43902525
BN1106_s346B000282.mRNA-1	521	Ribosomal protein L11	ps	1	1	1	0.000395805	0.0773	2	2	2	0.0005647	0.1215	2	2	3	0.0005975	0.1215	0.001557242	0.000657713	0.000657713	65.77134641
BN1106_s3478B000064.mRNA-1	523	Alpha-actinin	cs	1	1	3	3-4E-05	0.0181	1	1	*	*	*	1	1	2	0.0004565	0.0949	0.001155195	0.000421114	0.000421114	42.11404003
BN1106_s3478B000346.mRNA-1	522	Programmed cell death-involved prot s/apoptosis	cs	1	1	1	6.70E-05	0.2243	1	1	*	*	*	1	1	1	3.43E-05	0.0181	6.83836E-05	2.53693E-05	2.53693E-05	2.536929727
BN1106_s3509B000140.mRNA-1	524	Microtubule-associated protein 1	cs	2	2	2	0.00012287	0.0464	3	3	3	0.0002634	0.0653	3	3	4	0.0002477	0.0808	0.000430441	0.000252512	0.000252512	25.25199226
BN1106_s3540B000083.mRNA-1	528	Ribosomal protein	cs	2	2	3	0.000494312	0.1198	2	2	3	0.0009967	0.1843	4	4	6	0.0009967	0.1889	0.002433024	0.000902362	0.000902362	90.26157375
BN1106_s3547B000116.mRNA-1	529	Sodium/potassium-transporting ATP tr	tr	5	5	5	0.000806509	0.203	*	*	*	*	*	5	5	5	0.0010841	0.2707	0.001890646	0.000701401	0.000701401	70.14014251
BN1106_s3549B000112.mRNA-1	530	Voltage-dependent anion channel prc tr	tr	1	1	1	0.000132919	0.0409	2	2	2	0.00038	0.0855	*	*	*	*	*	0.000512873	0.000190268	0.000190268	19.02682847
BN1106_s3553B000143.mRNA-1	72	Heterogeneous nuclear ribonucleoep tm	cs	10	17	17	0.001986402	0.3072	9	9	15	0.0020501	0.2745	13	13	20	0.002356	0.4183	0.00684754	0.002540335	0.002540335	25.40335254
BN1106_s3580B000148.mRNA-1	532	ATP-dependent RNA helicase DDX5 ps	cs	2	2	3	0.000140034	0.0418	2	3	4	0.0002669	0.0535	2	2	2	9.41E-05	0.0418	0.000501013	0.000183868	0.000183868	18.38681005
BN1106_s3585B000136.mRNA-1	533	Myoferlin or Dysferlin	st	3	3	3	9.76E-05	0.0391	3	2	3	0.0001395	0.0273	4	4	4	0.0001312	0.0564	0.000683805	0.000136636	0.000136636	13.66357179
BN1106_s3590B000078.mRNA-1	534	FERM domain-containing protein st	cs	1	1	1	3-4E-05	0.0181	1	1	*	*	*	1	1	1	3.43E-05	0.0181	6.83836E-05	2.53693E-05	2.53693E-05	2.536929727
BN1106_s3592B000072.mRNA-1	535	Dnal (Hsp40) homolog	pm	1	1	1	0.000219357	0.092	1	1	*	*	*	1	1	1	0.0002312	0.092	0.000460508	0.000163422	0.000163422	16.34218356
BN1106_s3595B000059.mRNA-1	536	Glutathione S-transferase class-mu 2 detox/ox	cs	6	6	6	0.00113926	0.1618	3	3	8	0.001002	0.0711	7	7	15	0.0013253	0.1667	0.003466573	0.001286047	0.001286047	12.86046942
BN1106_s3607B000071.mRNA-1	538	40S ribosomal protein SA	ps	2	2	2	0.00036672	0.1231	3	3	*	*	*	1	1	1	0.0001849	0.1128	0.000515138	0.000204628	0.000204628	20.46278006
BN1106_s3606B000435.mRNA-1	74	Calumenin-B	st	2	2	2	0.000268356	0.094	1	1	1	0.0001921	0.0414	4	4	4	0.0005421	0.1391	0.001003024	0.000872107	0.000872107	8.721070878
BN1106_s3609B000200.mRNA-1	543	Heat shock protein	pm	7	7	7	0.000743352	0.1892	6	6	8	0.0005805	0.1414	9	9	10	0.0023474	0.2037	0.002342741	0.000869122	0.000869122	86.91219536
BN1106_s3703B000103.mRNA-1	545	Acetate:succinate Co-A-transferase	met/lipid	1	1	1	0.000203155	0.1193	1	1	1	0.0002904	0.1193	1	1	1	0.0002048	0.1193	0.000698333	0.000259071	0.000259071	25.90711189
BN1106_s3715B000086.mRNA-1	546	Carbonyl reductase	detox/ox	3	3	4	0.000428206	0.1228	3	1	1	0.0005396	0.2036	5	5	5	0.0005396	0.2036	0.000415817	0.000415817	0.000415817	41.58170852
BN1106_s3725B000198.mRNA-1	76	Histone H2A	nr	0	8	0	0.001238277	0.2251	0	0	3	0.0013274	0.2251	0	2	4	0.0006242	0.0996	0.003189849	0.000183386	0.000183386	18.33862004
BN1106_s3730B000290.mRNA-1	547	Cytoskeleton-B-like	s/protasee	9	14	9	0.000145937	0.2899	9	9	9	0.0003258	0.2377	9	9	21	0.0021942	0.2899	0.006039393	0.002561255	0.002561255	25.61255065
BN1106_s3747B000111.mRNA-1	548	Calponin/transgelin	tr	44	17	14	0.000828016	0.7158	14	14	32	0.008607	0.5316	19	19	48	0.008479	0.7211	0.009361798	0.009361798	0.009361798	93.61798534
BN1106_s3747B000112.mRNA-1	549	ST1 homolog	pe	1	1	1	0.00012415	0.0382	1	1	*	*	*	1	1	1	0.0001252	0.0382	0.000249315	9.24922E-05	9.24922E-05	9.24922962
BN1106_s3754B000092.mRNA-1	77	Large subunit ribosomal protein L21	ps	3	3	3	0.00066247	0.1304	2	2	2	0.0006348	0.1304	1	1	1	0.0002239	0.0683	0.001524975	0.000565743	0.000565743	56.57429791
BN1106_s3760B000232.mRNA-1	550	Staphylococcal nuclease domain-cont met/uc	cs	2	2	2	0.000128308	0.0299	*	*	*	*	*	2	2	3	0.0001294	0.0287	0.000257665	9.59901E-05	9.59901E-05	9.599005549
BN1106_s3780B000343.mRNA-1	544	Hypothetical protein	uc	4	4	5	0.000506448	0.0963	4	5	5	0.0007239	0.1955	4	4	4	0.0004085	0.0595	0.001638769	0.000607959	0.000607959	60.79588711
BN1106_s3834B000075.mRNA-1	552	Isocitrate dehydrogenase 2 (NADP+) detox/ox	cs	3	3	3	0.000414153	0.1969	*	*	*	*	*	2	2	2	0.0002784	0.1467	0.000692512	0.000256912	0.000256912	25.69119044
BN1106_s3864B000104.mRNA-1	79	Serpin	s/protinh	4	5	5	0.000614703	0.2206	3	3	3	0.0004393	0.1318	7	10	10	0.0010329	0.2951	0.002086872	0.000774198	0.000774198	77.41984234
BN1106_s3867B000081.mRNA-1	553	T-complex protein 1 subunit zeta - cl pm	cs	5	5	5	0.000456272	0.1296	5	5	5	0.0004663	0.0803	6	6	6	0.0003947	0.1097	0.00117684	0.000488841	0.000488841	48.88412514
BN1106_s3875B000176.mRNA-1	555	Carbonic anhydrase II	detox/ox	1	1	1	0.000181243	0.0663	1	1	1	0.000181243	0.0663	1	1	1	0.000181243	0.0663	0.00018124			

