

Gaps in the genome

On the eve of the Lorne Genome Conference, Melissa Trudinger takes a candid look at the state of genomics research in Australia.

AUSTRALIA HAS slipped behind other countries in genomics research, with little money available to fund large-scale genomics projects, and apparently little interest – with one notable exception – from state and federal governments in the science.

It's a frustrating situation for genomic scientists, and also for others who would like to avail themselves of the substantial resources that genome sequence data and maps provide to the biological sciences.

"It's disappointing that Australia hasn't made bigger contributions in this area," says Prof John Mattick, from Queensland's Institute of Molecular Bioscience. "All of our sciences rely on the contributions of other countries."

Australian researchers had little to do with the Human Genome Project, and since the end of that flagship project and the flowering of genome projects to sequence a wide variety of organisms, has not substantially increased its participation. In fact, Australia has participated in only a couple of major genome projects to date – the bovine genome project and the *Brassica* genome project, and has missed the boat on others.

Last year, the US National Institutes

of Health's National Human Genome Research Institute (NHGRI), which has coordinated many of the genome sequencing projects to date, chose to sequence a US marsupial – the opossum – rather than an

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Australian species, despite Australia being home to the vast majority of the marsupials. And the Americans are also sequencing the platypus, another iconic Australian species, with little or no input from Australian researchers.

According to the genome research community in Australia, though, it's not from lack of interest but from lack of funding of the scale required to participate in the expensive programs.

Neither the National Health and Medical Research Council nor the Australian Research Council, Australia's two major research funding agencies, have the funds

available for large-scale genomics projects, although funding is available through standard grants schemes for smaller targeted projects aimed at identifying specific genes, or sequencing the small genomes of pathogens.

"The ARC won't fund broad genome sequencing projects, although they will fund projects answering specific questions with direct biological outcomes," says Sue Forrest, the director of the Australian Genome Research Facility, a major national research facility that provides sequencing, genotyping, microarray and

other genetics and genomics services to Australian researchers. "It's disappointing, but at least it's a policy."

The NHMRC provided around \$8 million in funding in 2001 for four projects in medical genomics, and is currently seeking expressions of interests for another \$10 million round of funding, this time in medical bioinformatics, genomics and proteomics.

But large-scale genomics projects typically cost tens of millions of dollars, and there is nothing set up in Australia to provide that kind of funding.

Embarrassingly, a bid to sequence the

THE DIVERSITY OF GENOMICS RESEARCH

According to convener Alex Andrianopoulos, the major theme of this year's Lorne Genome Conference is turning out to be evolution and comparative genomics.

The theme is reflected by the choice of some of the international speakers who will be attending the conference. Patrick Keeling, a professor at the University of British Columbia's Canadian Institute for Advanced Research, will talk about his research into the molecular evolution of protists – single-celled eukaryotes. Keeling's lab uses molecular methods to study the evolution of these organisms, which provides insight into eukaryotic evolution, as well as hints about the evolution of parasitic relationships and the origin of organelles.

Another international speaker with an evolutionary interest is Sean Carroll, who is studying the evolution of developmental processes, using *Drosophila* as a basis and now branching out to compare *Drosophila* developmental processes to those of other organisms. And Celera Diagnostics' Michele Cargill will talk about the work she has done to compare genome evolution in mice, chimps and humans.

But other areas of genomics have not been forgotten. International speakers also include Affymetrix's Tom Gingeras, who will talk about his recent work on gene regulation; Alexander Johnson from the University

of California, San Francisco, who will describe his studies on the regulation of mating in yeast species *Saccharomyces cerevisiae*, and comparisons with the pathogenic yeast species *Candida albicans*; and Kent Hunter from the NIH's National Cancer Institute, who will describe the mapping of genes responsible for tumour metastasis in mice.

Australian speakers presenting at the conference include Julian Wells Medal winner Richard Harvey, from the Victor Chang Cardiac Research Institute, who will speak about his research into the molecular mechanisms underlying the development of the mammalian heart (see story, page 34). Researcher David Miller, from James Cook University in Queensland, will present details of his research into the developmental genomics of corals. And Frank Grutzner from the ANU will present his work on the unusual sex chromosomes of the platypus, which was recently published in *Nature*.

Andrianopoulos says there is also a move away from the purely technology-based talks of recent years, as researchers start to get a handle on the immense amount of genomic information that has been generated since the human genome project was completed. "Now it's the biology that's important," he says.

– Melissa Trudinger

tammar wallaby genome at a low level of coverage (2X) to supplement the sequence data from the opossum almost didn't go ahead due to the lack of funding available for the project, despite a pledge of matching funds from the NHGRI.

The Victorian government saved the day, upping its initial pledge of funding from \$1 million to \$4.5 million, which along with the \$1.5 million in support, mostly in the form of equipment and reagents, from Applied Biosystems, was enough to get the project off the ground.

