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Book Review

Genetics Twists of Fate
Stanley Fields and Mark Johnston,
MIT Press, 2011

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We are now, apparently, in an age of "personal genomics" brought about by new capabilities for cost-effective whole genome sequencing. There has been a concomitant rise in Direct-to-Consumer (DTC) testing through companies such as 23andMe, Knome (pronounced `know me'), deCODE Genetics, and Navigenetics to name but a few. Each of these offers to provide insights into our genetic fate. There also appears to be considerable public interest in knowing one's genetic risk[2].

In *Genetic Twists of Fate* Professors Fields and Johnston "set out to make human genetics fathomable to all those whose tax dollars generously support this research [into genetics]" (p.vii). Such an attempt is laudable given the apparent pervasiveness of genetic technologies. In part their aim is achieved, yet in other areas the text may be too technical for the reader without a reasonable level of science education.

The book itself is divided into four parts: 'What do genes do?'; 'The inheritance of the gene'; 'Finding the gene'; and 'The gene in evolution'. These four parts cover a total of 18 chapters in a book of 219 pages.

Part one provides an overview of what genes are, where they exist in the body and the basic composition of the DNA double helix – beginning with a DNA facts and figures section (Chapter 2). In Chapter 3 the authors progress the discussion to the role of genes in the production of proteins and the mechanism by which this occurs. Chapter 4 brings together the previous two chapters to show how DNA and proteins work to generate an embryo, whilst Chapter 5 considers the implications when these mechanisms fail to work as they should. In particular the authors consider how knowledge of transcription and translation processes can lead to treatment, with specific discussion of Severe Combined Immunodeficiency (SCID) and the potential of gene therapy. The final chapter of this first part harks back to Chapter 4 and looks at how knowledge of the cell specialization process can inform therapies, with a focus on stem cell therapy.

The second part of the book has, at its core, a discussion of inheritance with chapters on autosomal recessive (Chapter 7) and autosomal dominant (Chapter 8) forms of Mendelian inheritance. This introduction to inheritance patterns is followed by a discussion of more complex forms of inheritance (Chapter 9). The final chapter of this part considers additional complexities caused by gene-environment interactions and the area of behavioural genetics.

Part three consists of a number of chapters about the identification of disease-causing genes. This is introduced in Chapter 11 with a discussion of cancer-causing mutations through mistakes in DNA replication. Subsequent chapters then focus on how these mutations are

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located and identified through analyses of recombination (Chapter 12), the use of pedigrees (Chapter 13), and association studies (Chapter 14). The final chapter of the third part (Chapter 15), in a departure from the previous chapters, introduces the topic of pharmacogenetics within a review of Warfarin discovery and application.

The last part of the book, the shortest at only three chapters, considers two examples of the implications of genetic research and discovery. In Chapter 16 the authors recount the race to publish a theory of natural selection while in Chapter 17 the topic of genetics and race is reviewed. Whilst the authors end the chapter discussing population specific gene variants they do so without engaging with more difficult issues of stigmatisation, discrimination, or genetic reductionism. The final chapter, Chapter 18, provides a brief summary of the book.

Each of the chapters – which discuss different scientific advances in genetics, from the discovery of DNA as the inherited genetic material to the transmission of recessive and dominant disease alleles – are built around the stories of individuals. This narrative style serves to ground the abstract scientific discussions in real-life examples that provide illustrative case studies of the impacts of genetic disease. Indeed, the writing style of the authors should be applauded, as they utilise these cases both to introduce and to end each chapter and so provide discussions that would serve as stand-alone examples of the topics they are discussing.

However, on occasion the authors miss their mark with sections that delve into detail that may be beyond readers who "haven't thought much about the workings of genetics since their high school biology course" (p.vii). While the text is generally written in such a way that the non-specialist can pick up the book and gain an insight into genetics and the impact of genetics on health, some passages are jargon-filled and technically loaded. These include such convoluted portions as:

> In 1998 geneticists identified disease-causing mutations in the gene that encodes tau protein, but not in patients with Alzheimer's disease. Rather they found the tau mutations in patients suffering from a neurological disorder called frontotemporal dementia and Parkinsonism linked to chromosome 17, or FTDP-17 for short. People with this disorder have intracellular deposits of tau, but no deposits of amyloid-beta. The hypothesis that tau plays a role in this disease supports the idea that altered forms of tau cause neurodegeneration. (p.100)

Such complicated language may serve as a reflection of the complicated material with which the authors are trying to engage the audience, yet one can imagine that such language might deter the less enthused reader. Enthusiasm, however, is something that is not lacking from the authors who express an unwavering belief in the benefits of genetic science and its potential to do good – perhaps not surprising given that the book is written by a professor in genome sciences and medicine, and the editor-in-chief of the journal *Genetics*.

Yet there are occasions where a more nuanced critique of the scientific process would have been warranted. Chapter 3 provides one such example in which the authors, through a case study, relate the misdiagnosis of methylmalonic aciduria (MMA) in a child and subsequent

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imprisonment of the child's mother on suspicion of poisoning him with antifreeze. The example is used to illustrate the case of a mutation resulting in proteins being improperly formed or missing. Yet the authors fail to comment on the inconsistency of lab reports and the inappropriate self-regard of the prosecuting scientists. They write:

> Could MMA be confused with ethylene glycol poisoning? "Impossible!" said the experts that McElroy consulted. They maintained that there was no way MMA could cause high levels of ethylene glycol in the blood. Ryan may have MMA, they said, but there was no doubt that he had died of antifreeze poisoning. (p.27)

Later, they report the defendant's analysis of the lab reports:

> What about the traces of antifreeze found in the bottle Patty used to feed Ryan? The bottle had been washed in a dishwasher and filled with infant formula before testing, and the compound identified as ethylene glycol "could have been anything," Rinaldo concluded. "Their approach was: anything that showed up in a certain window in that chromatogram would automatically be labeled ethylene glycol. This is just…unacceptable," he said with a sad and disbelieving shake of his head. (p.32)

This would seem to be an example where a discussion about the potential for blinkered and predetermined analysis based on prior beliefs might be warranted, yet it is just presented with no commentary other than that justice was done in the end.

This is symptomatic of the one element that is lacking in the book: any real discussion of the sociological or ethical issues or implications raised by the technologies discussed. Whilst the authors cannot be expected to be specialists in all fields, a more thorough consideration would have been beneficial. Given that the authors discuss the potential for gene and stem cell therapies, behavioural genetics, and race in the context of genetic research, one would have anticipated a greater consideration of the issues these topics raise – particularly given the way in which the authors provide engaging real-world examples of the underlying genetic mechanisms. Indeed, given the difficulties encountered in attempts to progress both gene and stem cell therapies one might have thought that a discussion of the potential for scientific hubris and over-confidence in the scientific endeavor might have been justified.

While the authors may not have created a book for the lay audience, or one which engages in great detail with the ethical and social issues that accompany advances in genetic research, they have written an engaging volume on the key principles of genetics that would serve as a great introductory text for those wishing to study genetics at university, and which offers the somewhat informed reader a grounded understanding that could then be developed during further study.

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[2] T, Caulfield and A.L. McGuire. Direct-to-Consumer Genetic Testing: Perceptions, Problems and Policy Responses. *Annual Review of Medicine* 2011; 63: 1-11.

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