Volume 3
March 2007

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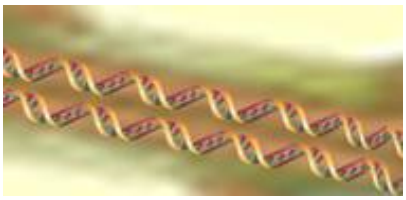
AUSTRALIAN PHENOMICS NETWORK

Phenomena

NCRIS 5.2 Funding to Support Animal Models of Disease

The National Collaborative Research Infrastructure Strategy (NCRIS) is a programme that was announced by the Australian Government in 2004 as part of Backing Australia's Ability – Building our Future through Science and Innovation.

The objective of the NCRIS lead investment is to greatly expand the number of human disease mouse models and significantly lower the cost of accessing these models.



The proposed infrastructure investment will allow for internationally leading research results, the achievement of much faster research programmes, and a growing internationalisation of the Australian medical research investment.

The $15 million the Government is committing through the (NCRIS) to systems biology infrastructure will greatly increase the ability of our researchers to study the observable characteristics of animals – their phenotypes – and how these relate to their genetic make-up. Mice have become indispensable in research into human biological systems because of their genetic similarities to humans. NCRIS funding is establishing an Australian Phenomics Network to increase the number of mouse models of human disease available to Australian researchers and so reduce the cost of accessing them.

The participating institutions in the Australian Phenomics Network are:

- The Australian National University
- Monash University
- Walter & Eliza Hall Institute
- The University of Melbourne
- Queensland Institute of Medical Research
- Menzies Research Centre, University of Tasmania

Further information on NCRIS 5.2 will be forthcoming in the next edition of Phenomena.

New Gene Variant Mouse Strains Available

Listed below are new heritable phenotypes discovered by APF staff from ENU-gene variant libraries. If you are interested in any of these strains please contact Dr Stuart Read: Stuart.Read@anu.edu.au

Gene Variant Strains:

T-Bird – mice develop a dull sparse coat which appears slightly greasy after ~60 days. The trait is recessive. Affected males are fertile, affected females breed poorly or not at all. Mice are viable and display normal behaviour.

Eddie - Generalised shaking, mild hypermetria, jerky movements, non progressive. First noted at weaning, trait is recessive. Affected mice do not breed but otherwise appear healthy

Tremors - Generalised tremors first noted close to weaning. Generalised tremors noted at around 70 days of age. Disease is progressive with marked shaking when stressed, generalised weakness and periods of head dropping or recumbency suggestive of seizures. Affected mice did not breed. Trait is recessive.

Pengu - Four shortened limbs with angular deformity, most pronounced in hind limbs. Some have kinked tail. The mice appear otherwise healthy.

Hipster - White stripe transverse across abdomen. Affected mice breed well. Trait is recessive.

Hypoglycaemia - Pups show weakness, shaking and seizures at around 2 weeks of age. Some show progression of symptoms, develop seizures and die. Some pups show only shaking and are normal after weaning. Temporary improvement in symptoms with administration of oral sucrose. Trait appears recessive.

Dorian – mice change coat colour from agouti or black to grey / white at approximately 40 days old.

APF–AGRF Establish Alliance to Facilitate Quality Service in mutation detection in mouse gene variant strains

The APF has recently formed an alliance with the AGRF (Australian Genome Research Facility) allowing a joint approach for providing a streamlined, consistent, high quality service spectrum for researchers. Belinda Whittle as Mapping and Genotyping Manager has written a proposal for the integration of a number of APF/AGRF services. This partnership will involve several services of the AGRF including the genotyping and mapping team utilising the Affymetrix and Sequenom technologies and the Sequencing, Bioinformatics and R&D teams. The APF will maintain a standing at the forefront of mouse variant strain mapping with the design and analytical expertise remaining centralised to the facility. However, in a forward approach the link with AGRF will allow the APF to utilise the latest mapping technologies and offer the best possible service for the most difficult of projects.

As part of this alliance the APF are using the AGRF's Affymetrix Gene Chip Mouse Mapping 5K SNP Kit. These chips offer a denser set of markers with the average informative marker density being greater than 1 per Mb, ensuring that linkage will be detected with multiple markers regardless of previous meioses. The first set of samples sent in late December produced some exciting linkage results for a Monash group that will now be confirmed by the APF mapping team using the Amplifluor system. Since January, linkage in a further eleven strains has been detected using the Affymetrix SNP chip technology. Nine of these strains form a major project involving phenotypic screens for Arthritis.

