Identification Of Genetic Variants Associated With Arterial Hypertension In A Hospital−based Romanian Cohort From ROMCAN Project

Andrei Alexandru Mircea1, Ioana Diana Gardus2, Ana Miloiu3, Elena Avram4, Dana Florentina Margine5, Larisa Simon6

Carol Davila" University of Medicine and Pharmacy, Bucharest – Romania 1,3
Department of Hematology Laboratory - Clinical Hospital of Infectious and Tropical Diseases 'Dr Victor Babes Hospital' – Bucharest – Romania2
Department of prevention and limitation of health care-associated infections "Children's Hospital 'Dr Victor Gomoiu" – Bucharest – Romania5
Department of Medical Genetics – 'Sibiu Clinical Hospital' – Sibiu, Romania 4
2nd Dermatology Department of "Colentina" Clinical Hospital - Bucharest – Romania6

Introduction: Arterial Hypertension (AH) is a multifactorial condition affecting 1.13 billion people worldwide. Both genetic and environmental factors are responsible for AH development. The contribution of genetic factors represents more than 30% from disease risk. However, the genetic variants predisposing to AH are still largely unknown. The objective of this study was to investigate the genetic variants associated with AH in a Romanian population.

Methods: A population sample of 5435 hospital−based Romanian patients from Bucharest Hospitals was used. The cohort was part of the ROMCAN Project ("Genetic Epidemiology of Cancer in Romania") conducted from 2012 to 2017.
It contained control group and hypertensive patients with or without different types of carcinomas. Whole genome sequencing was performed for every individual. A filtering process and association testing were performed with R-Studio v3.2.0 and Plink Genetics v1.07 software.

Results: From 91.917 variants, we identified 30 SNPs strongly associated with AH ($p<0.001$) from which 9 genetic markers expressed either in the cardiac tissue or organs whose dysfunction leads to greater risk of AH incidence. They were classified as markers that influence directly blood pressure (CNTN6, PRKAG2, ITPR2), indirectly (DNER, PLA2G16) or variants associated with inflammation associated with hypertension (TRAF3, ZNF836, HAUS8, TXNRD2).
Furthermore, we compared our results with similar genome-wide association studies on SNPs correlated with AH. There were 3 common variants already identified as corresponding to a higher risk of AH. These were rs4842666 ($p=0.04275$), rs284277 ($p= 0.3359$), respectively rs4842666 ($p=0.9143$).

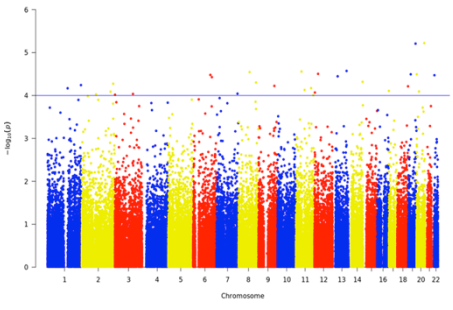

Fig.1 Manhattan plot summarizing the GWAS p-values

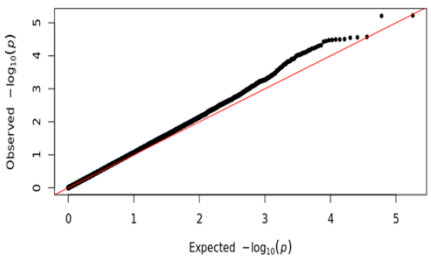

Fig. 2 Q-Q plot - differences between expected and observed p-values

Conclusion: This study found genetic variants related to hypertension susceptibility in the Romanian population. Further research may enable the development of a genetic prophylactic approach and a genetically personalized treatment for Romanian patients.