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Geo-ethnic diversity, hypertension and renal impairment in diabetes: Therapeutic consequences

Complications of type 2 diabetes (T2D) have been reported to be different between Asian and Caucasian populations with higher prevalence and severity of renal disease and stroke in Chinese, contrasting with lower myocardial infarction that could not be fully explained by differences in hypertension prevalence or treatment. Our objective was to determine whether ethnic heterogeneity exists within the Caucasian population with respect to phenotypic and genomic determinants of vascular complications of T2D. We analyzed the two main features of renal impairment: Increase of albuminuria as uACR and decline of estimated glomerular filtration rate as eGFR in Caucasian T2D patients followed during the 5 year period of the ADVANCE trial. Genetic ethnic origins of 5000 genotyped subjects were determined by principal component analysis with Eigenstrat software. The first principal component separated T2D individuals into two ethnic groups of Slavo-Baltic and Germano-Celtic origins. Phenotypic analyses and Genome Wide Association Studies (GWAS) for age of onset of T2D and changes in uACR and eGFR over the course of the study were performed in the two ethnic groups combined and separately. Patients of Slavo-Balticorigin had T2D at a significantly younger age and were more hypertensive in spite of higher number of antihypertensive drugs received. Baseline uACR was higher in individuals with a Slavo-Baltic genetic profile. The decline in eGFRCKD-EPI during the ADVANCE study was steeper among individuals with Germano-Celtic than with Slavo-Baltic genetic profile. Macrovascular events at baseline (myocardial infarction and stroke) were significantly higher in Slavo-Baltic subjects (p=1.3x10-2 and p=4.0x10-5) as was cardiovascular death (p=1.6x10-4) during the study. These characteristics persisted in Slavo-Baltic subjects living in Germano-Celtic environment suggesting a strong genetic contribution. A set of independent genetic variants (SNPs) were identified as markers of genes associated with early onset of T2D. They were used in a genetic risk score to predict age of death and response to therapy. Our studies revealed distinct genetic architectures of age of onset of T2D between two geo-ethnic groups within the Caucasian population that likely have clinical relevance.

Biography

Pavel Hamet is the holder of the Canada Research Chair in Predictive Genomics. He is Professor of Medicine at Université de Montréal, Adjunct Professor of Experimental Medicine at McGill University, and visiting professor at the First Faculty of Medicine at Charles University, Prague, Czech Republic. He is currently chief of Gene Medicine Services, member of the Endocrinology Service, and Director of the Ecogenomic Platform for Complex Diseases at the CHUM. He is also CEO and Chief Scientific Officer of Medpharmgene. He is the author or co-author of over 600 scientific publications, Dr. Pavel Hamet has received many honours, including the prestigious Wilder Penfield Award in 2001, was named Officer of the Ordre national du Québec in 2008 and received the Okamoto Award by the Japan Vascular Disease Research Foundation.

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