BN1106_s4448000267.mRNA-1	618	Peroxiredoxin 3	detox/ox	5	5	7	0.001214984	0.4515	0	1	1	0.0002481	0.0534	4	4	4	0.0007	0.199	0.002163013	0.000802446	0.000802446	80.24455352
BN1106_s4448000268.mRNA-1	619	Citrate synthase	met/energy	5	5	6	0.000489798	0.1233	3	3	5	0.0005834	0.1073	7	7	9	0.0007407	0.2123	0.000183788	0.000672922	0.000672922	67.29215896
BN1106_s4449800065.mRNA-1	622	Aldolase A, fructose-bisphosphat	met/carb	3	4	10	0.000976919	0.1721	4	2	3	0.0010834	0.0765	3	4	11	0.0029749	0.1749	0.000919746	0.000919746	0.000919746	91.97458712
BN1106_s4460000198.mRNA-1	621	40S ribosomal protein S8	ps	6	6	6	0.000949254	0.2655	5	3	4	0.0009045	0.1858	5	8	6	0.000957	0.2124	0.002810761	0.001047275	0.001047275	104.2750407
BN1106_s44799000057.mRNA-1	623	Glutathione S-transferase	detox/ox	7	7	14	0.000997158	0.1574	3	3	3	0.000509	0.0359	7	8	11	0.0007899	0.1315	0.002296647	0.000851949	0.000851949	85.17990724
BN1106_s4482000044.mRNA-1	624	Cathepsin B2-like	s/protease	14	16	47	0.001344	0.3124	16	14	40	0.004342	0.3384	17	22	49	0.003315	0.427	0.00441881	0.00441881	0.00441881	44.18809817
BN1106_s4499000179.mRNA-1	625	Clathrin complex	ps	7	7	10	0.000231575	0.0667	5	3	3	9.93E-05	0.0311	5	5	7	0.0001634	0.0415	0.000049288	0.000183377	0.000183377	18.3377162
BN1106_s45048000167.mRNA-1	626	Aldose 1-epimerase	met/carb	2	2	2	0.000188682	0.058	2	3	3	0.0004045	0.0897	2	2	2	0.0001902	0.058	0.000290638	0.000290638	0.000290638	29.06379648
BN1106_s45118000075.mRNA-1	627	Pyromycin-sensitive aminopeptidase	s/protease	3	3	4	0.000387591	0.0786	1	1	1	0.0001385	0.0325	3	3	3	0.0002931	0.0786	0.000819153	0.000303893	0.000303893	30.38934964
BN1106_s45128000085.mRNA-1	628	ADP-ribosylation factor	st	2	2	3	0.000592628	0.1381	1	*	*	*	*	1	1	1	0.0001992	0.0994	0.000791786	0.000293741	0.000293741	29.3740774
BN1106_s452B000151.mRNA-1	629	UDP-glucose 4-epimerase	prot	2	2	2	0.00037245	0.151	1	1	1	0.0002662	0.1094	2	2	2	0.0003755	0.151	0.00104111	0.00037622	0.00037622	37.62202034
BN1106_s452B000152.mRNA-1	630	UDP-glucose 4-epimerase	prot	4	4	7	0.001331312	0.2819	3	3	5	0.0013422	0.1915	4	4	7	0.0013422	0.2819	0.000432652	0.001496054	0.001496054	149.6053771
BN1106_s4543B000079.mRNA-1	631	Elongation factor 1-beta	ps	5	5	7	0.000997158	0.2311	6	6	9	0.0014362	0.239	7	10	10	0.0014362	0.2789	0.004265723	0.001582527	0.001582527	158.25219671
BN1106_s4543B0000331.mRNA-1	632	Actin-2	cs	0	52	0	0.14834619	0.8404	0	41	133	0.0180766	0.5213	0	54	161	0.0154533	0.859	0.04834649	0.017935822	0.017935822	1793.582659
BN1106_s4618B0000095.mRNA-1	634	Septin B	s/protein	3	3	5	0.000631718	0.1661	2	2	2	0.00035612	0.0671	4	4	4	0.0005095	0.1661	0.001502382	0.000557361	0.000557361	55.7361912
BN1106_s462B0000766.mRNA-1	635	Fibronectin-1	s/protein	10	10	12	0.000327182	0.0779	12	12	13	0.0003672	0.0912	9	9	11	0.0002192	0.0663	0.000823624	0.000305552	0.000305552	30.55521585
BN1106_s4644B0000085.mRNA-1	636	Heterogeneous nuclear ribonucleopro	tm	7	7	12	0.000953473	0.1533	7	7	3	0.0003407	0.0778	7	12	20	0.0009613	0.22	0.002254328	0.000836732	0.000836732	83.67320221
BN1106_s4651B0000094.mRNA-1	638	Stefin-1	s/protein	6	6	24	0.008667936	0.4949	4	4	11	0.0056782	0.3434	6	6	16	0.0058259	0.4949	0.020172005	0.007483513	0.007483513	748.3512815
BN1106_s4661B0001079.mRNA-1	639	Glutamine synthetase	met/aa	2	2	2	0.000299207	0.0962	2	1	1	0.0002138	0.046	1	1	1	0.0001508	0.046	0.000246281	0.000246281	0.000246281	24.62810707
BN1106_s4661B0001800.mRNA-1	640	Glutamine synthetase	met/aa	1	1	1	0.000148362	0.1079	*	*	*	*	*	*	2	2	0.0002991	0.1701	0.000447512	0.00016602	0.00016602	16.60201879
BN1106_s4672B0000098.mRNA-1	641	Rho GDP-dissociation inhibitor	st	5	5	11	0.002313574	0.4118	4	4	4	0.0014843	0.2647	5	7	7	0.00185047	0.3765	0.001855047	0.000500328	0.000500328	50.0328007
BN1106_s468B0000347.mRNA-1	642	SPARC protein	st	2	3	3	0.000576697	0.2043	2	2	3	0.0008243	0.1667	4	4	5	0.000969	0.3602	0.002369973	0.000679225	0.000679225	67.92254505
BN1106_s4703B0000028.mRNA-1	644	Chaperonin GROEL	pm	17	23	0	0.001302881	0.3487	15	15	23	0.0018627	0.1997	17	17	25	0.0014282	0.3185	0.004894211	0.001704384	0.001704384	170.4384567
BN1106_s4703B0000292.mRNA-1	644	Heat shock protein p36-like	pm	14	14	23	0.002071462	0.4181	15	14	21	0.0071032	0.3	13	26	32	0.00264158	0.6483	0.00264158	0.00264158	0.00264158	264.71579027
BN1106_s4759B0000058.mRNA-1	649	Nattenin-4	met/lipid	5	5	7	0.001245207	0.2637	3	3	3	0.0005085	0.1095	3	3	5	0.0008967	0.2189	0.002650408	0.000983262	0.000983262	98.32621816
BN1106_s476B0000184.mRNA-1	650	Adducin	cs	2	2	2	0.000206802	0.0749	3	2	2	0.0002549	0.0692	3	3	3	0.0003117	0.0865	0.000812279	0.000301343	0.000301343	30.13433343
BN1106_s4802B0000087.mRNA-1	654	Mitochondrial import receptor subun	tr	6	6	9	0.000911607	0.2181	3	3	5	0.0007239	0.153	5	5	8	0.0008169	0.1473	0.002452398	0.000909803	0.000909803	90.98032012
BN1106_s483B0000264.mRNA-1	657	Receptor expression-enhancing prot	st	1	1	1	0.00029796	0.1083	2	2	3	0.0012776	0.1083	3	4	4	0.0027741	0.2583	0.0027741	0.001030278	0.001030278	103.02778
BN1106_s487B000135.mRNA-1	90	Uncharacterized protein	uc	14	14	25	0.001835484	0.2895	8	8	12	0.0012592	0.1828	20	20	27	0.0019985	0.3655	0.005093246	0.001899518	0.001899518	188.9518105
BN1106_s488B000386.mRNA-2	653	Small subunit ribosomal protein S27	ps	2	2	2	0.000662134	0.1389	0	*	*	*	*	0	0	1	0.0003338	0.1111	0.000369467	0.000369467	0.000369467	36.94668621
BN1106_s495B0000230.mRNA-1	91	Heat shock 70 kDa	pm	5	21	44	0.002310177	0.2922	4	17	39	0.0029267	0.2188	6	23	47	0.0024879	0.2937	0.00772469	0.002865745	0.002865745	286.5744905
BN1106_s4986B0000028.mRNA-1	665	Saposin-1 (FHSAP1)	met/lipid	4	4	5	*	*	1	1	1	0.000501	0.1176	1	1	4	0.0003534	0.1176	0.000854425	0.000316979	0.000316979	31.69789995
BN1106_s499B0000146.mRNA-1	663	60S ribosomal protein L13	ps	4	5	5	0.000876354	0.2304	1	6	5	0.0012525	0.2794	4	4	6	0.0010602	0.2333	0.001183116	0.001183116	0.001183116	118.3116117
BN1106_s4999B0000040.mRNA-1	92	Integrin-linked protein kinase	st	3	3	5	0.000622914	0.1498	*	*	*	*	*	2	2	3	0.0003768	0.1045	0.00099717	0.00037088	0.00037088	37.08801545
BN1106_s4999B0000041.mRNA-1	667	Protein disulfide-isomerase A3-like	pm	13	13	23	0.001699112	0.3037	11	11	16	0.0016894	0.2335	15	15	21	0.001564	0.3409	0.004952542	0.001837319	0.001837319	183.731907
BN1106_s48B000834.mRNA-1	569	Calcium-binding protein	st	6	6	17	0.008089261	0.7826	2	2	5	0.0037032	0.2899	8	8	21	0.010971	0.7826	0.02348434	0.006912002	0.006912002	69.1200207
BN1106_s48B000836.mRNA-2	570	Calcium-binding protein	st	7	20	0	0.10363836	0.5797	11	11	27	0.0119971	0.9855	9	9	28	0.014628	0.9855	0.04498975	0.016692038	0.016692038	166.920387
BN1106_s5004B0000026.mRNA-1	669	Succinyl-CoA ligase	met/energy	1	1	1	0.000154785	0.0736	*	*	*	*	*	2	2	2	0.0003121	0.0779	0.000466885	0.000173207	0.000173207	17.3207209
BN1106_s500B000161.mRNA-1	668	Annexin A6	cs	13	13	51	0.005195205	0.3447	12	12	39	0.0056782	0.3219	14	14	46	0.0057888	0.3533	0.015597588	0.0047242	0.0047242	47.24236
BN1106_s502B0000344.mRNA-1	671	CG34417 - actin binding	cs	10	11	8	0.000532216	0.1353	8	8	11	0.0007607	0.1191	8	8	8	0.0003902	0.1326	0.001683126	0.000624415	0.000624415	62.44145829
BN1106_s503B0000225.mRNA-1	672	Insect uric acid	extrim	5	5	8	0.000625912	0.1405	5	5	5	0.0007032	0.3	3	3	3	0.0002366	0.0547	0.000825448	0.000319993	0.000319993	31.99925192
BN1106_s5073B0000165.mRNA-1	93	Majin saxifrage	st	1	1	1	0.000211569	0.0769	1	1	1	0.0003024	0.0769	1	1	1	0.0002133	0.0769	0.000727588	0.000269802	0.000269802	26.98018753
BN1106_s5073B0000167.mRNA-1	675	26S proteasome regulatory complex	s/prot	1	1	1	3.67E-05	0.0175	*	*	*	*	*	1	1	1	3.70E-05	0.0154	7.37195E-05	2.73488E-05	2.73488E-05	2.734883176
BN1106_s507B000153.mRNA-1	674	40S ribosomal protein S4	ps	2	2	2	0.000270873	0.0568	2	2	2	0.0005462	0.0606	3	3	4	0.00139773	0.000518553	0.000518553	0.000518553	0.000518553	51.85530112
BN1106_s5100B0000033.mRNA-1	677	Cathepsin L-like	s/protease	7	7	7	0.002191892	0.3142	4	4	14	0.0027412	0.1916	6	6	20	0.0027623	0.3027	0.007695357	0.002854863	0.002854863	285.4862735
BN1106_s5103B0000076.mRNA-1	678	Acetyl-CoA acetyltransferase 2	met/lipid	1	1	1	4.04E-05	0.0203	4	4	4	*	*	2	2	2	8.15E-05	0.0463	0.00021865	4.521E-05	4.521E-05	4.521001727
BN1106_s510B0000501.mRNA-1	676	26S proteasome non-ATPase regulat	prot	1	1	1	8.55E-05	0.0335	*	*	*	*	*	3	3	3	0.0002587	0.1005	0.000342523	0.000127713	0.000127713	12.77128431
BN1106_s5113B0000049.mRNA-1	679	Cotomeg protein complex	pe	1	1	1	3.98E-05	0.0289	1	1	1	5.68E-05	0.0289	*	*	*	9.66174E-05	3.58436E-05	9.66174E-05	3.58436E-05	3.58436E-05	3.584361933
BN1106_s5163B0000102.mRNA-1	95	Cathepsin B-like	s/protease	6	9	26	0.004284037	0.576	5	7	18	0.004239	0.3687	8	11	26	0.0043191	0.6406	0.012841225	0.004764237	0.004764237	47.64236874
BN1106_s5172B0000099.mRNA-1	680	Unknown product	uk	4	4	17	0.001324268	0.1598	7	4	17	0.001295	0.1501	8	17	26	0					

