Healthy genes, smaller jeans

We know what we look like. The mirror tells us so. We know our name and age. Our ID has the information. But who can tell us about the make-up of our genetic personhood? There are no talking genies in our DNA code. Only the aloof silence of our encrypted genes that write the script for our illnesses and wellness, whether we'll be fat or thin, tall or short. But is there no way to unravel this ciphered Pandora's box? Yes, indeed there is, says **DR STEPHEN RUDD**. He calls it the science of personal genomics. Rudd is a genome analyst, and Chief Scientific Officer with Malaysian Genomics Resource Centre Berhad.

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As interested readers of the scientific press, we are aware of the science of human genetics and understand that many diseases that blight humanity are in fact programmed into our genes. When we critically consider our immediate families we can all see evidence of the more common genetic diseases. Breast, prostate and colon cancers all have a well characterised genetic component. Alzheimer's disease, Parkinson's disease, obesity and osteoarthritis can also be explained by genetics.

Scientists across the world utilise research funding to characterise the molecular nature of human diseases, and with each scientific publication, we understand a little more about the roles of genetic disease. It is with this understanding of molecular and genetic etiology that a number of companies are championing the concept of personal genetics and now, as the price of human genome sequencing falls, even personal genomics.

The human genome was first described comprehensively a decade ago. In this seminal work, the full three billion letters of the human genetic code were collated together as a single corpus. It was discovered that if we compare any two humans there are only approximately three million differences in their genetic code. The vast majority of these differences are inherited from one's parents but a small fraction represents new mutations. Of these inherited differences, most are silent and inconsequential. Others are benign but confer subtle differences.

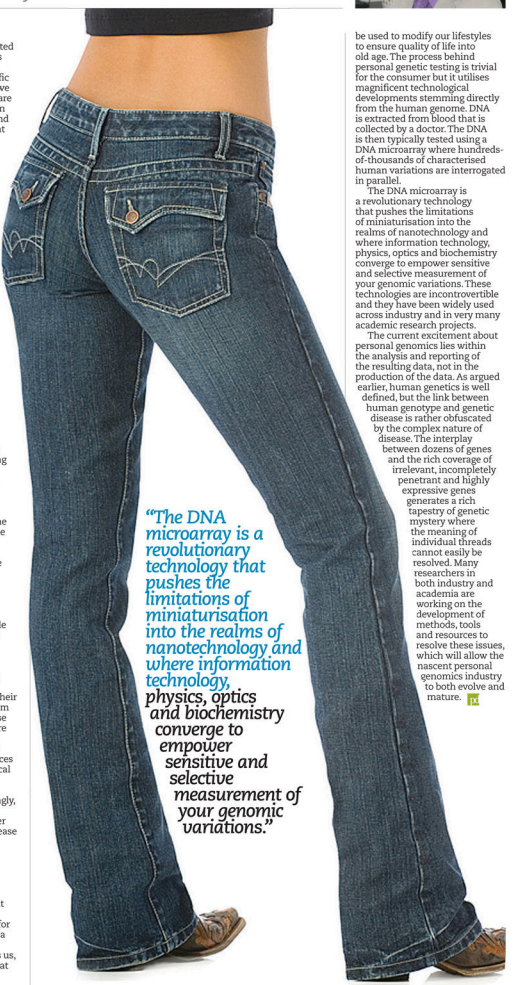
A variation (rs1726866) in the TAS2R38 gene is responsible for the perception of bitterness in foods. However, similarly benign differences are also responsible for more profound effects such as pharmaceutical efficacy and safety. For example, inherited genetic variation in the VKORC1 and CYP2C9 genes determines how well Warfarin (the anticoagulant drug) works, and hence the optimal dosage. Interestingly, the drug is much more effective at lower doses in some Asian populations than others. There are, of course, a small number of rarer inherited genetic variants that are directly implicated in human disease and health, and which form a significant burden for society. These variations include cancers.

The analysis of genetic variation is typically not so simple. Some diseases, such as schizophrenia, have been associated with dozens of genes and hundreds of individual variations. This is further complicated by penetrance and expressivity. Penetrance describes the correlation between a variation and a disease. A highly penetrant variant will explain most or all the genetic basis of a disease. Expressivity meanwhile explains the breadth of disease symptoms for completely penetrant variations with some genetic diseases having a wide range of severity.

Personal genetic testing is the science and technology that allows us, as interested consumers, to investigate our own genetic burden. What have we really inherited from our parents and what consequences might these variations have across our lives? This information can be used to modify our lifestyles to ensure quality of life into old age. The process behind personal genetic testing is trivial for the consumer but it utilises magnificent technological developments stemming directly from the human genome. DNA is extracted from blood that is collected by a doctor. The DNA is then typically tested using a DNA microarray where hundreds-of-thousands of characterised human variations are interrogated in parallel.

The DNA microarray is a revolutionary technology that pushes the limitations of miniaturisation into the realms of nanotechnology and where information technology, physics, optics and biochemistry converge to empower sensitive and selective measurement of your genomic variations. These technologies are incontrovertible and they have been widely used across industry and in very many academic research projects.

The current excitement about personal genomics lies within the analysis and reporting of the resulting data, not in the production of the data. As argued earlier, human genetics is well defined, but the link between human genotype and genetic disease is rather obfuscated by the complex nature of disease. The interplay between dozens of genes and the rich coverage of irrelevant, incompletely penetrant and highly expressive genes generates a rich tapestry of genetic mystery where the meaning of individual threads cannot easily be resolved. Many researchers in both industry and academia are working on the development of methods, tools and resources to resolve these issues, which will allow the nascent personal genomics industry to both evolve and mature.



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