Special Technical Feature

High-throughput Sequencing – a Transformative Technology

Guest Editorial

The use of hyperbole to describe breakthroughs in science and medicine often leaves us all rather jaded and cynical. There are times, however, when a new finding or a new technology is most definitely breathtaking. Those of you old enough to remember the late '70s will no doubt still remember with some awe the amazing accomplishments of those times which led to the era of molecular biology. The cloning of the first human gene (insulin) in 1978, while I was still an undergraduate, was certainly a stimulus for my lifelong interest in genes and how they functioned. Since then, there have been only a few similar disruptive events in biology – the development of the PCR technique in 1985 would no doubt qualify, as would the availability of automated DNA sequencing – and most advances have been of a more incremental nature. The recent advent of high-throughput sequencing is no doubt one of the single biggest technology changes that most practising molecular biologists have encountered in their careers. This sequencing method is also referred to as massively parallel sequencing or deep sequencing and is truly a transformative technology.

To illustrate the power of this technology, when the world was told of the sequencing of the first human genome with great fanfare in April 2003, we were also told that it had a cost of >US$3billion and had taken 13 years to complete (two fewer than expected – and that was only because of the public/private race initiated by Craig Venter and his colleagues). Now, it is possible to obtain a human genome sequence for a very small fraction of this cost – Illumina will charge less than $20,000 for its 'individual genome sequencing service', which provides 30-fold coverage. The sequencing of the giant panda genome, published earlier this year, using high-throughput sequencing only, was achieved in less than a year.

The details of the technology are well described in the articles in this Special Technical Feature, and there are a number of different technologies, each useful for different applications and biological questions. A glimpse of a few of the different approaches is seen in the accompanying articles, but there are many more. Deep sequencing is providing an unprecedented view of the genomes of many organisms, the epigenome (the packaging material of the genome) and the transcriptome (the output of the genome) of a cell or an organism. Beyond an individual organism, the technology is being used in exploratory ways to examine the microbial content of the gut or of soils, the oceans and beyond. Many new terms such as ecogenomics and metagenomics are arising to describe the use of these technologies in different settings. In clinical medicine, the ability to easily detect variation in the human genome is helping to bring the idea of personalised medicine closer to reality.

There are also exciting new developments on the horizon, an example being single molecule sequencing, which will lead to even faster and more accurate DNA sequencing data. It may not be long before every experimental biology lab will have a small benchtop sequencer (remember the old PCR machines?) capable of sequencing an entire genome at the press of a button in a few hours.

I hope that you will find these articles and the technology they describe as exciting as I do and think about adventurous new ways to apply it to your particular biological question.

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High-throughput DNA Sequencing

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Cover Illustration

A schematic diagram examining hypothetical RNAseq data in a genomic context. See page 17 of this issue for full caption.
Image courtesy of Sean Grimmond, Institute for Molecular Bioscience, University of Queensland.

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In December, Showcase on Research will be on **Control of Cell Growth** – *Guest Editor: Rick Pearson*

Australian Biochemist – **Editor** Rebecca Lew, **Editorial Officer** Liana Friedman