BN1106_s586B000372.mRNA-1	736	Cofilin	cs	8	8	15	0.003972804	0.5778	8	8	13	0.0049211	0.6222	8	8	12	0.0032042	0.6667	0.012098139	0.004488229	0.004488229	448.8229147
BN1106_s586B000374.mRNA-1	737	Fasciola/Schistosoma cross-reactive uc		12	12	21	0.004844258	0.7484	10	10	17	0.0056049	0.6452	12	12	20	0.0046513	0.7484	0.0151049	0.005602056	0.005602056	560.2056343
BN1106_s588B000098.mRNA-1	738	Masin	s/protease	2	2	2	0.000133664	0.0879	*	*	*	*	*	1	1	1	0.0045-05	0.0393	0.002001043	0.0056049	0.0056049	5.604936469
BN1106_s588B000487.mRNA-1	729	Degradation arginine-rich protein for pm		4	4	8	0.001330427	0.2047	*	*	*	*	*	4	4	6	0.001006	0.2047	0.002336406	0.000866772	0.000866772	86.67715849
BN1106_s596B000423.mRNA-1	740	Universal stress protein UspA	st	3	3	5	0.000976199	0.2131	2	2	2	0.0005585	0.153	4	4	4	0.0011819	0.2131	0.002773718	0.000800882	0.000800882	80.0084281
BN1106_s590B000431.mRNA-1	745	UV excision repair protein RAD23	nr	0	2	4	0.000401204	0.0753	0	0	2	0.0002787	0.065	3	3	4	0.0004973	0.1836	0.010004513	0.000408103	0.000408103	40.81032715
BN1106_s602B000099.mRNA-1	744	Tubulin polymerization-promoting p	cs	2	2	2	0.000444164	0.1366	0	0	2	*	*	3	3	3	0.0006717	0.1863	0.00115858	0.000413967	0.000413967	41.3966299
BN1106_s6031B000032.mRNA-1	746	Alpha crystallin-containing small hea pm		37	37	77	0.007077515	0.5861	24	24	55	0.0072255	0.4113	37	37	85	0.0078767	0.5733	0.022179704	0.000823391	0.000823391	82.8339391
BN1106_s6032B000034.mRNA-1	747	Unknown product	uk	4	5	9	0.000573613	0.1533	1	1	4	0.0003644	0.025	6	6	10	0.000426	0.1996	0.001580549	0.00058366	0.00058366	58.63600384
BN1106_s605B000203.mRNA-1	748	Putative rab GDP-dissociation inhibi	cs	3	4	8	0.000635649	0.1133	2	2	4	0.0003543	0.0489	3	3	5	0.0008011	0.12	0.001890961	0.000701518	0.000701518	70.15184945
BN1106_s605B000204.mRNA-1	749	Rab GDP dissociation inhibitor alpha st		3	4	8	0.000611201	0.1239	3	3	2	0.0002184	0.0491	3	3	5	0.0007702	0.1303	0.001599884	0.000595317	0.000595317	59.35166943
BN1106_s607B000421.mRNA-1	752	Transcription elongation factor B pol tm		4	4	5	0.001489801	0.35	4	4	5	0.0021293	0.4667	4	4	5	0.001502	0.3583	0.005121109	0.001899855	0.001899855	189.9854872
BN1106_s6083B000078.mRNA-1	753	Succinyl-CoA ligase subunit beta	met/energy	1	1	2	0.000701083	0.1176	1	1	3	0.0020041	0.3137	2	2	2	0.0007068	0.2059	0.00341969	0.00126579	0.00126579	126.5789642
BN1106_s613B000050.mRNA-1	754	Ribosomal protein	ps	1	1	2	0.00061647	0.1121	1	1	2	*	*	2	2	3	0.0005473	0.2845	0.001548734	0.000953457	0.000953457	95.34575286
BN1106_s617B000056.mRNA-1	755	Leucine amino peptidase 1 fragment	s/protease	11	11	20	0.001641822	0.4056	12	12	19	0.002477	0.3571	15	15	23	0.002115	0.4872	0.006233828	0.002312657	0.002312657	231.2657008
BN1106_s617B000057.mRNA-1	756	Leucine amino peptidase 1 fragment	s/protease	4	4	5	0.001232939	0.3172	4	4	2	0.0007049	0.0828	4	4	5	0.001243	0.3172	0.003180838	0.001180044	0.001180044	118.0043588
BN1106_s6241B000014.mRNA-1	757	Peptidyl-prolyl cis-trans isomerase	pm	6	6	11	0.003608327	0.4862	4	4	6	0.0028131	0.2385	4	4	7	0.0042992	0.5872	0.01072063	0.003977194	0.003977194	39.77193748
BN1106_s6277B000067.mRNA-1	759	Large subunit ribosomal protein L6e	ps	0	2	2	0.000290693	0.0488	2	2	2	0.0006232	0.0772	2	2	3	0.0004396	0.0772	0.001353515	0.000502134	0.000502134	50.21337065
BN1106_s638B000318.mRNA-1	764	Glutathione dehydrogenase	detox/ox	4	4	5	0.000530493	0.178	*	*	*	*	*	2	2	3	0.0002139	0.1009	0.000744425	0.00027617	0.00027617	27.61706267
BN1106_s639B000754.mRNA-1	764	Isochorismatase domain containin	1 pm	1	1	2	0.000342155	0.0766	*	*	*	*	*	2	2	2	0.000345	0.0766	0.000687108	0.000254907	0.000254907	25.49068147
BN1106_s638B000399.mRNA-1	760	CD59-like protein	imm	4	4	20	0.005630746	0.315	4	4	19	0.0053929	0.315	4	4	19	0.0053929	0.315	0.01866914	0.00525972	0.00525972	52.5972288
BN1106_s645B000322.mRNA-1	765	Aldehyde dehydrogenase	detox/ox	13	13	19	0.000991751	0.2336	7	7	14	0.0010445	0.1606	12	12	18	0.0009472	0.2672	0.00298344	0.00116813	0.00116813	116.813058
BN1106_s646B000009.mRNA-1	767	Histone H3		13	13	27	0.007098466	0.5515	3	3	10	0.0016755	0.5515	3	3	9	0.0006264	0.2513	0.02318938	0.008576781	0.008576781	85.76781185
BN1106_s647B000040.mRNA-1	767	Tropomyosin	cs	18	18	32	0.004323116	0.3694	18	34	34	0.0045845	0.3588	18	34	4	0.0040328	0.409	0.016488467	0.006116975	0.006116975	61.6975059
BN1106_s656B000153.mRNA-1	771	Laminin	4	2	2	0.000151505	0.0275	*	*	*	*	*	2	2	3	0.0001146	0.0275	0.000266063	0.978505E-05	9.785055E-05	9.785055E-05	9.785055061
BN1106_s6570B000050.mRNA-1	109	Cathepsin B1-like	s/protease	6	11	34	0.003798994	0.2938	4	8	22	0.0035134	0.2125	6	14	35	0.0039427	0.2938	0.011255082	0.004157468	0.004157468	41.57467566
BN1106_s6570B000051.mRNA-1	110	Cathepsin B3-like	s/protease	33	39	172	0.010846385	0.4462	27	31	143	0.0128866	0.3404	38	47	179	0.0113801	0.485	0.035115094	0.013027176	0.013027176	130.2717592
BN1106_s6573B000067.mRNA-1	773	Peptidyl-prolyl cis-trans isomerase F1 pm		4	4	4	0.000339711	0.1235	4	1	1	0.0001214	0.0333	2	2	2	0.0001712	0.0428	0.000623251	0.000234593	0.000234593	23.4592867
BN1106_s6576B000103.mRNA-1	774	Ubiquitin	prot	1	2	3	0.002336862	0.6444	*	*	*	*	*	1	1	1	0.0008011	0.3556	0.003184739	0.001181491	0.001181491	118.1490669
BN1106_s6635B000017.mRNA-1	775	Legumin-1	s/protease	3	5	11	0.001872893	0.1905	1	3	7	0.0017035	0.119	4	6	9	0.0015449	0.1905	0.005121249	0.001899907	0.001899907	189.9990696
BN1106_s666B000200.mRNA-1	777	mannosidase, alpha, class 2B	met/imm	14	14	15	0.000497061	0.2122	14	15	7	0.0003789	0.1029	10	10	11	0.0003675	0.1427	0.0012435	0.000461301	0.000461301	46.13012583
BN1106_s6720B000015.mRNA-1	778	CD59-like protein	imm	1	1	3	0.000879227	0.0984	2	2	4	0.0016755	0.1557	2	2	3	0.0008864	0.1557	0.003441177	0.001276625	0.001276625	127.6625456
BN1106_s674B000165.mRNA-1	781	Histone H3	nr	11	10	18	0.004723211	0.5515	1	8	20	0.0075153	0.5515	1	7	16	0.0042409	0.5515	0.016488467	0.006116975	0.006116975	61.6975059
BN1106_s678B000118.mRNA-1	780	Calmodulin-4	nr	4	4	4	0.000979595	0.1575	4	4	7	0.0024502	0.1644	4	4	5	0.0012345	0.1644	0.004664284	0.00173033	0.00173033	17.30379694
BN1106_s6797B000034.mRNA-1	781	Malate dehydrogenase	met/energy	12	12	23	0.004734311	0.8404	2	2	4	0.0010783	0.1117	4	4	13	0.0041101	0.8404	0.009871699	0.003662253	0.003662253	36.62252916
BN1106_s6800B000066.mRNA-1	782	Unknown product	uk	2	4	10	0.003471382	0.2816	1	6	10	0.0049615	0.3786	*	*	*	0.00452918	0.00128487	0.003128487	0.00128487	0.00128487	12.8486774
BN1106_s6840B000044.mRNA-4	784	Polubiquitin-A	prot	1	2	3	0.001650242	0.4462	1	1	2	0.0015724	0.2462	1	1	2	0.0011092	0.2462	0.00431822	0.001607041	0.001607041	16.07041428
BN1106_s686B000273.mRNA-1	785	14-3-3 protein gamma	st	13	15	24	0.003405261	0.5516	19	10	21	0.0042587	0.4603	11	13	25	0.0035761	0.3611	0.0124058	0.004169894	0.004169894	41.69893829
BN1106_s6922B000040.mRNA-1	788	Proteasome subunit beta type	prot	2	2	3	0.000734697	0.2466	2	2	*	*	*	1	1	2	0.0004938	0.1233	0.00455755	0.00045755	0.00045755	4.57546797
BN1106_s698B000162.mRNA-1	789	Small nuclear ribonucleoprotein D1 tm		2	2	6	0.001716251	0.256	2	2	5	0.0020442	0.256	2	2	6	0.0017303	0.256	0.005490687	0.002036963	0.002036963	20.36962774
BN1106_s6995B000048.mRNA-1	790	Cathepsin L4-like	s/protease	4	4	4	0.000543806	0.1483	1	1	4	0.0008929	0.0532	1	1	3	0.0006224	0.1483	0.002349117	0.000623093	0.000623093	6.23093229
BN1106_s6995B000049.mRNA-1	791	Cathepsin L3-like	s/protease	4	4	7	0.000770113	0.1692	*	*	*	*	*	2	4	4	0.0008873	0.1415	0.00614884	0.0014884	0.0014884	14.88442455
BN1106_s68B000373.mRNA-1	741	Arginine/serine-rich splicing factor	nc	*	*	*	*	*	2	2	3	0.0002954	0.0347	3	3	4	0.0002778	0.079	0.000573221	0.000212656	0.000212656	2.126564104
BN1106_s706B000207.mRNA-1	792	Methylmalonyl-CoA epimerase	met/lipid	4	4	4	0.000565059	0.1835	4	4	6	0.0013228	0.1835	5	8	8	0.0013228	0.2477	0.003385432	0.001259498	0.001259498	12.5949808
BN1106_s7079B000034.mRNA-1	113	Leucine aminopeptidase 2	s/protease	8	8	12	0.001159629	0.3162	3	3	3	0.0004414	0.0784	5	5	9	0.0008768	0.2	0.002450817	0.000909216	0.000909216	90.92164879
BN1106_s714B000190.mRNA-1	796	Ribosomal protein L30	ps	1	1	1	0.000262906	0.1176	*	*	*	*	*	1	1	1	0.0002651	0.1176	0.000529662	0.000195866	0.000195866	1.95865898
BN1106_s718B000363.mRNA-1	115	Ankyrin-2	cs	7	8	7	0.000189963	0.0655	3	3	3	0.000515	0.0236	8	9	10	0.0002128	0.059	0.000493261	0.000182992	0.000182992	18.29924597
BN1106_s725B000470.mRNA-1	797	Eukaryotic translation initiation facto	ps	*	*	*	*	*	1	1	1	0.0002156	0.0422	1	1	1	0.0001521	0.0422	0.000367727	0.000136421	0.000136421	13.64213416
BN1106_s7273B000044.mRNA-1	799	Major vault protein	cs	27	27	41	0.001602147	0.3913	17	17	26	0.0014521	0.2098	26	26	40	0.0015758	0.3858	0.004630127	0.001717708	0.001717708	17.17709944
BN1106_s7278B0000176.mRNA-1	822	LM domain protein 3	cs	10	29	0.000587620	0.8478	11	10	11	0.00095278	0.7119	13	13	25	0.0025927	0.8136	0.025927926	0.009627926	0.009627926	96.27926126	
BN1106_s7307B000022.mRNA-1																						

