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Genetic Susceptibility to Type 2 Diabetes Mellitus (T2DM) and Associated Phenotypes: Role of Molecular Markers in the Disease Prevention and Personalization of Medicine

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Editorial

Diabetes mellitus is defined as a chronic condition characterized by raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively [1]. According to the International Diabetes Federation (IDF) in its 8th edition, in 2017, there were more than 318 million adult persons at high risk of developing diabetes, in the same year, 425 million adults had diabetes and by 2045 this number is projected to get to 629 million [2]. Type 2 diabetes mellitus (T2DM), resulting from relative insulin deficiency, insulin resistance or both represent more than 90% of diabetes cases. Like most cardio-metabolic diseases such as obesity, hypertension, ketosis prone diabetes (KPD), T2DM is a multifactorial disease with a complex interactions of environmental and genetic factors. Also people with a family history of these diseases are at a higher risk of developing T2DM [3].

T2DM constitutes a major public health problem. Substantial progress has been made in research to avoid its installation, reduce its progression or related complications. In this way, in addition to physical exercise programs, blood sugar monitoring and balanced diet, the number of available classes of drugs used to treat or reduce the complications related to T2DM have drastically increased in these two past decades [4]. To date with the increasing numbers of newly diagnosed cases [2], the challenge is to identify specific genetic markers which could be used to prevent T2DM and associated phenotypes, or used in the personalization of medicine. In fact, profiling of individual responsiveness to the existing diabetes treatment classes would tremendously advance clinical practice and lower the disease burden. Starting by the family based linkage analyses and focused candidate gene studies, large scale surveys of association between common DNA sequence variants and disease that have used to identified hundreds of genetic variants implicated in T2DM and other cardio-metabolic diseases, the exploration of the entire human genome has allowed for a much clearer idea

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and to understand the genetic architecture of these diseases.

As described in review by Erik Ingelsson and Mark I McCarthy "*Genome-wide association studies have also provided a critical starting point for discovering new biology relevant to these traits. Expectations are high that these discoveries will foster development of more effective strategies for intervention, through optimization of precision medicine approaches*" [5], suggesting that precision or personalize medicine using molecular markers or populations genetic characteristics is a direction to follow in the future. An interesting genetic markers was recently identified as a master switch gene for multiple metabolic phenotypes [6]. This master switch gene called Kruppel Like Factor 14 (KLF14) gene, as demonstrate by Civelek and Lusis is a master trans regulator of a network of genes who expression level is implicated to the predisposition to many metabolic phenotypes or disorders (in parentheses): TPMT (HDL-C, TG, BMI, INS, HOMA); ARSD (HDL-C, TG, BMI, INS, GLU, HOMA); SLC7A10 (LDL-C, WHR, HDL-C, TG, BMI); C8orf82 (T2DM, BMI); APH1B (HDL-C, INS, HOMA); PRMT2 (BMI); NINJ2 (LDL-C); KLF13 (LDL-C, WHR); GNB1 (HDL-C, TG, BMI, INS) and MYL5 (BMI) [7].

Added to data generated by researchers on this gene, the Cameroonian research team used a computational approach focused on this master gene to generate its regulation network and provides a variety drug development targets in the form of signal pathways that can reduce the progression of T2DM and associated phenotypes or the risk of their complications [8]. At this stage, it is important to pool existing data in this domain to develop clinical genetic testing based on specific molecular markers that can help to predict the occurrence of T2DM and other cardio-metabolic disorders; or used potential targets identified in the regulatory network of these genes or in the protein-protein interactions network of proteins expressed from these genes and their expression levels to develop drugs and used them in the personalization of medicine approach as demonstrated by Guewo-Fokeng and co-authors [8].

In this special issue of Journal, the articles featuring are not only based on the genetic of T2DM and other cardio-metabolic disorders, also on others topics of great interest that could contribute to the better understanding and manage of these conditions.

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