"It's particularly disappointing that we have found it difficult to raise funding to sequence our national icon, despite the US offer to pay half," says Mattick, who is on the board of the AGRF, which – along with the ARC's Special Research Centre for Kangaroo Genomics led by Prof Jenny Graves at the ANU – is spearheading the wallaby genome project. "With the notable exception of the Victorian government, none of the other state or federal governments have seen the importance of doing this."

The problem, according to Mattick, is a lack of understanding by research funding agencies and governments of

the importance of genome research as an underpinning to other biological sciences research. He says the view that genes lead to proteins is a limited one, and that more information on the workings of the genome is required.

One way or another, the consensus from genomics researchers is clear – they would like to see more money for large-scale genomics in Australia. And it isn't likely that the money would be thrown at random projects – the genome projects currently being planned or conducted bring with them strategic as well as scientific benefits.

"It's not as if we'd be sequencing any old genome," Forrest says. "For projects to be proposed they have to be important just to get the consortium together."

University of Melbourne geneticist Phil Batterham, who is behind the two insect genome projects – the sheep blowfly and the cotton bollworm moth – with the promise of substantial agricultural benefits downstream, says genomics will provide a solid platform for continuing research into insect pests in a more targeted fashion, to identify the mechanisms of developing resistance

to insecticides, vulnerable points in the life cycle, and so on.

"For some of these organisms, tens of millions of dollars have been spent so far with little effect," he says.

A MIXED PORTFOLIO

One thing to consider is how to fund the genome projects. Mattick says it would be best to fund them completely separately from the existing research funding agencies – and that it's important that any funding designated for genome research doesn't result in a diminishing of general research funding by the NHMRC or ARC.

"There should be a targeted genomics program in Australia that could be modelled on the either that of the US or of Canada," he says.

While the US genomics program, which is coordinated by the NHGRI, takes a strategic look at what genomes should be sequenced and why, Genome Canada provides funding to projects submitted based on merit.

"It would be good to look at the stronger aspects of those two countries," Mattick says.



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TRUE BLUE GENOMICS

Here is a selection of the current and future plans for large-scale genome mapping and sequencing projects in Australia.

Bovine: US\$53m, international project, involves NHGRI, US Dept of Agriculture, State of Texas, Genome Canada, CSIRO Livestock Industries, and NZ's Agritech Investments, Dairy Insight and AgResearch. Due for completion 2005.

Tammar wallaby: AUD\$6m, matched by NHGRI, led by led by ARC Special Research Centre for Kangaroo Genomics and AGRF, supported by Victorian government, Applied Biosystems, Human Genome Sequencing Centre at Baylor College of Medicine (Texas). Due for completion 2006.

Sheep blowfly: AUD\$1.4m from Australian Wool Innovations to Australian and NZ researchers led by the University of Melbourne's Phil Batterham, to map the genome of the sheep blowfly *Lucilia cuprina*.

Cotton bollworm moth: Batterham is also lobbying for funding for the genome sequencing of the cotton bollworm moth *Helicoverpa armigera*.

Brassica: Victorian Department of Primary Industries' Plant Biotechnology Centre (PBC), La Trobe University, researchers working to sequence a chromosome from the *Brassica rapa* A genome as part of the Multinational Brassica Genome Project (MBGP), joining other researchers from the US, Europe,

Canada, China and Korea. Supported by Grains Research and Development Corporation, Horticulture Australia, Victorian government. Whole genome sequence expected to be available by end 2007.

Eucalyptus: Scientists from Australian universities, CSIRO, various government departments and the AGRF, as well as from South Africa, Brazil, France and the USA, formed a consortium in 2004 to map and sequence the genome of the southern blue gum, *Eucalyptus globulus*. It is unclear what the scope of Australia's participation will be in the project, or whether it will go overseas.

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In any case, he says, the genome portfolio should be mixed, with projects of economic and scientific interest – preferably both. Budget-wise, Mattick believes that Australia should invest about half the amount that Genome Canada has to date, given that Australia is about two thirds the size of Canada.

The Canadian government has so far invested C\$386 million into Genome Canada, with a further \$469 million raised through contributions from provincial governments, industry and foreign support.

Forrest says she can see the need for Australia to have about 10 major sequencing projects underway, in addition to other kinds of large-scale genomics projects such as linkage studies. In addition, smaller scale studies to map genomes and generate databases of ESTs would be necessary for biological discovery, she says.

"If we can fund manageable genome projects, then we have a significant advantage in capturing intellectual property locally – that's a major issue," Forrest says.

"We're not asking to sequence everything under a rock in this country – it's about choosing relevant projects. If we don't do these projects, we will find it difficult to stay in or even maintain our position – we risk slipping backwards and losing our position of strength and scientific capability."



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