



CONNECTIONS

Bioplatforms Australia Quarterly Newsletter | Q2-2010

UNDERGRADS SEQUENCE WOLLEMI PINE

Universities have faced difficulties keeping pace with advances in instrumental techniques when training students in Molecular Genetics and Genomics

The Ramaciotti Centre at UNSW has started a program to redress this by giving students access to next-generation sequencing. In the first application of this policy, the Centre donated time on the next-generation sequencers to third year students who have sequenced the chloroplast genome of the ancient Wollemi Pine – a world first that could reveal how a “dinosaur” of the tree kingdom survived 200 million years of

remote rainforest canyon in Wollemi National Park, 150 kilometres north-west of Sydney. Fewer than a hundred trees are known to be growing wild, in three localities not far apart. These trees show an extremely low level of genetic diversity and are threatened by introduced fungal diseases and climate change. The Wollemi is being protected from extinction by secrecy surrounding the locations of the wild populations, and by widespread cultivation of the pine in Australia and around the world.

The students' preliminary findings show that the Wollemi chloroplast DNA is unique but shares some features with other pines such as the Kauri and Norfolk Island Pine. Further analysis of the data will provide clues to the evolution of the Wollemi and other pines. The students presented their original findings as a poster at the Australasian Microarray and Associated Technologies Association Conference (<http://www.amata.org.au/>) in October 2009.



WOLLEMI PINE PROJECT

University of NSW students at work on the Wollemi Pine Project

shifting continents and changing climates. Using next-generation sequencing machines in the Ramaciotti Centre for Gene Function Analysis, the students have produced a draft sequence of the approximately 180,000 nucleotides of the DNA code of the Wollemi's chloroplast genome.

The Wollemi (*Wollemia nobilis*) was known to science from fossil records but was thought to be extinct until 1994 when David Noble discovered it in a

The research project exposed students to leading-edge technology that allowed them to take part in actual research rather than set experiments and to get a feel for the real process of research. Exposure to this technology is rare in degree-level science programs and was made possible by the outstanding sequencing research facilities at UNSW and an ongoing collaboration between researchers at UNSW and the Royal Botanic Gardens Sydney.

METABOLOMICS AUSTRALIA FORGE NEW LINKS IN RESEARCH

Metabolomics Australia facilities within the Bio21 Institute and School of Botany at the University of Melbourne have been used to establish strong links with many University and Institute research groups around Melbourne providing access to state-of-the-art metabolomics technologies for a number of new research projects. Two examples follow:

Novel biomarkers for diabetic nephropathy

The Metabolomics Australia node at The University of Melbourne is partnering with Dr John Wentworth from the Walter Eliza Hall Institute to identify novel biomarkers for early stage diagnosis of diabetic kidney disease in order to provide more effective treatment options.

A long standing diabetic condition often leads to kidney disease especially when sugar blood levels are badly managed. Kidney disease is expensive to treat and often leads to early death. While diabetic kidney disease can be diagnosed using a number of clinical markers established for blood and urine, all are non-specific and do not correlate with disease onset or progression. The current tests are important for medical intervention aimed at slowing kidney disease, however, most people still suffer kidney failure as irreversible damage has already occurred.

Research will centre on the urine samples of 60 diabetic patients collected over ten years. Half the patients have developed nephropathy allowing critical metabolic comparisons between the two cohorts. Once metabolic markers are identified and validated, the next phase of the project will seek collaboration with Proteomics



Over the next three years, BioplatformsAustralia will co-ordinate an additional \$50 million in infrastructure investments

and Genomics Australia to explore complementary markers for instance peptides, proteins or small RNA fragments.

The generous financial support of the Cass Foundation (<http://www.cassfoundation.org/>) will allow a broad range of complementary analytical platforms to be employed. Metabolomic techniques such as gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) will be used for untargeted screening and quantitative metabolite analyses will utilise LC-MS and NMR to measure, quantify and compare thousands of small molecules. Metabolomics Australia will provide the sophisticated bioinformatics support required for statistical analysis and expert capabilities in multivariate analysis to develop mathematical models for identifying potential metabolic markers.

Cancer research

A major project established with researchers from the Peter MacCallum Cancer Research Institute, East Melbourne, is directed at understanding the mode of action of new generation anti-cancer drugs. Dr Rick Pearson and his team have access to over 50 different cancer cell lines with defects in specific signaling pathways and varied metastatic potential. These cell lines are being treated with a library of compounds provided by big Pharma and metabolic responses will be determined using a range of analytical approaches, including gas chromatography-mass spectrometry.

