Gene dreams

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I remember sitting in one of my genetics lectures in the early days of university and being in awe of the complexity of the human being but also at science's ability to probe it. We were in the thick of The Human Genome Project's culmination and all that it promised for the future of medicine. My mind wandered from the nitty-gritty of base pairs to imagine a time when one's personalised blueprint would be an essential tool in the doctor's armament, as commonplace and essential as a full blood examination or electrocardiogram.

A good 10 years has passed since I was sitting in that lecture theatre and in one sense, it seems that dream of gene-based medicine is as far away as it was back then. Cystic fibrosis in many ways led the charge on the gene therapy front. It was one of the earliest identified causative mutations, discovered in 1989,[1] and by 1998 there was promising clinical trial evidence of effective *CFTR* gene transfer via viral vectors to the sinuses by a group from the USA.[2] This group went on to have success with transfer to the lungs by 2001.[3] These promising beginnings, however, have failed to deliver on all-important clinical outcomes to date. A Cochrane review on the subject, updated in 2013,[4] found that there is currently no evidence for the use of *CFTR* gene transfer agents as a treatment for cystic fibrosis lung disease.

Cystic fibrosis has also featured prominently in the area of gene-related therapeutics commonly known as 'personalised medicine'. The positive results in this arena have been more forthcoming: improved clinical outcomes have been seen with compounds developed to directly target specific mutations in the *CFTR* gene and modulate its function.[5] Personalised medicine has also been heralded to be the next big thing in cancer medicine and while there have been real breakthroughs – notably the development of transtuzumab for breast cancer – the results have not perhaps been as widespread or disease-changing as initially hoped.[6]

Despite the slow progress, genetics does continue to walk through our consulting room doors in various forms. In this month's issue, Blashki et al[7] provide a very practical guide regarding the form those consultations are likely to take in 2014. Their article serves as a helpful reference for managing issues that we need to think about less commonly than hypertension and sports injuries..

Antenatal screening is possibly the sphere of genetic medicine where clinically significant advances have been made most swiftly. The newly available noninvasive prenatal testing (NIPT) is truly a breakthrough in that it allows, for the first time, examination of fetal genetic material detected in maternal serum, to screen for the more common aneuploidies with a high degree of sensitivity and specificity. Woolcock and Grivell outline its advantages and disadvantages, important counselling points for women intending to undergo testing, and discuss the likely place of this testing in our approach to antenatal care in the future.[8]

NIPT, like many forms of genetic testing, inevitably raises ethical and social concerns, both in terms of accessibility and the possible consequences of genetic knowledge. Ever since humans unlocked our genetic code with the completion of the Human Genome Project in 2003, we have had the ability to map our individual genetic blueprints, but not necessarily the ability to fully and meaningfully interpret them.[9] In the name of autonomy and self-determination, commercial enterprises have evolved that will deliver results of DNA genetic testing directly to the individual; testing is almost exclusively performed offshore and as such, is largely unregulated, at least in Australia. Professor Ronald Trent attempts to unpick some of the difficulties inherent in this direct-to-consumer DNA testing and arm the general practitioner with a reasoned response should our patients ask us to be involved in either the initiation of such tests or interpretation of the results.[10]

From a day-to-day clinical perspective, how powerful it would be if we could identify and manage those illusive genetic factors that contribute to the development of diabetes, obesity and cardiac disease, and perhaps prevent patients from ever developing them? Implausible yes, but I wonder if Mendel ever imagined the existence of something like DNA or that one day, with a simple saliva sample, scientists could decode an individual's genotype? Perhaps we'll never get there, but it's still awe-inspiring to daydream about the possibilities.

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