BN1106_s9069B000006.mRNA-1	870	Legumain-1	s/protease	2	4	12	0.00326068	0.2248	2	4	9	0.0035654	0.2248	2	4	8	0.0022355	0.2248	0.009126958	0.003385965	0.003385965	338.5965319
BN1106_s9080B000601.mRNA-1	868	LIM domains protein 2	cs	7	7	10	0.001496035	0.3431	5	5	10	0.0021382	0.251	8	8	12	0.0018099	0.3975	0.005444189	0.002019713	0.002019713	201.9712869
BN1106_s9130B0000051.mRNA-1	872	Hydroxycyglutathione hydrolase	detox/ox	3	3	3	0.000430786	0.1647	1	1	1	0.0002052	0.0442	3	3	3	0.0004343	0.1647	0.00107033	0.000397076	0.000397076	39.70764706
BN1106_s914B000124.mRNA-1	873	40S ribosomal protein S20	ps	5	5	5	0.001528002	0.3846	*	*	*	*	*	2	2	3	0.0009243	0.2393	0.002452298	0.000909766	0.000909766	90.97658492
BN1106_s915B000136.mRNA-1	874	Tetraspanin-1	st	0	1	1	0.000120388	0.0572	0	1	1	0.0001721	0.0572	0	1	1	0.0001214	0.0572	0.000413827	0.000153524	0.000153524	15.3523526
BN1106_s916B000192.mRNA-1	875	Alpha-1,4 glucan phosphorylase	met/carb	19	21	42	0.002021157	0.3472	10	10	14	0.0009629	0.1373	21	22	39	0.0018921	0.3311	0.004876215	0.001809003	0.001809003	180.9003051
BN1106_s917B000270.mRNA-1	876	Ferritin	hrp	3	3	5	0.001027449	0.4598	2	2	4	0.0011748	0.2816	2	2	3	0.0006215	0.2816	0.002823759	0.001047573	0.001047573	104.7572549
BN1106_s9189B0000015.mRNA-1	877	Peptidyl-prolyl cis-trans isomerase	pm	1	1	3	0.002103249	0.2745	*	*	*	*	*	1	1	3	0.0021204	0.2745	0.004223693	0.001566927	0.001566927	156.6927184
BN1106_s925B000539.mRNA-1	881	Tubulin	cs	0	3	6	0.000488682	0.0547	1	4	4	0.0004656	0.0478	1	4	8	0.0006569	0.0729	0.001611223	0.00059774	0.00059774	59.77398954
BN1106_s925B000543.mRNA-1	882	Tubulin	cs	15	17	21	0.001483913	0.2885	7	9	11	0.001111	0.168	10	12	18	0.0012823	0.2273	0.003877189	0.001438379	0.001438379	143.8379443
BN1106_s925B000547.mRNA-1	883	Tubulin alpha-3	cs	1	2	4	0.001014333	0.1702	0	3	3	0.0010873	0.1348	1	2	4	0.0010226	0.1702	0.003124274	0.001159059	0.001159059	115.9058957
BN1106_s9271B0000022.mRNA-1	884	Thioredoxin-glutathione reductase	detox/ox	2	2	2	0.000541746	0.3561	*	*	*	*	*	1	1	1	0.0002731	0.2727	0.000814833	0.000302291	0.000302291	30.2291069
BN1106_s928B000210.mRNA-1	885	Unknown product	uk	*	*	*	*	*	1	1	3	0.0019164	0.15	1	2	2	0.0009012	0.15	0.002817582	0.001045281	0.001045281	104.5280884
BN1106_s937B000520.mRNA-1	890	Myosin	cs	12	27	12	0.00614899	0.6688	9	9	19	0.0061845	0.4841	14	14	26	0.0059697	0.6688	0.018303186	0.006790209	0.006790209	679.0209016
BN1106_s9429B0000021.mRNA-1	893	Large subunit ribosomal protein LPl	ps	2	6	6	0.001881855	0.1491	*	*	*	*	*	2	2	4	0.0012648	0.1491	0.003146681	0.001167372	0.001167372	116.7371636
BN1106_s945B000218.mRNA-1	894	Annexin A11	cs	10	10	20	0.001459397	0.2898	5	5	10	0.0010429	0.1633	8	8	16	0.0011771	0.202	0.003679395	0.001365001	0.001365001	136.5000771
BN1106_s945B000221.mRNA-2	895	Ubiquitin-related modifier	prot	*	*	*	*	*	0	2	3	0.0016485	0.2366	0	2	3	0.0011628	0.2366	0.002811335	0.001042963	0.001042963	104.296316
BN1106_s9461B000006.mRNA-1	128	Heat shock 70 kDa	pm	5	14	29	0.00207796	0.2465	3	9	15	0.0015362	0.1703	5	14	28	0.0020227	0.2325	0.005636855	0.002091189	0.002091189	209.1189019
BN1106_s947B000845.mRNA-1	896	RNA-binding protein	tm	2	2	3	0.000174985	0.0326	2	*	*	*	*	2	2	2	0.0001176	0.0326	0.000292595	0.000108548	0.000108548	10.85484229
BN1106_s949B000142.mRNA-1	899	Dynein light chain	cs	2	2	4	0.001288477	0.1532	2	2	4	0.0018416	0.1532	2	2	5	0.0016238	0.1532	0.00475382	0.001763596	0.001763596	176.3596134
BN1106_s949B000146.mRNA-1	900	Dynein light chain LC8	cs	7	7	10	0.003505415	0.4608	7	7	9	0.0045092	0.451	6	6	9	0.0031807	0.451	0.011195242	0.004153268	0.004153268	415.3267758
BN1106_s9797B0000034.mRNA-1	901	Cubilin-related protein	tr	3	4	4	0.000468921	0.177	*	*	*	*	*	2	2	2	0.0002364	0.0984	0.000705299	0.000261655	0.000261655	26.16552204
BN1106_s986B000164.mRNA-1	903	RNA polymerase II transcription elor tm	tm	3	3	3	0.000858126	0.224	3	3	3	0.0012265	0.144	3	3	3	0.0008651	0.224	0.002949759	0.001094316	0.001094316	109.4316406
BN1106_s986B000166.mRNA-1	904	Unknown product	uk	1	2	1	0.003250476	0.5909	1	1	2	0.0046458	0.5909	1	2	2	0.003277	0.5909	0.011173328	0.004145138	0.004145138	414.5137903
BN1106_s988B000745.mRNA-1	129	Titin	cs	44	44	49	0.000312412	0.1168	38	38	40	0.0003645	0.099	39	39	43	0.0002764	0.1041	0.000953317	0.000353667	0.000353667	35.36665331
BN1106_s988B000759.mRNA-1	902	Leukotriene-A4 hydrolase	s/protease	5	5	7	0.000477646	0.1183	4	4	5	0.0005503	0.084	6	6	8	0.0005503	0.1508	0.001515622	0.000562273	0.000562273	56.22733054
BN1106_s992B000187.mRNA-1	905	APEX nuclease	met/nuc	1	1	1	0.000111387	0.053	2	2	2	0.0007301	0.1857	1	1	1	0.0001123	0.053	0.00023685	8.29837E-05	8.29837E-05	8.298368265
BN1106_s995B000144.mRNA-1	906	protein MEMO1	st	*	*	*	*	*	2	2	2	0.0002575	0.1071	1	1	1	0.0002575	0.1071	0.000987537	0.000366362	0.000366362	36.63615196
BN1106_s9961B000006.mRNA-1	907	Puromycin-sensitive aminopeptidase	s/protease	5	5	7	0.000930434	0.2677	4	4	4	0.0007599	0.197	6	6	7	0.000938	0.2639	0.002628382	0.000975091	0.000975091	97.50905357
BN1106_s999B000190.mRNA-1	908	Unknown product	uk	4	4	7	0.001276973	0.3214	2	2	4	0.0010429	0.0918	5	5	9	0.0016552	0.3112	0.003975152	0.001474722	0.001474722	147.4722247

Anexo D

Tabelas com as anotações funcionais de proteínas e valores de NSAF feitos com a base de dados de *Bos taurus* do capítulo I

