Bioplatforms Australia

Written by Graeme O'Neill[1] with contributions from Andrew Gilbert[2], Lisa Sampson[3] and Nick Hayward[4]

[1]Science Ink, [2]Bioplatforms Australia, corresponding author, agilbert@bioplatforms.com, [3]Melanoma Institute Australia, [4]Queensland Institute of Medical Research

Australian scientists have launched the Melanoma Genome Project, a major initiative to pry open the cellular black box of melanoma, and shed light on the mechanisms that drive the development and spread of one of the most dangerous human cancers.

The national bioscience infrastructure organisation Bioplatforms Australia, will employ biomedical science's most advanced analytical tools to explore the genetic and biochemical events that transform a normal pigment-producing melanocyte, or melanocyte precursor cell into a melanoma. The multi-million dollar study is led by world leading melanoma research centre Melanoma Institute Australia.

Commonwealth Government investment, through Bioplatforms Australia, will be augmented with a major philanthropic commitment from Melanoma Institute Australia, which is actively raising funds in support of this critical project.

Melanoma Institute Australia was opened in 2012 after a $40 million donation from the Australian businessman and philanthropist Greg Poche AO, the greatest gift by an Australian to a single cause in Australia's history. Mr Poche has donated $1m to the study.

Professor Graham Mann, his colleague Professor Richard Scolyer, and Professor Nick Hayward, are three of Australia's leading experts on the biology of melanoma. Together they have access to an invaluable resource for melanoma research: a tissue bank, containing more than 1,550 tissue samples and 3,500 blood specimens and a database of over 33,000 melanoma patients meticulously collected since the 1960s by the Sydney Melanoma Unit (now Melanoma Institute Australia).

A malignant melanoma is a fast-replicating aggregation of out-of-control cells whose genetic and metabolic activity and behaviour differs so greatly from those of healthy melanocytes, that they effectively become a hostile alien entity in the body.

"We're going to study melanoma as an organism, to see what makes it tick," said Professor Nick Hayward, a molecular geneticist with the Queensland Institute of Medical Research, and one of the project's leaders.

"We just can't afford to wait another 20 years," says Professor Graham Mann, co-director of research at Melanoma Institute of Australia. "We urgently need to understand melanoma."

The figures, and the trend, are alarming. The incidence of melanoma in Australia, already the highest in the world, is rising. In females, it rose by 0.7% a year between 1993 and 2003, or 6.8% overall. In men, it rose by 1.7% a year, an 18.7% increase overall.

Cancer is typically a disease of advanced age, but melanoma mainly affects people in their most productive years, between age 15 to 44. Melanoma is the most prevalent cancer in this age group. Although melanoma represents only 2.3% of all skin cancers, it accounts for almost 76% of all skin-cancer deaths. Australia treats more than 11,000 cases a year, and metastatic melanoma caused 1279 deaths in 2007 alone.

The Melanoma Genome Project will be one of Australia's largest and most complex biomedical research projects.

Its first phase will sequence the genomes – the complete DNA blueprints – of 100 melanoma cell lines from a tissue bank established by the Melanoma Foundation 12 years ago and the Queensland Institute of Medical Research. The aim is to characterise over 500 tumours and compare them with what is considered a "normal" human cell.

The task, equivalent to 200 Human Genome Projects, could not have been contemplated a decade ago. The Human Genome Project took 15 years to sequence the 3.5 billion DNA bases ("letters") of the human genome, and cost some $3 billion when it was completed 2003.

Today, an ultra-fast next-generation DNA sequencer no larger than a desktop printer can complete a human genome sequence in a few days, for less than $10,000.

Researchers will compare patterns of mutation, and consequent changes in gene activity, protein production patterns, and metabolic activity in each line.

The aim is to characterise patterns of activity common to the majority of melanomas, while looking for atypical melanomas that have arisen through rare mutations, or reflect the influence of rare gene variants in some individuals.

Prof Hayward says the aim is to assign tumours to broad classes, for prognostic and therapeutic purposes, no two tumours will be the same because every person is genetically unique.

"A driving reason for the study is that, until recently, we have had no effective therapies for treating metastatic melanoma," Prof Hayward said. "But we have recently seen the emergence of promising therapeutic agents that target very specific mutations."

"We have to use our most advanced technologies to pull it apart. A comprehensive, unbiased exploration of every aspect of its development will greatly improve our prospects of making the right correlations, and drawing correct conclusions."

"Over the next two to three years, we expect to have data on thousands of melanomas, and statistically meaningful patterns will emerge, revealing the variety of molecular abnormalities involved in initiating and driving primary and metastatic melanoma.

"It will reveal common combinations of mutations, and suggest how to deal with them. While we will target the most common mutations, we don't want to miss the outliers.

"There are more than 20,000 human genes, so we might expect around 10% of patients to have uncommon mutations, and 1% might carry very rare mutations."

Professor Mann said projects like the melanoma project will generate data sets linking all aspects of cellular biology. "They will be of huge value, not only for cancer research, but for researchers across the biological sciences.

"They will drive biological research for the next generation. With the data from all the experiments we do, we will have 100 times more information about cancer cells, with all their abnormalities, than we do for normal tissues, because of the sheer number of variations.

"They will give us the power to correlate what happens in cancerous cells with normal cell activity. It can be difficult to find or engineer a cell line with a particular mutation, but 20 years hence, you go to the cancer databases, you'll have comprehensive information on the physical and metabolic effects of different mutations in your gene of interest, for as many as 1300 different human cancers.

"We predict there will be massive spinoffs that rapidly find application across the biological sciences, and in the biotechnology industry."