The APF mapping resource has not only been involved in mapping ENU variant strains but within the past 6 months has also attracted researchers wanting to map spontaneous mutants and causative polymorphisms between two inbred strains. The APF's recent mapping success can be attributed to the new Affymetrix technology and the in-house custom Amplifluor Genome scans that have also identified initial linkage in a number of strains on C57Bl/6 x C57Bl/10 crosses. These include several immunological variant strains with B- and T-cell defects and an ANA positive strain.

The APF now offers a full mapping service beginning with design and initial chromosomal location through to resequencing and identification of a mutation. In January the facility acquired a software package (produced by Nancy Hong formally of Phenomix, USA) that will greatly improve the efficiency of searching for genes in a mapped interval and designing primers for resequencing. The script for interval analysis enables gene and exon annotation including candidate gene searches through OMIM and JAX files. While the primer picking script enables primer selection appropriate for PCR sequencing. This package will now be used for all mapping projects within the facility. In addition, the AGRF sequencing service will now perform the high throughput mapped interval resequencing runs. The introduction of a 454 Sequencer to the AGRF will also be a future advantage to all mapping projects with the possibility of performing resequencing of larger genomic intervals more efficiently at lower costs.

For more information please contact the Mapping and Genotyping Manager, Belinda Whittle on 61 2 61257756 or Belinda.Whittle@anu.edu.au.

APN to Sign MOU With NorCOMM

Dr. Geoff Hicks, from the Manitoba Institute of Cell Biology, who is leading the North American Conditional Mouse Mutagenesis (NorCOMM) project along with Dr. Janet Rossant (Toronto) in Canada, spent the morning at the APF along with his colleagues Reno Pontarollo, CSO Genome Prairie/Project manager-NorCOMM and Allen Sturko, Life Science Branch Government of Manitoba. They discussed Australia's needs for gene targeted mouse models of animal disease and an MOU will be signed between the 2 parties, enabling the APF to act as a point of contact for the distribution of gene-targeted ES cells to Australian researchers.

Geoff Hicks (centre) sits between Chris Goodnow and Moira O'Bryan. Key members of the APN-NorCOMM agreement.

http://norcomm.phenogenomics.ca/index.htm

APF Visits Singapore

APF members Robert Wells, Steve Winslade, Adrienne McKenzie and Ed Bertram visited Singapore in late October 2006 to explore ongoing collaborations and commercial opportunities.

They visited the A*STAR Research Centres at the Biopolis including Mr Rob Kozma and Dr Thomas Luftkin from Genome Institute, Dr Neal Copeland and Dr Nancy Jenkins from The Institute of Molecular and Cell Biology, Dr Jean-Pierre Abastado from Centre of Molecular Medicine and Dr Andre Wan, Director of the Biomedical Research Council toured the Resource Centre with Dr Sathi Ponniah. http://www.a-star.edu.sg/astar/index.do.

The team also met with Ms Loh Chin Siew, Associate Director (Investments) for BioOne Capital and met representatives of Singapore based companies including Dr Sarah Lynagh from Maccine, Dr Michael Richardson from Vanda Pharmaceuticals and Steve Breen from Kios.

L-R: Steve Winslade, Andre Wan, Adrienne McKenzie, Ed Bertram, Ken Kakihara and Robert Wells/ Discussing opportunities over dinner at the Botanic Gardens.

APF Visits RIKEN at Tsukuba

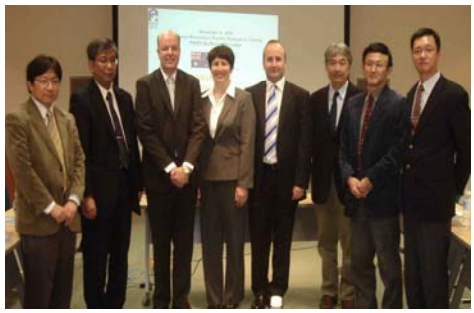
After meeting with Ken Kakihara, RIKEN representative in Singapore, the APF team travelled to Tsukuba, just out of Tokyo to visit Dr Yuichi Obata, Director of RIKEN BioResource Center. The APF were the first Australian group to tour this facility and were warmly welcomed.