Adult ESP

Accession number	Seq number	Description	Class	DB	evaluc	Coverage	Run #1 (UniquePeptideCount)	Run #1 (PeptideCount)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePeptideCount)	Run #2 (PeptideCount)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePeptideCount)	Run #3 (PeptideCount)	Run #3 (SpecCount)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	Contig/Total	Sum total NSAF	Contig/Total	x10000
sp A217N0 SPA34_BOVIN	48	Alpha-1-antitrypsin_like	s/protin	CDD	0	100.2	3	12	19	0.0006846	0.2798	1	16	24	0.0008656	0.3528	*	*	*	*	*	0.0015502	0.032434	0.0477955	0.032434	324.3396
sp A6QPQ2 SPA38_BOVIN	54	Alpha-1-antitrypsin_like	s/protin	CDD	0	100.8	*	*	*	*	*	1	8	13	0.000461	0.11	1	1	2	9.68E-05	0.0813	0.0005578	0.0116712	0.0477955	0.0116712	116.71217
sp O46375 TTHY_BOVIN	11	Transferrin	tr	GO	8E-80	100	2	2	3	0.0003022	0.2245	2	2	3	0.0003025	0.2245	*	*	*	*	*	0.0006047	0.0126526	0.0126526	126.52593	
sp P00442 SODC_BOVIN	12	Superoxide dismutase Cu-Zn	detox/ox	GO	8E-86	100	17	17	40	0.0038968	0.5066	18	18	42	0.0040962	0.4408	5	5	8	0.0010647	0.3026	0.0009057	0.01895093	0.01895093	189.5093	
sp P00760 TRY1_BOVIN	27	Cationic trypsin	s/protease	GO	0	100	3	3	6	0.0003612	0.0488	2	2	9	0.0005423	0.0488	*	*	*	*	*	0.0009035	0.0189038	0.0189038	189.03815	
sp P01044 KNG1_BOVIN	103	Kininogen-2	s/protin	GO	0	100.3	0	4	12	0.0002861	0.0483	0	3	8	0.000191	0.0483	0	2	2	6.52E-05	0.0145	0.0005423	0.0113456	0.0113456	113.45562	
sp P0CH28 UBC_BOVIN	110	Polyubiquitin-C	prot	GO	0	100	0	8	100	0.0021461	0.0696	0	6	131	0.0028144	0.058	0	5	29	0.0008502	0.0478	0.0058108	0.1215753	0.1215753	1215.7528	
sp Q1JPB0 ILEU_BOVIN	41	Leukocyte elastase inhibitor	s/protin	GO	0	100	1	1	1	3.93E-05	0.0451	1	1	1	3.93E-05	0.0451	*	*	*	*	*	7.86E-05	0.0016445	0.0016445	16.445014	
sp Q29463 TRY2_BOVIN	28	Antionic trypsin	s/protease	GO	0	100	0	2	3	0.0001799	0.1093	0	2	3	0.0001801	0.1093	0	1	1	8.19E-05	0.0486	0.0004418	0.0092437	0.0092437	92.436573	
sp Q3Y5Z3 ADIPO_BOVIN	25	Adiponectin	met/lipd	GO	0	100	2	2	4	0.0002468	0.0833	1	1	4	0.0002471	0.0833	1	1	1	8.43E-05	0.0833	0.0005782	0.0120965	0.0120965	120.96502	
sp Q56K04 CRIP1_BOVIN	1	Cysteine-rich protein 1	crp	Q-VERTEB	5E-44	100	2	2	18	0.0034616	0.1169	2	2	23	0.004428	0.1169	*	*	*	*	*	0.0078896	0.1650699	0.1650699	1650.6988	
sp Q7SIH1 A2MG_BOVIN	137	Alpha-2-macroglobulin	imm	GO	0	100	5	5	5	4.90E-05	0.0344	4	4	5	4.91E-05	0.0344	*	*	*	*	*	9.812E-05	0.0020529	0.0020529	20.529041	
sp Q9TTE1 SPA31_BOVIN	49	Alpha-1-antitrypsin_like	s/protin	CDD	0	100.2	5	17	49	0.0017654	0.365	4	20	117	0.00422	0.2774	4	7	35	0.0017227	0.1484	0.0077082	0.1612737	0.1612737	1612.7372	
tr A5D977 A5D977_BOVIN	18	Ras-related protein Ral-B	st	GO	0	100	0	1	1	7.19E-05	0.068	0	1	1	7.20E-05	0.068	*	*	*	*	*	0.0001438	0.0030096	0.0030096	30.095973	
tr A5PJE3 A5PJE3_BOVIN	100	Fibrinogen alpha chain precursor	hrp	GO	0	100	0	1	1	2.41E-05	0.0211	0	1	1	2.41E-05	0.0211	*	*	*	*	*	4.818E-05	0.0010081	0.0010081	10.080927	
tr F1MB22 F1MB22_BOVIN	29	cellular vesicular exosome - metal ion binding - depho	st	GO	0	96	0	1	2	0.0001069	0.0253	0	1	2	0.000107	0.0253	*	*	*	*	*	0.000214	0.0044764	0.0044764	44.763685	
tr F1MLW7 F1MLW7_BOVIN	23	Ig kappa chain V-II	imm	Q-VERTEB	1E-74	66.1	0	3	3	0.0001851	0.125	0	2	2	0.0001235	0.125	*	*	*	*	*	0.000214	0.0044764	0.0044764	44.763685	
tr F1MLW7 F1MLW7_BOVIN	23	Immunoglobulin lambda-like polypeptide 1 precursor	imm	Q-VERTEB	0	100	0	5	20	0.0012656	0.1325	0	5	21	0.0013304	0.1325	0	3	5	0.0004323	0.0769	0.0030283	0.0633588	0.0633588	633.58807	
tr F1MSZ6 F1MSZ6_BOVIN	69	rombin is a serine proteinase inhibitor - probable fra	s/protin	CDD	0	100	1	3	3	9.55E-05	0.0602	0	1	1	3.19E-05	0.0602	*	*	*	*	*	0.0001274	0.0026658	0.0026658	26.658356	
tr F1MUY2 F1MUY2_BOVIN	94	Keratin	cs	MEROPS	1E-17	23.7	0	2	4	0.0001037	0.0385	0	2	3	7.79E-05	0.0368	*	*	*	*	*	0.0001816	0.0037999	0.0037999	37.999113	
tr F1N514 F1N514_BOVIN	63	CD5 antigen-like precursor	imm	GO	0	100	2	2	2	6.54E-05	0.0486	2	2	2	6.54E-05	0.0486	*	*	*	*	*	0.0001308	0.0027372	0.0027372	27.372055	
tr G3N0V0 G3N0V0_BOVIN	33	innate immune response - Fe-gamma receptor signali	imm	GO	0	100.9	18	18	43	0.0019532	0.2117	19	19	43	0.0019553	0.2454	9	9	10	0.0006205	0.1779	0.0045291	0.0947593	0.0947593	947.5931	
tr G3N0V2 G3N0V2_BOVIN	98	Keratin	cs	MEROPS	2E-21	25.7	2	2	3	7.33E-05	0.0429	2	3	3	7.34E-05	0.0578	*	*	*	*	*	0.0001467	0.0030692	0.0030692	30.691933	
tr G5E5A9 G5E5A9_BOVIN	148	Fibronectin	extmat	GO	0	100	0	1	1	5.98E-06	0.0056	0	2	2	1.20E-05	0.0121	*	*	*	*	*	1.794E-05	0.0003754	0.0003754	3.7535748	
tr G8JKW7 G8JKW7_BOVIN	50	Alpha-1-antitrypsin_like	s/protin	CDD	0	100.2	3	14	25	0.0008985	0.2306	2	18	34	0.0012234	0.2985	2	5	6	0.0002946	0.1432	0.0024165	0.0505591	0.0505591	505.59147	
tr M0QVY0 M0QVY0_BOVIN	95	Keratin	cs	MEROPS	7E-18	23.7	0	2	4	0.0001037	0.0385	0	2	3	7.79E-05	0.0368	*	*	*	*	*	0.0001816	0.0037999	0.0037999	37.999113	
tr Q17QG8 Q17QG8_BOVIN	8	Histone H2A	nr	GO	5E-75	100	0	1	2	0.0002071	0.2028	0	1	1	0.0001037	0.2028	*	*	*	*	*	0.0003108	0.0065021	0.0065021	65.02065	
tr Q3SYR8 Q3SYR8_BOVIN	13	Immunoglobulin J chain	imm	Q-VERTEB	2E-87	100	1	1	1	9.43E-05	0.0955	1	1	1	9.44E-05	0.0955	*	*	*	*	*	0.0001887	0.0039489	0.0039489	39.488983	

NEJ ESP

Accession number	Seq number	Description	Class	DB	evalue	Coverage	Run #1 (UniquePeptideCount)	Run #1 (PeptideCount)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePeptideCount)	Run #2 (PeptideCount)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePeptideCount)	Run #3 (PeptideCount)	Run #3 (SpecCount)	Run #3 (NSAF)	Run #3 (Coverage)	Run #3 (Coverage)	Sum NSAF	Contig/T total	Sum total NSAF	Contig/T total	x10000
sp A11595 K1C17_BOVIN	58	Keratin, type II cytoskeletal	cs	MEROPS	1E-43	28	0	2	4	0.000712473	0.0363	0	3	3	0.000534299	0.0363	2	5	13	0.001383555	0.1361	0.00263	0.05011	0.05249	0.05011	501.086	
sp P00760 TRY1_BOVIN	27	Cationic trypsin - metal ion s/protase	GO		0	100	3	3	4	0.001277238	0.0407	3	3	3	0.000957828	0.1341	4	4	4	0.000763162	0.0976	0.003	0.05712	0.05712	0.05712	571.173	
sp P06394 K1C10_BOVIN	86	Keratin	cs	MEROPS	6E-41	22.5	0	3	6	0.000896009	0.0532	0	5	5	0.000746596	0.0532	0	6	14	0.001249206	0.076	0.00289	0.05509	0.05509	0.05509	550.9	
sp P08728 K1C19_BOVIN	43	Keratin, type I cytoskeletal	cs	MEROPS	4E-42	23.4	0	2	4	0.00078747	0.0401	0	3	3	0.000590541	0.0401	*	*	*	*	*	*	0.00138	0.02625	0.02625	262.516	
sp P0CH28 UBC_BOVIN	110	Polyubiquitin-C	prot	GO	0	100	0	2	2	0.000227682	0.0261	0	1	2	0.000227658	0.013	0	2	4	0.000272084	0.013	0.00073	0.01386	0.01386	0.01386	138.577	
sp Q29S21 K2C7_BOVIN	70	Keratin type II cytoskeletal	cs	GO	0	100	4	5	15	0.002528438	0.0515	0	4	12	0.002022539	0.0515	2	4	35	0.003525119	0.0665	0.00808	0.15385	0.15385	0.15385	1538.52	
tr E1BGJ5 E1BGJ5_BOVIN	109	Complement component C	imm	GO	0	100	1	1	4	0.000475341	0.0303	1	1	4	0.000475292	0.0303	1	1	25	0.00177513	0.0303	0.00273	0.05193	0.05193	0.05193	519.267	
tr E1BJB1 E1BJB1_BOVIN	60	Tubulin	cs	CDD	0	100	0	3	3	0.000529551	0.1056	0	1	1	0.000176499	0.0337	*	*	*	*	*	*	0.00071	0.01345	0.01345	134.505	
tr F1MC11 F1MC11_BOVIN	73	Keratin	cs	MEROPS	2E-44	26.7	0	2	4	0.000658701	0.0335	1	4	4	0.000658633	0.0335	1	4	13	0.001279136	0.0755	0.0026	0.04946	0.04946	0.04946	494.636	
tr F1MFW9 F1MFW9_BOVIN	75	Keratin	cs	MEROPS	1E-44	28.3	2	3	14	0.002286283	0.0541	2	4	11	0.001796177	0.0541	2	3	20	0.001951536	0.0541	0.00603	0.11495	0.11495	0.11495	1149.5	
tr F1MIH7 F1MIH7_BOVIN	112	Small GTPase mediated sig	st	GO	0	100	1	1	3	0.000337608	0.0143	1	1	3	0.000337573	0.0143	1	1	10	0.000672413	0.0143	0.00135	0.02567	0.02567	0.02567	256.721	
tr F1MUY2 F1MUY2_BOVIN	94	Keratin	cs	MEROPS	1E-17	23.7	0	3	8	0.001100527	0.021	0	4	15	0.002063273	0.0543	0	3	10	0.000821969	0.0543	0.00399	0.07593	0.07593	0.07593	759.303	
tr F2Z4I6 F2Z4I6_BOVIN	6	Histone H2A	nr	GO	1E-67	100	0	2	3	0.001812695	0.3692	0	1	2	0.001208337	0.2231	*	*	*	*	*	*	0.00302	0.05755	0.05755	575.517	
tr G3N0V2 G3N0V2_BOVIN	98	Keratin	cs	MEROPS	2E-21	25.7	4	4	13	0.001685069	0.0759	6	7	15	0.001944107	0.0908	4	5	12	0.000929395	0.0528	0.00456	0.08684	0.08684	0.08684	868.423	
tr M0QVY0 M0QVY0_BOVIN	95	Keratin	cs	MEROPS	7E-18	23.7	0	3	8	0.001100527	0.021	0	4	15	0.002063273	0.0543	0	3	10	0.000821969	0.0543	0.00399	0.07593	0.07593	0.07593	759.303	
tr Q17QG8 Q17QG8_BOVIN	8	Histone H2A	nr	GO	5E-75	100	0	2	4	0.002197207	0.3357	0	1	3	0.001647733	0.2028	0	1	3	0.000984639	0.2028	0.00483	0.09201	0.09201	0.09201	920.051	

