Editorial

Prevention and management of type 2 diabetes: Potential role of genomics

Type 2 diabetes is a disease with a growing public health burden. Nearly 26 million people already have it and 79 million more have prediabetes.[1] Prevention and intervention are important. Innovative solutions are required to tackle it. Precisely because of the same reason, the American Medical Association Council on Science and Public Health decided to review current genomic strategies to control type 2 diabetes and improve clinical care.[2]

More than 65 genetic variations have been identified, which can increase the risk of type 2 diabetes by 10–45%. The Ser/Thr protein kinase mechanistic target of rapamycin (mTOR) is one such variant, which plays a significant role in regulating insulin signaling. In combination with several other molecules, mTOR can form two complexes, mTORC1 and mTORC2. Each complex has a distinct role in regulating insulin sensitivity - mTORC1 inhibits insulin signaling via its substrate S6K1, whereas mTORC2 has been shown to have a positive effect on glucose uptake and tolerance.[3] A quantified algorithm of all these risk factors can add value to diabetic risk prediction.

Individualizing therapy on the basis of the patient's genotype is another field of interest. For example, patients with gene variants for cytochrome P450 2C9 (P4502C9*3 allele) have decreased tolbutamide metabolism and thus have larger decreases in blood glucose. Such variants require a lower dose of tolbutamide to regulate their serum blucose levels.[4] Similarly, patients with genetic variations in organic cation transporter 1 (OCT1) that reduce liver uptake of metformin (OCT1-420del allele) show less glucose-lowering response (more dose required), compared to those without this genetic variant.[5] Carriers of other variants of enzymes that regulate glucose metabolism also show variation in response with antidiabetic drugs; like a variant of peroxisome proliferator-activated receptor-γ (Pro12Ala) shows more blood sugar lowering with pioglitazone therapy.[6]

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Further perspectives of genetic polymorphism in Type 2 diabetes lay in predicting Type 2 diabetes complications, such as retinopathy, peripheral neuropathy, and nephropathy. The promise is there, but for the time being the potential has not been tapped fully and the small studies so far have not yet changed clinical practice. However with the advent of next-generation sequencing and whole-genome sequencing, genomics has many potential future uses in diabetes risk assessment, prevention, and management.

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