

Diabetes Research and Treatment

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Over the past few years, various international research centres have been involved in the study and identification of genes predisposing to Type 2 Diabetes Mellitus (T2DM). Using different strategies like candidate gene, linkage and genome-wide association studies, a large number of variants have been identified in many genes which have highlighted the role of genetics in the development of T2DM. The number of known T2DM variants has risen to over 60 including confirmation of variants identified earlier by candidate gene and linkage studies. This has led to identification of genes and pathways involved in the development and progression of the disease and have significantly improved our knowledge of one of the most serious health problems in the world.

Currently, however, genetic studies on T2DM can explain only 10 % of its heritability. Despite all of the loci that have been found to be associated with T2D, there are still many more T2D-associated variants that remain to be discovered. Hence, future research should aim towards the identification of rare genetic variants with a stronger association, rather than common variants with a relatively small effect on the disease. Because GWAS approaches are best suited to identify common variants within the population, it is believed that the remaining variants are rare. In order to uncover these missing variants, modifications to the genome-wide approaches used to date are

necessary. It is evident that if a genetic variant confers a high susceptibility to T2DM it may become a useful biomarker to search for. The genetic studies in T2DM may integrate and improve our knowledge about the molecular mechanisms underlying the pathophysiology of this disease. The focus of current ongoing research efforts include (1) detailed functional characterization of the identified T2D susceptibility variants and the search for missing heritability; and (2) utilization of the knowledge for clinical applications, as well as future investigations for further understanding of the genetic basis of T2D.

Despite the progress in clinical and laboratory investigations, the fundamental cause of T2DM remains uncertain. How the identified genes and pathways impact on T2DM still remains largely unknown due to the multifactorial nature of the disease. Understanding the pathogenesis of T2DM is necessary to enable the identification of prognostic and predictive biomarkers, as well as new therapeutic targets, which in turn should lead to improved outcomes in affected patients. The exciting results generated by GWAS have led to intense discussion of their clinical utility. It will be a challenge to translate the GWAS findings into improved care for patients with diabetes. However, recently, several reports have shown statistically significant interactions between genetic variants and medications for glycemic outcomes. These promising results show the potential of using genetic variation to tailor therapy for type 2 diabetes prevention and management. After the completion of Human Genome Project in 2003, it was expected that translation of the human genome into clinical practice will be done easily but it

has proven to be more challenging than was expected. According to the plan published by the National Human Genome Research Institute on February 2011, the impact of

human genome data on health care will begin to build only after 2020. We still have a long way to go.