Session P24 - GWAS

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P24.015.B / B - Genetic variability of 6p22.1 in sepsis susceptibility: a fine mapping association study of the HLA

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Authors

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Disclosures

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Abstract

Introduction: Sepsis is a severe inflammatory response to infections with a high death rate. We previously conducted the first GWAS of copy number variations in 839 sepsis cases from the Gen-Sep Network and 1,453 controls, highlighting 6p22.1 as one of the significant loci linked to sepsis susceptibility. Due its importance in inflammatory and immunological diseases, here we performed a fine mapping of the Human Leukocyte Antigen (HLA) region contained in that locus. **Methods:** We used SHAPEIT v2.837 for phasing the haplotypes and Impute2 to impute the classic HLA alleles, amino acids, and single nucleotide polymorphisms (SNPs). Association analyses were performed by logistic regressions using EPACTs v3.2.6. A Bonferroni correction was applied to identify significant classic HLA alleles (p<2.58E-4) and amino acids (p<4.91E-5). For SNPs, a significance threshold was established at p<1.50E-5 based on the number of independent variants. **Results and conclusions:** We analyzed a total of 194 classic HLA alleles, 1,019 amino acids and 10,919 SNPs. None of the classic HLA alleles (p_{lowest}=0.01), amino acids (p_{lowest}=0.01), or SNPs (p_{lowest}=9.84E-4) were significantly associated with sepsis. Given the complexity of this phenotype, these results suggest that the HLA genetic variation is not a major driver of sepsis susceptibility or has a modest effect size. **Funding**: *Instituto de Salud Carlos III (CD19/00231, FI17/00177, PI17/00610, PI20/00876), Ministerio de Ciencia e Innovación (RTC-2017-6471-1; AEI/FEDER, UE), and agreement OA17/008 with*

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