

Genetics in Diabetes: Type 2 Diabetes and Related Traits

AL Gloyne, MI McCarthy

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In this book, the groundbreaking work of Mendel, Crick and Watson is extended into the 'human genome age'. The availability of sophisticated investigative techniques has enabled researchers to interrogate human genetic characteristics to determine more subtle and multigenic factors in human disease. These techniques have been applied to the investigation of the genetic determinants of type 2 diabetes (T2DM) and obesity.

A number of findings are of particular interest. Genome-wide association studies (GWAS) have identified 70 genomic regions associated with T2DM predisposition. However, this is associated with only 5–10% of T2DM predisposition. There were few ethnic differences. Fine mapping of the T2DM susceptibility loci and whole genome and exome sequencing are providing insights into the relative contribution of

common (weakly associated) and low-frequency (more strongly associated) variants of T2DM risk. GWAS of glycaemic and obesity traits suggest that for glycaemia the strongest factors relate to insulin secretion rather than insulin resistance; those related to obesity (as measured by body mass index) are located near genes expressed in the brain and hypothalamus; those associated with fat distribution are associated with genes that act in peripheral tissues affecting metabolic factors such as adipogenesis.

Next-generation sequencing is being used to characterise single-gene mutations that cause various forms of monogenic diabetes and are important because of their treatment implications. These most commonly involve mutations in transcription factors HNF1 α and HNF4 α , which affect insulin secretion, and are treated with low-dose sulphonylureas. Glucokinase abnormalities, whereby the body's 'glucostat' is reset upwards, are benign and require no treatment. Forms of neonatal diabetes, diagnosed at age <6

months, and in some instances associated with other abnormalities, are treated with high-dose sulphonylureas.

Potential mechanisms for epigenetic modifications, whereby genes and environment interact to modify T2DM risk, are discussed in this book, particularly in relation to obesity and physical inactivity, as well as the fetal environment.

This book has been written by researchers at the forefront of their field. The chapters are logically sequenced and provide information that is up-to-date and of potential future relevance and importance to clinical practice. However, it is highly technical and hard to digest. While it would be of interest to geneticists and diabetes researchers, it is not a book that will influence current diabetes care and, as such, will not be a useful addition to a clinician's personal library.

Clinical Associate Professor Alison Nankervis
Royal Melbourne Hospital