SSP NEJ

Accession number	Seq number	Description	Class	DB	evalue	Coverage	Run #1 (UniquePeptideCount)	Run #1 (Peptide Count)	Run #1 (SpecCount)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (UniquePeptideCount)	Run #2 (Peptide Count)	Run #2 (SpecCount)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (UniquePeptideCount)	Run #3 (Peptide Count)	Run #3 (SpecCount)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	Contig/total	Sum total NSAF	Contig/Total	x10000
sp P06394 K1C10_BOVIN	86	Keratin	cs	MERC	6E-41	22.5	0	12	26	0.001767369	0.1977	0	14	24	0.002331733	0.1616	0	13	27	0.00185035	0.2129	0.005949452	0.02309	0.25761	0.02309	230.944
sp P68138 ACTS_BOVIN	40	Actin-2	cs	CDD	0	99.2	3	28	95	0.00900994	0.4032	3	26	83	0.011250974	0.3687	3	30	105	0.010039769	0.4032	0.030300682	0.11762		0.11762	1176.2
sp Q29821 K2C7_BOVIN	70	Keratin type II cytoskeletal 7	cs	GO	0	100	0	6	13	0.000997464	0.0687 *	*	*	*	*	*	1	5	12	0.000928263	0.088	0.001925727	0.00748		0.00748	74.7523
sp Q3MHM5 TB4B_BOVIN	59	Tubulin	cs	CDD	0	100	0	15	30	0.002410465	0.3326	2	9	10	0.0011484	0.1843	0	17	32	0.002592183	0.4045	0.006151049	0.02388		0.02388	238.769
sp Q5XQNS K2C5_BOVIN	97	Keratin	es	MERC	1E-17	23.6	0	7	13	0.000773408	0.0749	0	8	12	0.001020376	0.0899	0	5	10	0.000599793	0.0649	0.002393576	0.00929		0.00929	92.9131
tr A4IFP2 A4IFP2_BOVIN	91	Keratin	es	MERC	6E-19	23.9	0	4	11	0.000716407	0.0528 *	*	*	*	*	*	0	3	6	0.000393962	0.0528	0.00111037	0.00431		0.00431	43.102
tr E1BJB1 E1BJB1_BOVIN	60	Tubulin	cs	CDD	0	100	0	14	27	0.002169419	0.3056 *	*	*	*	*	*	0	16	29	0.002349166	0.3258	0.004518585	0.01754		0.01754	175.401
tr F1MC11 F1MC11_BOVIN	73	Keratin	es	MERC	2E-44	26.7	4	10	13	0.000974461	0.1866	6	12	16	0.001714174	0.2432	7	11	13	0.000982428	0.2138	0.003671064	0.01425		0.01425	142.502
tr F1MFW9 F1MFW9_BOVIN	75	Keratin	es	MERC	1E-44	28.3	2	5	17	0.001263699	0.0686	1	4	9	0.000956205	0.0665	2	4	14	0.001049201	0.0686	0.003269104	0.01269		0.01269	126.899
tr F1MU2 F1MU2_BOVIN	94	Keratin	es	MERC	1E-17	23.7	0	8	16	0.001001898	0.0911 *	*	*	*	*	*	0	6	9	0.000568175	0.0841	0.001570073	0.00609		0.00609	60.9466
tr F1N169 F1N169_BOVIN	149	Filamin-A isoform X1	cs	GO	0	100	*	*	*	*	*	1	1	1	1.93E-05	0.0049	1	1	1	1.36E-05	0.0049	3.29121E-05	0.00013		0.00013	1.27757
tr F1N775 F1N775_BOVIN	143	Myosin motor domain - probabl	cs	CDD	0	100.7	1	3	7	5.54E-05	0.0139 *	*	*	*	*	*	1	2	2	3.72E-05	0.0139	9.25972E-05	0.00036		0.00036	3.59441
tr F6S1Q0 F6S1Q0_BOVIN	56	Keratin, type II cytoskeletal 80	cs	GO	0	100	1	3	7	0.000583419	0.0373	1	3	4	0.000476492	0.0373	1	2	4	0.000336108	0.0373	0.001396019	0.00542		0.00542	54.1902
tr G3MXL3 G3MXL3_BOVIN	101	Keratin	cs	MERC	2E-21	7.4	1	9	20	0.001160884	0.1071	1	7	9	0.000746647	0.0747	1	6	11	0.000643706	0.0812	0.002551237	0.0099		0.0099	99.0331
tr G3MZ71 G3MZ71_BOVIN	102	Keratin	cs	GO	0	101.7	0	3	10	0.000578564	0.0534	0	3	5	0.000413461	0.0469 *	*	*	*	*	*	0.000992025	0.00385		0.00385	38.5081
tr G3NOV2 G3NOV2_BOVIN	98	Keratin	cs	MERC	2E-21	25.7	6	10	24	0.001416049	0.1023	3	8	13	0.001096287	0.0842	6	8	16	0.00095175	0.0924	0.003464086	0.01345		0.01345	134.468
tr M0QVY0 M0QVY0_BOVIN	95	Keratin	cs	MERC	7E-18	23.7	1	8	17	0.001064517	0.0911	1	8	14	0.001252983	0.0946	2	7	11	0.000694436	0.1016	0.003011936	0.01169		0.01169	116.916
tr F1MJ28 F1MJ28_BOVIN	122	Glycogen phosphorylase	met/carb	GO	0	100	0	3	3	0.000127394	0.0344 *	*	*	*	*	*	0	2	2	8.56E-05	0.0261	0.000213018	0.00083		0.00083	8.26885
sp Q2KJ5 G3PT_BOVIN	42	Glyceraldehyde-3-phosphate de	met/energy	MERC	1E-17	10.2	2	3	6	0.000543118	0.0759	3	4	9	0.001164391	0.0759	0	3	5	0.000456298	0.0759	0.002163806	0.0084		0.0084	83.994
tr E1BBP7 E1BBP7_BOVIN	5	Histone H4	nr	GO	3E-54	100	0	13	42	0.014439614	0.5769	0	8	32	0.015724252	0.5769	0	12	42	0.014557664	0.5769	0.044721531	0.1736		0.1736	1735.99
tr F2416 F2416_BOVIN	6	Histone H2A	nr	GO	1E-67	100	0	7	20	0.005500805	0.4923	0	6	19	0.00746902	0.4615	0	6	17	0.00471391	0.4615	0.017683736	0.06864		0.06864	686.442
tr Q17Q8 Q17Q8_BOVIN	8	Histone H2A	nr	GO	5E-75	100	10	15	49	0.012251794	0.5245	4	9	30	0.010721081	0.5245	9	14	47	0.011847796	0.5245	0.034820671	0.13517		0.13517	1351.66
sp Q19120 HSP7C_BOVIN	108	Heat shock 70 kDa protein	pm	CDD	0	100	3	16	32	0.001760258	0.1954	1	10	28	0.002201395	0.1585	2	15	33	0.001830106	0.1862	0.005791759	0.02248		0.02248	224.823
sp Q76LV2 HS90A_BOVIN	116	Heat shock protein 83 kDa	pm	CDD	0	102.1	1	3	4	0.000195117	0.0368	1	2	4	0.000278875	0.0286	2	3	5	0.000245891	0.0246	0.000719883	0.00279		0.00279	27.9442
sp P0CH28 UBC_BOVIN	110	Polyubiquitin-C	prot	GO	0	100	0	5	10	0.000518192	0.0536	0	2	5	0.000370318	0.0261	0	3	6	0.000313457	0.0261	0.001201966	0.00467		0.00467	46.6575
sp P00760 TRY1_BOVIN	27	Cationic trypsin - metal ion binc s/protease	GO	GO	0	100	3	4	4	0.000581386	0.1585	3	3	5	0.001038696	0.1585	3	3	5	0.000732674	0.0732	0.002352755	0.00913		0.00913	91.3285
sp P00974 BPT1_BOVIN	2	Pancreatic trypsin inhibitor	s/proteinh	GO	9E-56	100	3	4	21	0.0075086	0.37	5	6	22	0.01124284	0.48	4	5	22	0.007930461	0.48	0.026681901	0.10357		0.10357	1035.73
tr F1MNL7 F1MNL7_BOVIN	4	Pancreatic trypsin inhibitor	s/proteinh	GO	5E-56	100	1	2	15	0.005363285	0.28	1	2	15	0.007665573	0.28	1	2	14	0.005046657	0.28	0.018075515	0.07016		0.07016	701.65
tr G3X7A8 G3X7A8_BOVIN	3	Spleen trypsin inhibitor I	s/proteinh	GO	2E-55	100	0	2	13	0.004648181	0.26	0	2	14	0.007154535	0.26	0	2	13	0.004686181	0.26	0.016488897	0.06401		0.06401	640.061
tr E1BC58 E1BC58_BOVIN	20	Ras-related protein Rab-2B	st	GO	0	100	0	1	1	0.000165533	0.0556	0	1	1	0.000236592	0.0556	0	1	1	0.000166887	0.0556	0.000569012	0.00221		0.00221	22.0877
tr F1N306 F1N306_BOVIN	53	Advanced glycosylation end pro st	GO	GO	0	100	0	1	1	8.60E-05	0.0312	0	1	1	0.000122846	0.0312 *	*	*	*	*	*	0.000208796	0.00081		0.00081	8.10497
tr F1N764 F1N764_BOVIN	71	Noelin isoform X2	st	MERC	6E-55	21	1	1	1	7.66E-05	0.0236	1	1	1	0.00010943	0.0236 *	*	*	*	*	*	0.000185994	0.00072		0.00072	7.21984
tr E1BBB8 E1BBB8_BOVIN	134	Zinc finger transcription factor 'tf	GO	GO	0	100	1	1	1	2.77E-05	0.0131	1	1	1	3.95E-05	0.0131 *	*	*	*	*	*	6.71764E-05	0.00026		0.00026	2.60763
sp Q56K04 CRIP1_BOVIN	1	Cysteine-rich protein 1	tr	REFSI	5E-44	100	3	3	8	0.00371483	0.2727	2	2	7	0.004645802	0.2727	2	2	8	0.0037452	0.2727	0.012105832	0.04699		0.04699	469.92
tr G3X757 G3X757_BOVIN	121	Endoplasmic reticulum ATPase tr	CDD	GO	0	98.9	0	5	13	0.000576697	0.0844 *	2	*	*	*	*	0	5	10	0.00044724	0.0868	0.001023937	0.00397		0.00397	39.7469
tr G3MZ6 G3MZ6_BOVIN	104	WD repeat domain 76	uk	GO	0	101.4	1	1	1	5.68E-05	0.027	1	1	1	8.11E-05	0.027 *	*	*	*	*	*	0.000137872	0.00054		0.00054	5.35185