Alterations in the steady state levels of key metabolites can be used to identify specific metabolic processes that are altered in the cancerous cell line as well as those that are being targeted by the drugs. This approach can be used to identify novel biomarkers for different cancer cell types and aid diagnosis.

This project has resulted in a close collaboration between researchers at the Peter MacCallum and Metabolomics Australia's Bio21 Institute. Researchers from both laboratories have been involved in the development of new methods for metabolically quenching the cancer cells, metabolite extractions, experimental design and data analysis.

Data analysis remains a major challenge with 'omic investigations, including metabolomics datasets, however, the Metabolomics Australia bioinformatics team at Melbourne University have made considerable progress. The team is developing a range of statistical and multivariate analysis to identify the metabolic pathways potentially affected. This data will be coupled with other 'omic' datasets, including transcript and proteomic analyses generated by the Peter MacCallum Institute research groups, to provide a comprehensive view of the cellular response of different cancer cell lines to new drugs.

SYSTEMS BIOLOGY SEMINAR IN CAPITAL CITIES

Bioplatforms Australia aims to promote systems biology and showcase Australia's 'omics capabilities with the seminar "Lessons in winemaking: An example of integrated 'omics at work".

Dr Paul Chambers, Research Manager of the Australian Wine Institute will offer invaluable insights on the benefits and challenges of a systems biology approach as demonstrated by a multi-disciplinary wine yeast project. As highlighted in our last edition, this ambitious project aims to build a

knowledge base of wine yeast genetic and biochemical systems which can then be used to engineer novel wine yeast strains to improve the commercial performance of yeast in winemaking.

The seminar is being offered in capital cities throughout August. Dr Chambers will be joined by speakers from Genomics Australia, Proteomics Australia and Metabolomics Australia. Please see <http://www.bioplatforms.com.au/news-and-resources/news-and-events>, for further details.

NEW STUDY ON COMMUNICATION NETWORKS IN MICROBES

Macquarie University has been awarded two ARC Super Science Fellowships to undertake an 'omics based study on microbial communication and interaction networks.

The Commonwealth funded fellowships will train early career postdoctoral scientists in new biomolecular technologies, particularly in the areas of genomics, proteomics and glycomics, to quantify and characterise how microorganisms interact with each other and their environment.



SYSTEMS BIOLOGY SEMINAR
the Australian Wine Institute



BIOMEDICAL SCIENTISTS FROM MACQUARIE UNI.

Paul Haynes, Mark Molloy, Helena Nevalainen, Nicki Packer and Ian Paulsen

The project will focus on the infectious bacterium, *Pseudomonas aeruginosa* and its interactions in the tissue it infects (such as lungs) as well as with fungi including those that co-colonise cystic fibrosis patients. Research efforts will use proteomic and transcriptomic analyses of *P. aeruginosa* grown in artificial lung sputum medium and sputum samples to study how the bacteria aggregate in the lungs. Glycomic and proteomic analyses will be combined with functional genomics in order to identify microbial binding proteins. Functional genomics, proteogenomics and glycomics analyses will also be used to investigate the unique lifestyle of bacteria and fungi cohabitation.

'The Commonwealth funded fellowships will train early career postdoctoral scientists in new biomolecular technologies

The research will take a system-wide approach and utilise the unique collective expertise in proteomics, glycomics and genomics at Macquarie University. Results should offer valuable insights into the importance of previously uncharacterised genes,

proteins and glycans in human pathogenic microorganisms and their impact on the human tissues they infect. Such information will provide new treatment leads for associated diseases.

The fellows will work with a highly experienced team of biomolecular scientists (Paul Haynes, Mark Molloy, Helena Nevalainen, Nicki Packer and Ian Paulsen) and have access to the renowned expertise of APAF (Australian Proteome Analysis Facility) and the complimentary research strengths of the MQ Biomolecular Frontiers Research Centre. The project also offers strategic advantages by providing invaluable multi-discipline training for early career researchers while supporting the emergence of systems biology in Australia. It also leverages the first grade 'omics research capacities of Macquarie University.



