Notification No: 515/2022

Date of Award : 18-05-2022

Name of the Scholar : Kavita Sharma

Name of the Supervisor : Dr. Syed Mansoor Ali

Name of the Department/Centre : Department of Biotechnology/Faculty of Natural Sciences

Topic of Research : Large-scale association and functional analysis to identify the genetic variants of essential hypertension

Finding

Essential hypertension (EH) is influenced by environmental changes, such as the normobaric to hypobaric hypoxic. To identify the genetic variants associated with hypertension (HTN) we conducted a two-staged study. The stage one included GWAS with 2.5 million SNPs in the high altitude (HA) cohort (≥2500 MASL; meters above sea level); its association analysis revealed >60,000 significant SNPs (P<0.05). The stage two included 96 SNPs in two additional cohorts, namely, north-east (NE) cohort (>1000 MASL) and sea level (LA) cohort (>200 MASL). It provided with a differential distribution with 21, 45 and 15 SNPs associating with HTN in the three cohorts of HA, LA and NE, respectively. Also, multi-locus interactions in GWAS revealed 3937 risk haplotypes (P<0.05; OR≥1.62) and 5833 risk gene-gene interactions (P<1.00E–04; OR≥4.53). Here, *NOS3* with highest number of SNP associations emerged as one of the critical genes. Functional validation, hence, was restricted to *NOS3* most significant SNP rs1799983G/T that revealed the deleterious effects on the gene expression and protein level due to an allele change. Our findings are encouraging, albeit, further validation of additional variants may help identify contributing factors to the pathophysiology of HTN, as well as categorize potential targets for medical intervention strategies.