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Book Review

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A Century of Mendelism in Human Genetics. Eds. Milo Keynes, A. W. F. Edwards & Robert Peel. CRC Press. 2004.

This book comprises the Proceedings of a symposium organised at the Galton Institute and held at the Royal Society of Medicine, London in 2001. Why the long delay to print and does it matter? If some of the delay owed to the editing process then it was worth the wait and no, unlike all too many Proceedings, this largely reflective volume is still worth reading and will remain so for years ahead. Thanks to the consistently high quality contributions, the editors have produced an excellent and timely summary of the many major contributions of Mendelism to the field of human genetics. The century is marked not by the publication of Mendel's seminal work, but rather by that of Bateson's 'Problems of heredity as a subject for horticultural investigation' published in 1901 and now widely recognised as a key trigger for expansion of Mendelism and it is usefully reprinted here. Thus defined, the first and second half of the century divides rather conveniently into pre- and post-DNA and it will be of particular interest to the current generation of researchers to realise just how many of the fundamental principles and methodological developments preceded the practical advances that derived from knowing the structure of DNA and being able to manipulate, interrogate and interpret it's information content directly.

The first five chapters (by Milo Keynes, Michael Bulmer, Eileen Magnello, A. W. F. Edwards and Patrick Bateson) chart and reflect upon the legacy of the first 50 years and do so with a well researched, consistent authority and passion. Each justifies thorough and repeated reading. In the second half, Newton Morton kicks off by taking us through linkage and allelic association with great clarity. Week on week fresh claims are made in the literature for 'a gene for disease X', but how many of us are confident in the interpretation of linkage or association analysis? This chapter will set you straight on the underlying assumptions and experimental approach. There then follow chapters from Lucio Luzzatto (Malaria and Darwinian selection in human populations), Malcolm Ferguson-Smith (Chromosome genetics and evolution), Timothy Cox (Mendelian disorders in man: the development of human genetics) and Alfred Knudson (Human cancer genetics), all interesting and valuable in their own way for summarising the respective experimental approaches and advances made through genetics. For a contemporary take on the subject, John Bell (The genetics of complex disease) and David Weatherall (Genetics and the future of medicine), two visionaries and frequent commentators on the future promise of medical genetics, when taken together provide a balanced view of just some of the opportunities and challenges ahead.

What this book makes clear is how the elegantly simple rules of Mendelian genetics can be brought to bear upon the complexities of human genetics and inherited disease and how this is a truly international, eminently accessible and transferable science.

It was not until 1990 and the launch of the Human Genome Project and with it the era of large scale DNA sequencing and related genomic sciences, that genetics became 'big' science driven by a small number of well endowed research laboratories. The Galton Institute Proceedings however remind us of the prominent role made by the UK community in starting the human genetics revolution, in developing the theory and methodology, in discovering the structure of DNA, and indeed the often under played role in arguing for the human genome project (by Ed Southern, Sidney Brenner and John Sulston, in particular). The Wellcome Trust and Sanger Centre (now Institute), largely through the determination of the first Director, Sir John Sulston, played a vital role, initially against strong political forces, to ensure that DNA sequence was released immediately to the community without restriction. The Sanger Centre also made the largest single contribution to the publicly available, finished human genome sequence. This, more that anything else, has ensured that the human genetics door is wide open to all who will make the conceptual and practical advances over the next century. Some contributors (notably John Bell and David

Weatherall) do take a look into the post-genome (or more correctly the genome) era, but there is no equivalent of the Bateson paper that portends the next 100 years. Are there other obvious shortcomings? What does seem like an omission is any specific treatment of epigenetics or epistasis. One of the 'hot' areas of genome biology is so called systems biology, but far from being 'new', we can arguably trace back it's conceptual framework back to the 1950's and early 70's and work of two Edinburgh luminaries, Conrad Waddington and his epigenetic landscape and Henrik Kascer's flux control theory, or Metabolic Control Analysis. What will be seen as the landmarks and key staging posts of the second century of Mendelism in Human Genetics? Certainly the Human Genome Project, perhaps the advent of gene therapy as a robust and curative contribution of genetics to medicine and, just perhaps, a fully worked genetic approach to the systems biology of complex pathways, processes and whole organisms. But whatever and wherever progress is made, it will always pay to look back and reflect upon these foundations of genetic science.

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