GWAS on Romanian Population: Lung Cancer Susceptibility Loci on Chromosome 1

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Introduction: According to data provided by the Romanian National Institute for Public Health, the incidence of lung neoplasm in 2018 was the highest in both sexes, among all malignancies. In the past years, Genome-Wide Association Studies (GWASs) opened new perspectives over the traditional methods of analyzing genetic modifications connected to various pathologies. On these accounts, we are aiming to discover novel susceptibility loci for lung cancer in Romanian population, by conducting a GWAS.

Methods: A case-control study was performed in a previously unscreened Romanian population, counting 1386 lung cancer patients and 1437 controls. Data was collected from four hospitals in Bucharest between 2014 and 2018, during the ROMCAN project. The study was funded by the EEA grant "Integrated Applied Genetics Training- AppGENEdu", ID:EY-COP-0029. Whole blood samples and buccal swabs were processed at deCODE Genetics (Reykjavik, Iceland), using Infinium OmniExpress-24 bead chips (Illumina) for genotyping. Data quality control, data processing and analysis were performed with R Studio and PLINK tool for GWASs. Out of 716.503 SNPs, 91.897 variants entered data processing. PubMed and SNP databases were interrogated regarding information available over the significant variants.

Results: Out of 69 statistically significant SNPs (p-value<10-5), we found 7 relevant SNPs on chromosome 1, one of which had a p-value lower than 10-8. Although none of these variants had clinical relevance reported in the available databases, after a thorough interrogation, we discovered multiple connections to cancer pathogenesis. We identified the rs10494126, rs659580, rs340835 coding variants for DRAM2, PRRX1 and PROX1 genes, which were previously linked to lung cancer. Subsequently, we determined three other variants on SCP2(rs10493170), COL24A1(rs12568614) and PRSS38(rs12565154) genes, all of which are associated with malignancies. The 7th variant (rs4656525) is in a non-coding region and we could not identify any links to carcinogenesis.

Conclusion: Our study identified 69 statistically significant SNPs, 7 of them on chromosome 1, 6 of them corresponding to genes: three involved in carcinogenesis and three associated with lung neoplasm, in particular. We advocate for further research to be directed so as to determine the clinical implications of these variants in the pathogenesis of pulmonary cancer.

Keywords: GWAS; lung cancer; chromosome 1; PROX1