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Pharmacogenomic aspects in the treatment of type 2 diabetes

Oral antidiabetic drugs are used for more than a half century in the treatment of type 2 diabetes. Only in the last five years intensive research has been conducted in the pharmacogenetics of these drugs based mainly on the retrospective register studies, but only a handful of associations detected in these studies were replicated. The gene variants in CYP2C9, ABCC8/KCNJ11 and TCF7L2 were associated with the effect of sulfonylureas. CYP2C9 encodes sulfonylurea metabolising cytochrome P450 isoenzyme 2C9, ABCC8 and KCNJ11 genes encode proteins SUR1 and Kir6.2, respectively. Those proteins constitute the ATP-sensitive K⁺ channel which is a therapeutic target for sulfonylureas. TCF7L2 is a gene with the strongest association with type 2 diabetes that influences insulin secretion. SLC47A1, ATM and SLC2A2 gene variants were associated with the response to metformin. SLC47A1 and SLC2A2 encode MATE1 metformin transporter and GLUT2 glucose transporter, respectively. The function of a gene variant near ATM (ataxia-telangiectasia mutated) gene is probably related to activation of AMPK. In the recent years, the first studies related to the pharmacogenetics of response to DPP-4 inhibitors were published, although none of them was replicated so far. Among identified genes are TCF7L2, CTRB1/2 encoding chymotrypsinogen, and GLP1R encoding the downstream therapeutic target for gliptins – GLP-1 receptor. With the accumulating pharmacogenetic evidence in type 2 diabetes there are reasonable expectations that genetics might help in the adjustment of drug doses to reduce severe side effects, as well as to make better therapeutic choices among the drugs available for the treatment of diabetes.

Biography

Ivan Tkac has completed his MD in 1982 and PhD in 1991 in the Šafárik University in Košice, Slovakia and his postdoctoral studies in the University of Toronto, Canada. He is a professor and the head in the Department of Medicine, University of Kosice. He has published more than 50 papers in renowned journals including Diabetes Care, Diabetes, Obesity and Metabolism, Nature Genetics, Clinical Pharmacology and Therapeutics, and Arteriosclerosis, Thrombosis and Vascular Biology. His research focuses on the topics of pharmacogenetics of oral antidiabetic drugs and atherosclerosis in diabetes..

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