

**GLUTATHIONE S-TRANSFERASES AND CYTOCHROME P450 ENZYMES POLYMORPHISMS AS SUSCEPTIBILITY FACTORS TO SYSTEMIC LUPUS ERYTHEMATOSUS IN SOUTHERN BRAZILIAN PATIENTS**

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Background: There is evidence that different factors may contribute to the occurrence of Systemic Lupus Erythematosus (SLE), including genetic ones. Cytochrome P450 (CYP) and Glutathione S-transferases (GST) enzymes are related to the production of elements that facilitate the excretion of toxic products and xenobiotics. Polymorphisms in the CYP and GST genes can alter the expression and catalytic activity of enzymes, being responsible for differences regarding the capacity of transforming xenobiotics and may be useful as markers of susceptibility of SLE. Objectives: Evaluate the influence of three GST and two CYP polymorphisms in SLE predisposition. Methods: This study included 370 SLE patients and 329 control patients who were followed at Hospital de Clínicas de Porto Alegre. The CYP polymorphisms were genotyped by PCR-RFLP and the GST ones by multiplex PCR and PCR-RFLP. Results: Analyses were performed subdividing the individuals according to their ethnic origin. European-derived individuals had a lower frequency of GSTP1\*Val heterozygosis in SLE patients compared to controls (36% vs. 48%,  $p=0.0047$ ; OR 0.63 CI 95% 0.43 - 0.93 in relation to GSTP1\*Ile/Ile and OR 0.49 95% CI 0.26 - 0.92 in relation to GSTP1\*Val/Val). In African-derived group, the CYP2E1\*5B allele was significantly more frequent in patients than in matched controls (11% vs. 5%,  $p=0.038$ , OR 2.69 95% CI 1.00 - 8.42). No association of the CYP and GST polymorphisms with the SLE clinical manifestations was observed. Conclusions: Our data suggest a protective role of the GSTP1\*105Ile/Val heterozygosis in Europeanderived and a possible influence of the CYP2E1\*5B allele in SLE susceptibility among African-derived. Our findings may indicate new mechanisms of interaction of factors and triggering of SLE.