BOOK REVIEW

A vision of personalised medicine revealed through modern genomics and open science

Exploring Personal Genomics

First Edition by Joel T Dudley and Konrad J Karczewski

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Exploring Personal Genomics delivers an interesting and comprehensive education for any postgraduate student embarking on a career in genetic epidemiology or genetic medicine, but it can also be dipped into by those interested in just one or two of the topics covered. Each chapter is individually accessible to the reader because the subjects, ranging from human ancestry to pharmacogenetics, are described from first principles. There are ample illustrations and useful summary boxes that elaborate on definitions, concepts, and case scenarios.

Part I of the book provides the reader with the scientific and social context for understanding genomic medicine. It also includes detailed narratives about its applications in genealogy or in predictive and personalised medicine. Complex traits and genome architecture are discussed alongside the experimental tools used to identify and understand genetic variation; from genome-wide association studies (GWAS) and whole-genome sequencing to principal component analysis.

Pharmacogenomics is highlighted as the field with the most immediate promise for clinical application. Pharmacogenetic variants can be considered to be quantitative trait loci (QTL) with potential clinical utility if they can explain a significant proportion of the variability of the response between individuals. In chapter 7, known functional variants that impact the pharmacokinetics and pharmacodynamics of commonly prescribed medicines are discussed and a comparison is made with the use of dosing

algorithms that incorporate genetic data, with standard protocols that do not.

A unique selling point for this book is its emphasis on active, enquiry-based learning. The authors encourage the reader to investigate and try particular tools and databases that are in the public domain (<http://www.pharmgkb.org/>; <http://www.pdb.org/>; <http://www.snpedia.com/>; <http://www.drugbank.ca/>; <http://www.interpretome.com/>; <http://genetics.bwh.harvard.edu/pph2/>; <http://www.genome.gov/gwastudies/>). This is particularly so in part II of the book, which considers personal physiology, private mutations, and structural variants and is aimed at the more expert reader. A plethora of open access data coupled with freely available software and analytical platforms are described; examples are given for the cascading use of *Interpretome*, *DrugBank*, and *PolyPhen*. The authors take care to distinguish tools that could be of use to a keen novice from those that require specialised expertise. This adds to the atmosphere pervading the field of human genomics; it is democratic and its ultra-rapid progress is dependent on open science and a generous, non-paternalistic attitude.

In silico experiments are described that could result in more rational and focused empirical studies than existing GWAS deliver. We can use a variety of platforms and software to predict which variants in a personal genome are likely to affect complex phenotypes by virtue of their functional and deleterious impact on gene products. However, pitfalls with this approach are also identified for software that is not yet integrated for

systems biology; predictions for individual variants can be made but this is without reference to the redundancy that exists within chaotic cellular pathways. The authors provide a glimpse into the future by discussing strategies and the potential for systematically measuring 'pathway mutational load' and concomitant physiological impacts.

Chapter 9 explores methods for the identification of genetic drivers of personal physiology by integrating expression-QTL data, allele frequency data, and personal genome data. Genotypes that were homozygous for rare variants and associated with unusual physiological levels of gene transcript were identified to be of putative phenotypic importance to the individual. Using a published proof-of-principle case study, the authors show that it is possible to make predictions about the disease risks of an individual that were corroborated by their medical history. The complex integration of data described in this section of the book was fascinating to read about but was also a stark reminder of why the use of personalised medicine still remains elusive in the clinic for complex, polygenic traits.

I have a few gripes that may relate to the book's review and editorial process. Firstly, there are some typos, and frankly, errors, that should have been corrected – for example; uracil is a pyrimidine or base, and not a nucleic acid. Secondly, one of the appealing and fresh qualities of this book, is that the authors are in collaboration with the reader, rather than overly didactic. This ethos however, jars with reminders to *consult a physician (or other) for how one's genome may affect one's disease risk or drug response*; it is clear that the authors do not present any arguments for genetic determinism, making such statements superfluous. However, overall I will strongly recommend the book to medical students, postgraduate students and clinical colleagues, and will undoubtedly re-read many sections myself.

Aspects of personalised medicine are in sight and the tools for their delivery are growing exponentially. For those interested in clinical utility we do not yet have a high-definition image, but the resolution is improving at a pace. The authors of this book are contributing to, and describe with great clarity, a revolutionary shift towards participatory and predictive medicine.

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