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Book Reviews

Genetics in diabetes: Type 2 diabetes and related traits, A.L. Gloyn, M.I. McCarthy, editors (Karger, Basel, Switzerland) 2014. 192 pages. Price: USD 233.00 / CHF 198.00 / EUR 185.00
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The past decade has seen unprecedented progress in the understanding of the genetic basis of type-2 diabetes (T2D), fuelled largely by technological advancement. This has led to large scale studies such as various genome-wide association studies (GWAS). The undercurrent of this book is in defining the genetic basis of T2D and related traits from the perspective of current advancement in genomic sciences and technologies.

This book is divided into six sections comprising of 14 chapters in all. The sections have been well laid out covering gene discovery efforts for T2D initially, moving onto the glycaemic and metabolic traits and then to monogenic disorders of β-cell dysfunction and insulin resistance. This is followed by the 'Omics' technologies of T2D and related traits, study of molecular mechanisms and culminating in translation of the results in clinical set-up.

The opening section of the book, 'Gene Discovery Efforts for Type 2 Diabetes' comprises three chapters touching upon GWAS studies in T2D which led to the identification of around 70 genomic loci. The authors have put forth the challenges of these studies succinctly and delineated clearly how even in the absence of mechanistic understanding GWAS signal patterns still provide insights into disease pathogenesis. They argue that the variants associated with T2D have been predominantly through insulin secretion rather than peripheral insulin sensitivity. A similar case is presented in traits such as obesity and body mass index (BMI). That these genetic variants have a physiological and pathological role is evident. GWAS data have shown that physiological variation in fasting glucose levels does not overlap with those implicated in pathological deterioration of glycaemic control often. This has been explained by the authors through MAGIC (the Meta-Analyses of Glucose and Insulin-related traits Consortium) study.

Chapter 2 is on fine mapping of T2D susceptibility loci. A range of approaches for assaying genetic variation across complex human traits loci and the methodologies for fine mapping causal variants in these regions have been delineated. The author has pointed out how to appreciate the genetic architecture and pathophysiological mechanisms underpinning the diseases, fine mapping of loci is very important.

Chapter 3 deals with whole genome and exome sequencing of T2D. The advent of next generation sequencing (NGS) has stepped up the tempo for discovery and interrogation of the full catalogue of human genetic variation. Unlike the Sanger sequencing, NGS could generate a huge amount of data. This has been well captured in this chapter. The chapter also poses very important questions that need to be answered to understand the simple genetic architecture of T2D and it is believed that technological advancement will lead to answering these questions.

The book goes on to describe the MAGICal journey of GWAS studies of glycaemic traits, posing first, the question on glycaemic traits and then answering that disease sub-classification is possible through glycaemic traits which are highly regulated within each individual and that the identification of genetic loci that influence glycaemic traits is an avenue to understand this. The authors have also pinpointed on how international collaborative efforts are the best way to generate massive data to understand the genetic underpinning of T2D.

Chapter 5 deals with obesity and related traits touching upon the genetic architecture of obesity traits such as WHR, BMI and also stressing the need for *in vitro* experiments and experiments on model organisms to elucidate the biological mechanism of obesity.

The book moves on to the next section on gene discovery efforts for monogenic disorders of β-cell dysfunction and insulin resistance. While T2D is affected by a combination of genes and environment, monogenic forms of T2D are more genetically enriched. The advent of NGS has helped in the diagnosis of monogenic diabetes and also in the discovery of novel aetiologies. This chapter describes the application of targeted NGS for clinical diagnostic testing or screening of known genes and exome analysis for novel gene discovery. The strategy for discovery and diagnosis of gene variants in neonatal diabetes and MODY (maturity onset diabetes of the young), has been detailed. The importance of genetic testing and treatment changes due to mutations in genes with high translational potential is also emphasized.

In the next section on 'Omics' of T2D and related traits, the new field of epigenetic modifications in T2D is reviewed well. Studies from islet transcriptome and the insight gained in β-cell biology and T2D pathogenesis are also explained. How transcriptome analysis serves as a tool for disease biology understanding is well accounted for. This is followed by genomics of adipose tissue and advancement in understanding of its role in obesity and its traits.

In the next section translational aspects of genetic association signals is dealt with. The importance of continuing genetic, epigenetic and transcript data to understand the importance of gene variants discovered by GWAS has been discussed. A good account on the future directions of functional translation which will deliver to clinical medicine is also available. The book, next discuss the advancements in the study of mouse models for understanding molecular mechanisms of diabetes and obesity. The *FTO* gene has been identified as one of the obesity associated genes.

The last section of the book deals with clinical translation. The challenges of defining drug response in diabetes have been discussed along with the potential and future of this area of research. Whether it is possible to get the right drug at the right dose for the right person is a million dollar question. But the potential of genomic research is taking us closer to that objective. The last chapter gives an account on the translation of genetics of diabetes into the clinic. The clinical impact of genetic diagnosis is discussed, taking MODY as an example. The chapter ends with a discussion on the myriad clinical potentials of genomics, where patient stratification, prediction of risk of diabetes and its complications, therapeutic stratification and the discovery of novel therapeutic targets are possible.

This book is written by experts in various domains of genomics of diabetes mellitus, so, the perspectives in each area have been brought out succinctly. The need for international collaboration comes out strongly in the book. Thorough referencing and a well connected idea is one of the major features of this volume. Clinicians interested in diabetes and researchers in the field of genetics of T2D, will benefit by reading this book. This book is motivating and leaves the reader full of new ideas. This book is recommended for clinicians and scientists working in the field of genomics of T2D.

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