Foram analisados dados de 73.399 adolescentes de 12-17 anos que participaram do ERICA, um estudo transversal, nacional e de base escolar. Considerou-se PAE a PA sistólica ou diastólica maior ou igual ao p95 das duas referências ou > 130/80mmHg, quando adequado. Para avaliação do risco cardiometabólico, 6.185 adolescentes reclassificados de forma ascendente pela referência brasileira para PAE e com dados laboratoriais disponíveis foram pareados 1:1 com adolescentes da mesma idade, sexo e percentil de altura, mas normotensos pelas duas referências. Os parâmetros avaliados foram: sobrepeso/obesidade, circunferência da cintura, colesterol total, triglicerídeos, LDL-c, HDL-c, glicemia em jejum, HbA1c e HOMA-ir. Prevalências e intervalos de confiança (IC) de 95% foram calculados. A classificação de acordo com os percentis de PA brasileiros resultou em maior prevalência de PAE (14,0%, IC95% 13,2-14,8), quando comparado com os percentis da AAP (10,6%, IC95% 10,0-11,2). Para os seguintes subgrupos, utilizar a referência brasileira resultou em maiores prevalências de PAE: sexo feminino (13,7%, IC95% 12,5-15,0 vs. 7,4%, IC95% 6,7-8,2), idade entre 12-14 anos (15,0%, IC95% 14,0-16,1 vs. 9,0%, IC95% 8,3-9,6), peso normal (9,7%, IC95% 8,8-10,6 vs. 7,2%, IC95% 6,6-7,9), sobrepeso (26,5%, IC95% 25,0-28,1 vs. 20,5%, IC95% 19,3-21,7) e obesidade (38,2%, IC95% 35,1-41,4 vs. 30,2%, IC95% 27,6-33,0). A análise de casos e controles mostrou que adolescentes reclassificados quanto à PA pelos percentis brasileiros apresentam maior prevalência de todos os fatores de risco cardiometabólicos avaliados, exceto glicemia e HbA1c, se comparados com aqueles normotensos. Portanto, utilizar a curva de PA proposta pelo ERICA é um método sensível para o rastreamento de adolescentes brasileiros com PAE e maior risco cardiometabólico, além de apresentar maior validade externa em nossa população.

1364

DAMAGE-ASSOCIATED MOLECULAR PATTERNS (DAMPS) RELATED TO IMMUNOGENIC CELL DEATH ARE DIFFERENTIALLY TRIGGERED BY CLINICALLY RELEVANT CHEMOTHERAPEUTICS IN LUNG ADENOCARCINOMA CELLS

CATEGORIA DO TRABALHO: PESQUISA

Jose Ignacio Gonzalez Solari, Esteban Alberto Gonzalez, Emily Pilar, Vitória Brum da Silva Nunes, fabricio figueiro, Eduardo Cremonese Filippi-chiela, cristiano feijo andrade, Fabio Klamt
UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

Introduction: Chemotherapeutics can stimulate immune antitumor response by inducing immunogenic cell death (ICD), which is activated by Damage-Associated Molecular Patterns (DAMPs) like the exposure of calreticulin (CRT) on the cell surface, the release of ATP and the secretion of High Mobility Group Box 1 (HMGB1). Methods: Here, we investigated the levels of ICD-associated DAMPs induced by chemotherapeutics commonly used in the clinical practice of non-small cell lung cancer (NSCLC) and the association of these DAMPs with apoptosis and autophagy. A549 human lung adenocarcinoma cells were treated with clinically relevant doses of cisplatin, carboplatin, etoposide, paclitaxel and gemcitabine. We assessed ICD-associated DAMPs, cell viability, apoptosis and autophagy in an integrated way. Results: Cisplatin and its combination with etoposide induced the highest levels of apoptosis, while etoposide was the less pro-apoptotic treatment. Cisplatin also induced the highest levels of ICD-associated DAMPs, which was not incremented by co-treatments. Etoposide induced the lower levels of ICD and the highest levels of autophagy, suggesting that the cytoprotective role of autophagy is dominant in relation to its pro-ICD role. High levels of CRT were associated with better prognosis in TCGA databank. In an integrative analysis we found a strong positive correlation between DAMPs and apoptosis, and a negative correlation between cell number and ICD-associated DAMPs as well as between autophagy and apoptosis markers. We also purpose a mathematical integration of ICD-associated DAMPs in an index (IndImunnog) that may represent with greater biological relevance this process. Cisplatin-treated cells showed the highest IndImmunog, while etoposide was the less immunogenic and the more pro-autophagic treatment. Conclusions: Cisplatin alone induced the highest levels of ICD-associated DAMPs, so that its combination with immunotherapy may be a promising therapeutic strategy in NSCLC.