Anexo E

Tabelas com as anotações funcionais de proteínas e valores de NSAF feitos com a base de dados de *Fasciola hepatica* do capítulo II para os PES de NEJ (*L.viatrix*)

Accession number	Hyperlink	First residue	Seq size	Description	Class	Run #1 (Unique Peptide Count)	Run #1 (Peptide Count)	Run #1 (Spec Count)	Run #1 (NSAF)	Run #1 (Coverage)	Run #2 (Unique Peptide Count)	Run #2 (Peptide Count)	Run #2 (Spec Count)	Run #2 (NSAF)	Run #2 (Coverage)	Run #3 (Unique Peptide Count)	Run #3 (Peptide Count)	Run #3 (Spec Count)	Run #3 (NSAF)	Run #3 (Coverage)	Sum NSAF	Contig/Total	Sum total NSAF	Contig/Total	x10000	x100.000
BN1106_s10139800014.mRNA-1 transcr		M	290	Cathepsin L-like	s/protease	1	6	32	0.027322	0.2172	1	5	30	0.026842	0.1621	2	11	44	0.024942	0.2448	0.079107	0.027601	2.866107	0.02665	266.5016	2665.016
BN1106_s1018000531.mRNA-1 transcr		M	376	Actin-2	cs	0	1	1	0.000659	0.0426	0	1	2	0.000874	0.0426	0	2	2	0.000874	0.0426	0.002913	0.001016	0.000981	9.814051	98.14051	
BN1106_s102788000009.mRNA-1 transcr		K	162	Saposin-like protein SAP-3	met/lipid	0	1	1	0.001528	0.0802	0	1	1	0.001602	0.0802	0	2	3	0.003044	0.1481	0.006174	0.002154	0.00208	20.801	208.01	
BN1106_s108908000012.mRNA-1 transcr		M	206	Peptidase inhibitor 16P	erp	2	2	3	0.003606	0.1796	2	2	3	0.003779	0.1796	3	3	6	0.004788	0.2381	0.012173	0.004247	0.004101	41.00887	410.0887	
BN1106_s109478000008.mRNA-1 transcr		M	167	Legumain-1	s/protease	1	1	1	0.001483	0.1138	1	1	1	0.001554	0.1138	1	1	2	0.001969	0.1138	0.005005	0.001746	0.001686	16.86193	168.6193	
BN1106_s11108000106.mRNA-2 transcr		M	259	Cubilin-like	tr	3	3	5	0.00478	0.1699	2	2	4	0.004007	0.1274	2	2	4	0.002539	0.0811	0.011326	0.003952	0.003816	38.15694	381.5694	
BN1106_s14448000095.mRNA-1 transcr		M	89	Dynein	cs	1	1	1	0.002782	0.236	1	1	2	0.005831	0.236	1	1	2	0.003694	0.236	0.012307	0.004294	0.004146	41.46161	414.6161	
BN1106_s146668000004.mRNA-1 transcr		M	93	Pro-cathepsin B2	pm/protease	*	*	*	*	*	1	1	2	0.00558	0.1935	1	2	3	0.005303	0.2796	0.010883	0.003797	0.003666	36.6399	366.639	
BN1106_s16148000280.mRNA-1 transcr		M	156	Thioredoxin peroxidase	detox/ox	*	*	*	*	*	1	1	1	0.001663	0.141	1	1	3	0.003161	0.141	0.004825	0.001683	0.001625	16.25386	162.5386	
BN1106_s16578000161.mRNA-1 transcr		M	302	Tetraspanin-CD63 receptor	st	2	2	2	0.00164	0.106	1	1	1	0.000859	0.0728	2	2	3	0.001633	0.106	0.004132	0.001442	0.001392	13.92028	139.2028	
BN1106_s176228000002.mRNA-1 transcr		A	309	Cubilin-like isoform 1	tr	1	3	10	0.008013	0.1327	1	2	8	0.006718	0.0421	2	5	26	0.013832	0.1424	0.028563	0.009966	0.009623	96.22674	962.2674	
BN1106_s18408000150.mRNA-1 transcr		M	248	Cathepsin B4-like	s/protease	0	4	15	0.014976	0.1331	0	4	12	0.012555	0.1331	0	5	13	0.008617	0.1371	0.036149	0.012613	0.012178	121.7813	1217.813	
BN1106_s19858000403.mRNA-1 transcr		M	397	onucleotide pyrophosphatase/phosphodiester	nr	1	1	1	0.000624	0.0378	*	*	*	*	*	1	1	1	0.000414	0.0378	0.001038	0.000362	0.00035	3.496174	34.96174	
BN1106_s20878000065.mRNA-1 transcr		M	409	Legumain-1	s/protease	8	8	23	0.013924	0.2421	8	8	31	0.019667	0.2372	10	10	41	0.01648	0.2714	0.050071	0.01747	0.016868	168.6814	1686.814	
BN1106_s23038000143.mRNA-1 transcr		M	179	Cathepsin L6-like	s/protease	1	4	20	0.027666	0.3128	1	4	20	0.028992	0.2626	1	5	22	0.020205	0.2737	0.076862	0.026818	0.025894	258.939	2589.39	
BN1106_s23858000108.mRNA-1 transcr		M	230	Lysosomal alpha-glucosidase	met/carb	2	2	6	0.006459	0.1	3	3	5	0.005641	0.1913	2	2	3	0.002144	0.1	0.014244	0.00497	0.004799	47.98752	479.8752	
BN1106_s2858000844.mRNA-1 transcr		M	452	Tubulin	cs	0	1	2	0.001096	0.0332	0	1	1	0.000574	0.0332	*	*	*	*	*	0.001627	0.000583	0.000562	5.624917	56.24917	
BN1106_s29078000133.mRNA-1 transcr		M	420	Actin-2	cs	0	1	1	0.00059	0.0381	0	1	2	0.001236	0.0381	0	2	2	0.000783	0.0381	0.002608	0.00091	0.000879	8.785912	87.85912	
BN1106_s29078000134.mRNA-1 transcr		M	451	Actin-2	cs	0	1	1	0.000549	0.0355	0	1	2	0.001151	0.0355	0	2	2	0.000729	0.0355	0.002429	0.000847	0.000818	8.182002	81.82002	
BN1106_s30018000132.mRNA-2 transcr		M	207	Cubilin-like	tr	0	2	2	0.002392	0.1159	0	2	2	0.002507	0.0531	3	3	6	0.004765	0.1981	0.009664	0.003372	0.003256	32.58099	325.8099	
BN1106_s30018000132.mRNA-2 transcr		M	233	Cubilin-like	tr	0	2	2	0.002125	0.103	1	2	3	0.003341	0.0472	*	*	*	*	*	0.005466	0.001907	0.001842	18.41521	184.1521	
BN1106_s30088000074.mRNA-1 transcr		M	301	Cathepsin L3-like	s/protease	6	31	112	0.092133	0.6412	6	30	111	0.095687	0.608	7	39	174	0.095031	0.6645	0.282851	0.098688	0.095289	952.8916	9528.916	
BN1106_s31738000376.mRNA-1 transcr		M	618	Alpha-glucosidase	met/carb	12	12	24	0.009616	0.2945	15	15	31	0.013016	0.322	15	30	0.00798	0.3269	0.030612	0.010681	0.010313	103.1276	1031.276		
BN1106_s3188000274.mRNA-1 transcr		M	73	Kunitz-type proteinase inhibitor (Fh-KTM)	s/protein	3	3	9	0.030527	0.6438	2	2	5	0.017772	0.3425	4	5	17	0.038283	0.6438	0.086583	0.030209	0.029169	291.6862	2916.862	
BN1106_s32278000227.mRNA-1 transcr		M	549	Enolase	met/carb	4	4	4	0.000772	0.0273	3	3	1	0.000473	0.0273	3	3	3	0.000898	0.1148	0.001371	0.000478	0.000462	4.618582	46.18582	
BN1106_s3738000290.mRNA-1 transcr		M	345	Cathepsin B-like	s/protease	1	1	12	0.008612	0.058	3	3	15	0.011282	0.058	3	3	9	0.004289	0.0986	0.024183	0.000847	0.008147	81.4679	814.679	
BN1106_s40268000080.mRNA-1 transcr		M	104	Thioredoxin	detox/ox	2	2	9	0.021428	0.2692	2	2	7	0.017465	0.2692	4	4	13	0.020549	0.4135	0.059441	0.020739	0.020205	200.2509	2002.509	
BN1106_s41878000060.mRNA-1 transcr		M	383	Cathepsin L-like	s/protease	1	6	26	0.016809	0.1749	1	6	24	0.01626	0.1749	*	*	*	*	*	0.033068	0.011538	0.01114	11.4036	114.036	
BN1106_s41878000061.mRNA-1 transcr		M	239	Cathepsin L3-like	s/protease	3	28	101	0.014638	0.569	3	25	95	0.013139	0.5858	2	33	157	0.010799	0.6067	0.315767	0.110173	0.106378	1063.78	10637.8	
BN1106_s44828000044.mRNA-1 transcr		M	461	Cathepsin B2-like	s/protease	13	15	73	0.039209	0.3145	12	14	73	0.041088	0.3124	11	13	82	0.029241	0.308	0.109539	0.038219	0.036902	369.0223	3690.223	
BN1106_s4558000331.mRNA-1 transcr		M	376	Actin-2	cs	0	1	1	0.000659	0.0426	0	1	2	0.00138	0.0426	0	2	2	0.000874	0.0426	0.002913	0.001016	0.000981	9.814051	98.14051	
BN1106_s46518000094.mRNA-1 transcr		M	99	Stefin-1	s/protein	1	1	6	0.015007	0.1515	1	1	3	0.007863	0.1515	2	2	2	0.003321	0.2525	0.026191	0.009138	0.008823	88.2326	882.326	
BN1106_s48008034.mRNA-1 transcr		M	69	Calcium-binding protein	st	2	2	5	0.017943	0.3623	2	2	4	0.015042	0.3623	2	2	6	0.014295	0.3623	0.04728	0.016496	0.015928	159.2796	1592.796	
BN1106_s5100800033.mRNA-1 transcr		M	261	Cathepsin B-like	s/protease	5	7	16	0.015179	0.2299	4	6	18	0.017895	0.2146	8	10	19	0.011967	0.3755	0.045041	0.015715	0.015174	151.7383	1517.383	
BN1106_s51638000012.mRNA-1 transcr		M	217	Cathepsin B-like	s/protease	7	9	69	0.078732	0.5806	10	12	74	0.088485	0.5806	8	12	91	0.068939	0.7143	0.236156	0.082396	0.079558	795.5814	7955.814	
BN1106_s51728000090.mRNA-1 transcr		M	513	Unknown product	uk	3	5	16	0.007723	0.1306	3	4	11	0.005564	0.076	3	6	25	0.008011	0.1092	0.021298	0.007431	0.007175	71.74976	717.4976	
BN1106_s56028000083.mRNA-1 transcr		M	249	Cathepsin L4-like	s/protease	3	4	11	0.010939	0.2129	1	4	9	0.009379	0.2129	1	4	11	0.007262	0.2129	0.027579	0.009623	0.009291	92.9189	929.189	
BN1106_s56898000026.mRNA-1 transcr		M	205	Natterin-4	met/lipid	5	5	7	0.008455	0.439	4	4	7	0.00886	0.3854	4	4	7	0.005613	0.2927	0.022928	0.008	0.007724	77.24319	772.4319	
BN1106_s65708000050.mRNA-1 transcr		M	320	Cathepsin B1-like	s/protease	6	6	18	0.013928	0.2969	5	5	19	0.015406	0.2969	6	7	23	0.011816	0.3156	0.04115	0.014357	0.013863	138.6295	1386.295	
BN1106_s65708000051.mRNA-1 transcr		M	567	Cathepsin B3-like	s/protease	26	26	113	0.049347	0.4356	26	26	106	0.048509	0.4004	32	33	241	0.069874	0.4374	0.16773	0.058522	0.056506	565.0614	5650.614	
BN1106_s65768000103.mRNA-1 transcr		M	45	Ubiquitin	prot	1	1	1	0.005502	0.3556	*	*	*	*	*	1	1	2	0.007306	0.3556	0.012809	0.004469	0.004315	43.15114	431.5114	
BN1106_s66358000017.mRNA-1 transcr		M	210	Legumain-1	s/protease	1	2	5	0.005895	0.1143	1	2	4	0.004942	0.1143	3	5	15	0.011742	0.1905	0.02258	0.007878	0.007607	76.06986	760.6986	
BN1106_s6668000200.mRNA-1 transcr		M	1079	Mannosidase, alpha, class 2B	met/carb	5	5	7	0.001606	0.1046	5	5	8													