HPLC AT AUST. PROTEOME ANALYSIS FACILITY

\$50 MILLION IN NEW FUNDING

To further expand the national infrastructure network managed by Bioplatforms Australia, the Commonwealth government has provided new funding from the Education Investment Fund Super Science initiative.

Over the next three years, Bioplatforms Australia will co-ordinate an additional \$50 million in infrastructure investments to further enhance Australia's 'omics capabilities.

Host universities and research institutions have been identified and sub-contracts are presently being executed in order for instrument purchases to get underway. Most new instrumentation will be commissioned by the end of the year enabling a host of novel research projects and a whole range of new 'omics services for the broader scientific community.

BIOINFORMATICS BOOST

Super Science funding will be used to advance Australia's bioinformatics analytical environment to ensure software, databases and information technology become integrated with the latest generation of 'omics capabilities.

In particular, Bioplatforms Australia will kick off an exciting initiative to create the strategic datasets needed to advance systems biology in Australia.

Large scale datasets are critical to employing a systems biology approach, however, available funding within disciplinary boundaries is rarely sufficient to generate such significant data mass. Bioplatforms Australia hope to overcome this bottleneck by supporting the genomic, proteomic and metabolomic analysis of nationally prioritised specimens and samples. Priorities will be based on potential economic, scientific and/or social benefits and include wheat, barley, cancer types and unique Australian flora and fauna. The datasets will become a centrally managed resource that can be utilized by all sectors of the research community.



By investing in the latest advances in imaging mass spectrometry, the University of Adelaide will harness some remarkable gains

NEW TISSUE IMAGING MASS SPECTROMETER AT THE ADELAIDE PROTEOMICS CENTRE

The University of Adelaide will invest Super Science funding to acquire the latest imaging mass spectrometer to gain new capabilities in tissue imaging.

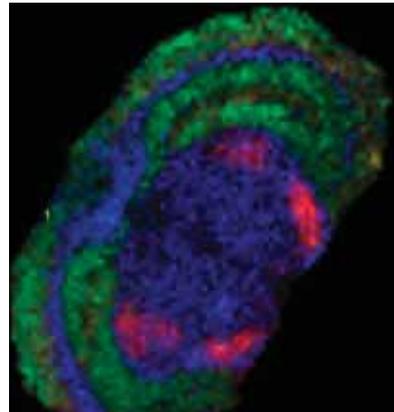
Matrix-assisted laser desorption/ionization (MALDI) mass spectrometry is a powerful tool for investigating proteins and small molecules in animal and human tissue samples. Although the technology is relatively young, it is rapidly advancing and making considerable contributions to understanding diverse areas of human health. Consequently,



PETER HOFFMAN WITH THE LAST GENERATION MALDI TOF/TOF MS

MALDI mass spectrometry is fast becoming a critical tool for cutting edge proteomics studies, however, the required investment is significant. Instrumentation costs are around \$700,000-800,000 with additional expenditure needed for automated matrix deposition instrumentation, software as well as computers powerful enough to handle the massive data analysis required.

By investing in the latest advances in imaging mass spectrometry, the University of Adelaide will harness



MALDI TISSUE IMAGE OF MOUSE BRAIN SECTION

some remarkable gains in sensitivity, robustness and automation. New developments in the laser alone, offers almost a five-fold improvement in time to analyse a tissue section when compared to previous laser technology. Other advances in automation and visualisation offer significant labour savings and decreases in processing time. Such advances propel the potential of the technology for diagnostic applications and those related to assessing drug effectiveness.

The University of Adelaide will apply the instrument to deciphering the biological processes underlying disease with projects on ovarian cancer and a collaboration to study brain tissue samples with the Australian Multiple Sclerosis Society.

The University of Adelaide will finalise its purchase in the next few months and seek to have the new imaging

mass spectrometer commissioned and put to work by the end of the year. The instrument will also form part of the national infrastructure established and co-ordinated by Bioplatforms Australia enabling broader access to the technology through the research services offered by the Adelaide Proteomics Centre at the University of Adelaide.

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AUSTRALASIAN METABOLOMICS SYMPOSIUM 2010

The second Australasian Metabolomics Symposium will be held at the University of Melbourne from 3 to 5 October 2010.

The symposium follows a three day metabolomics workshop for novices interested in the field.

Further information available at www.bioplatforms.com or contact Dr Ute Roessner u.roessner@unimelb.edu.au.



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