Anexo F

Tabelas com as anotações funcionais de proteínas e valores de NSAF feitos com a base de dados de *Bos taurus* do capítulo II para os PES de NEJ (*L.viatrix*)

Annotation

Seq name	Seq size	First residue	Seq size	Description	class	database	E-value	coverage	Best match to BLASTN/NCBI Database	E-value	Match	Score	Extend of match	Length of best match	% identity	% similarity	% Coverage	Mismatch rate	Gaps	First residue of match	First residue of sequence	Number of regions	Best match to BLASTN/ ENPHIGT database	E-value	Match	Score	Extend of match	Length of best match	% identity	% similarity	% Coverage	Mismatch rate	Gaps	First residue of match	First residue of sequence	Number of regions	Species of best match	Best match to BLASTN/ SWISSP protein database	E-value	Match	Score	Extend of match	Length of best match	% identity	% similarity	% Coverage	Mismatch rate	Gaps	First residue of match	First residue of sequence	Number of regions	Species of best match	
spTROMETER1_BOVIN	7	M	266	Cytosine tRNA	poly(A)	BLASTN/NCBI	0	100	cytosine tRNA-procavia	1E-141	100	246	246	100	100	100	0	0.00E+00	1	1	1	spP07502	1.0E-144	100	246	246	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07502	506	246	246	100	100	100	0	0	0	1	1	1	1	Blattella germanica	
spTROMETER12_BOVIN	16	M	326	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.27E-097	100	426	426	100	100	100	0	0	1	1	1	spP07504	1.0E-144	100	426	426	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07504	1048	426	426	100	100	100	0	0	0	1	1	1	1	Blattella germanica	
spTROMETER13_BOVIN	25	M	600	polyubiquitin C	prot	BLASTN/NCBI	0	100	polyubiquitin C	6.85E-075	137	600	600	100	100	100	0	0	1	1	1	1	spP07512	0.00E+00	100	600	600	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07512	1137	600	600	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER14_BOVIN	8	M	377	Acute-phase reactant protein 1	ca	BLASTN/NCBI	0	100	acute-phase reactant protein 1	6.85E-066	767	377	377	100	100	100	0	0	1	1	1	1	spP07518	0.00E+00	100	377	377	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07518	767	377	377	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER15_BOVIN	13	M	466	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.81E-018	100	466	466	100	100	100	0	0	1	1	1	1	spP07521	0.00E+00	100	466	466	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07521	899	466	466	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER16_BOVIN	20	M	601	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.80E-011	1164	601	601	100	100	100	0	0	1	1	1	1	spP07523	0.00E+00	100	601	601	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07523	1164	601	601	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER17_BOVIN	15	G	481	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	84	Kanata type II cytochrome P450	6.82E-044	100	406	406	100	100	100	0	0	1	1	1	1	spP07524	0.00E+00	100	406	406	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07524	753	406	406	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER18_BOVIN	18	M	371	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.81E-021	1125	371	371	100	100	100	0	0	1	1	1	1	spP07525	0.00E+00	100	371	371	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07525	968	371	371	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER19_BOVIN	5	M	130	Hemolysin A	nr	BLASTN/ENPHIGT	8.00E-69	100	Hemolysin A type 2A-like	6.80E-69	254	130	130	100	100	100	0	0.00E+00	1	1	1	1	spP07528	0.00E+00	100	130	130	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07528	254	130	130	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER20_BOVIN	21	M	406	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.81E-011	1164	406	406	100	100	100	0	0	1	1	1	1	spP07529	0.00E+00	100	406	406	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07529	968	406	406	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER21_BOVIN	19	M	571	Kanata type II cytochrome P450	nc	BLASTN/NCBI	0	100	Kanata type II cytochrome P450	6.81E-011	1121	571	571	100	100	100	0	0	1	1	1	1	spP07530	0.00E+00	100	571	571	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07530	970	571	571	100	100	100	0	0	0	1	1	1	1	Blattella germanica
spTROMETER22_BOVIN	6	M	142	Hemolysin A	nr	BLASTN/ENPHIGT	3.00E-76	100	Hemolysin A-like	6.80E-76	277	142	142	100	100	100	0	0.00E+00	1	1	1	1	spP07531	3.00E-76	100	142	142	100	100	100	0	0	0	1	1	1	1	Blattella germanica	spP07531	278	142	142	100	100	100	0	0	0	1	1	1	1	Blattella germanica

PES NEJ

Accession number	Annotation	Class	Run #1 (UniqueP eptideCo unt)	Run #1 (PeptideC ount)	Run #1 (SpecCou nt)	Run #1 (NSAF)	Run #1 (Coverag e)	Run #2 (UniqueP eptideCo unt)	Run #2 (PeptideC ount)	Run #2 (SpecCou nt)	Run #2 (NSAF)	Run #2 (Coverag e)	Run #3 (UniqueP eptideCo unt)	Run #3 (PeptideC ount)	Run #3 (SpecCou nt)	Run #3 (NSAF)	Run #3 (Coverag e)	Sum NSAF	Contig/T otal	Sum total NSAF	NSAF/To tal	x100000	x100,000
sp P00760 TRY1_BOVIN	Cationic trypsin	pm/protease	2	2	3	0.00302	0.0732	1	1	1	0.001055	0.0976	4	4	5	0.003341	0.0732	0.007416	0.072532	0.102241	0.072532	725.3154	7253.154
sp P06394 K1C10_BOVIN	Keratin, type I cytoskeletal 10	uc	0	3	4	0.001883	0.0418	0	3	4	0.001973	0.0513	0	7	10	0.003125	0.0932	0.006981	0.068285		0.068285	682.8453	6828.453
sp P0CH28 UBC_BOVIN	Polyubiquitin-C	prot	0	2	3	0.001077	0.0362 *	*	*	*	*	*	0	2	3	0.000715	0.0362	0.001791	0.01752		0.01752	175.2042	1752.042
sp P68138 ACTS_BOVIN	Actin, alpha skeletal muscle	cs	0	1	1	0.000657	0.0424	0	1	2	0.001377	0.0424	0	2	2	0.000872	0.0424	0.002905	0.028417		0.028417	284.1736	2841.736
sp Q29S21 K2C7_BOVIN	Keratin, type II cytoskeletal 7	uc	1	3	9	0.004782	0.0644	1	2	10	0.005568	0.0494	1	2	8	0.002822	0.0494	0.013172	0.128837		0.128837	1288.372	12883.72
sp Q5XQN5 K2C5_BOVIN	Keratin, type II cytoskeletal 5	uc	0	4	9	0.003708	0.0682	0	3	7	0.003022	0.0566	0	3	7	0.001915	0.0566	0.008645	0.084553		0.084553	845.5344	8455.344
tr F1MFW9 F1MFW9_BOVIN	keratin type I cytoskeletal 24	uc	1	1	5	0.002574	0.0395	2	2	4	0.002158	0.0395	2	4	6	0.002051	0.0541	0.006782	0.066337		0.066337	663.3656	6633.656
tr F1MUY2 F1MUY2_BOVIN	in, type II cytoskeletal 59 kDa, compon	uc	0	4	7	0.003035	0.0718	0	3	5	0.002272	0.0595 *	*	*	*	*	0.005308	0.051912		0.051912	519.1242	5191.242	
tr F2Z416 F2Z416_BOVIN	Histone H2A	nr	0	2	2	0.003809	0.3692	0	2	4	0.007984	0.3692	0	1	1	0.001265	0.2231	0.013058	0.127715		0.127715	1277.154	12771.54
tr G3N0V2 G3N0V2_BOVIN	keratin type II cytoskeletal 1	uc	2	3	5	0.002043	0.0231	3	3	7	0.002997	0.038	5	5	14	0.003798	0.0776	0.008838	0.086443		0.086443	864.4335	8644.335
tr M0QVY0 M0QVY0_BOVIN	keratin type II cytoskeletal 6A	uc	0	4	7	0.003035	0.0718	0	3	5	0.002272	0.0595	2	4	5	0.00144	0.0771	0.006747	0.065992		0.065992	659.9206	6599.206
tr Q17QG8 Q17QG8_BOVIN	Histone H2A	nr	0	2	4	0.006926	0.3357	0	2	5	0.009073	0.3357	0	1	4	0.004598	0.2028	0.020597	0.201456		0.201456	2014.557	20145.57