A day of talks from key RIKEN personnel including Kuniya Abe, Head of the Technology and Development Team for Mammalian cellular Dynamics, Atsuo Ogura, Division Head, Bioresource Engineering Division, Shigeharu Wakana, Team Leader, Mouse mutation Resource Exploration Team and Atsushi Yoshiki, Head of the Experimental Animal Division was followed by a tour of the facility. For information on RIKEN Bioresource centre and gene-variant mouse strains available to the research community, please go to:

http://www.brc.riken.jp/inf/en/

Both APF and RIKEN are founding members of FIMRe:

http:// www.fimre.org



Dr Yuichi Obata (second from left), Director of RIKEN BioResource Centre and colleagues with Steve Winslade (third from left), CEO of APF and team.

Professor Marc Feldmann Visits APF

Professor Feldmann (from file)

Professor Marc Feldmann is Head of the Kennedy Institute of Rheumatology Division at Imperial College , London. He has made important contributions to our understanding of the pathogenesis and treatment of chronic autoimmune and inflammatory disorders. Over the past 20 years his pioneering studies on the role of cytokines in autoimmunity have led to the development of an effective therapy for patients with resistant rheumatoid arthritis and Crohn's disease.

Professor Feldmann, an Australian, has lived overseas for many years but maintains close contacts with Australian scientists and institutions. He was a joint recipient of both the Crafoord Prize of the Royal Swedish Academy of Sciences in 2000 and the Albert Lasker Clinical Medical Research Award in 2003.

During his visit to ANU and the Australian Academy of Sciences, of which he became a corresponding member, he visited the APF and gave a presentation at JCSMR titled: "The dual face of NGkB/TLR pathways: vaccination and autoimmunity"

Professor William Paul Visits the APF

In September 2006, the APF was privileged to host Professor William Paul, Chief, Laboratory Of Immunology, National Institutes of Allergy and Infectious Disease. He met with APF staff and discussed strategies to utilise the facility for infectious disease research. He gave the seminar titled "Th2 Differentiation: Transcription factors and Repertoire-determined Immunopathology" at the new John Curtin School of Medical Research.

Dr. Paul is a leading immunologist, well known for his discovery of interleukin-4 (IL-4) and the characterization of its receptor and its signaling mechanisms.

Dr. Paul was Director of the Office of AIDS Research at NIH and established the office as the prime mover in determining national AIDS research policy. Under his leadership, the OAR developed a comprehensive plan and a unified budget for all NIH-sponsored AIDS scientific activities and placed a major emphasis on HIV vaccine research. Dr. Paul is a member of the U.S. National Academy of Science and of its Institute of Medicine. He is a fellow of the American Academy of Arts and Sciences. He received the 1980 Founder's Prize of the Texas Instruments Foundation, the 1988 3M Life Sciences Award and the Tovi Comet-Wallerstein Prize of Bar-Ilan University. He is the recipient of honorary doctorates from the State University of New York, the Hebrew University of Jerusalem and the Medical University of Cluj-Naporca, Romania. Dr. Paul has been president of the American Society for Clinical Investigation and of the American Association of Immunologists. He is founding editor-in-chief of the Annual Review of Immunology and the editor of the advanced textbook, Fundamental Immunology, now in its fifth edition.

Chris Goodnow (CSO of APF) with Bill Paul.

New NHMRC Australian Phenome Bank Available Online:

The Australian Phenomics Facility has developed an Internet-accessible database of murine strains housed in Australia. This database, which is accessible to all researchers, can be accessed online at: http://pb.apf.edu.au/phenbank.
In association with the Phenome Bank database the APF is offering a sperm cryopreservation service. The service is free of charge if the strain(s) are distributable to other researchers.

Professor Lu, President, Chinese Academy of Sciences Visits APF

Professor Lu Yong Xiang (from file)

Professor Lu Yong Xiang was inducted as a corresponding member into the Australian Academy of Science following his presentation at the Shine Dome "Future Perspectives of China." Earlier in the day he met with Professor Chris Goodnow and Dr Ed Bertram at the APF to discuss strategies for collaborations between Chinese and Australian Scientists in mouse genome-phenome research along with Cao Jinghua, Deputy Director General, Bureau of International Cooperation and Yongguan Zhu, Assistant Director General.

Professor Lu Yong Xiang has served as the President of the Chinese Academy of Sciences since 1997 and actively promotes the development of scientific research and education. He is currently Vice Chairman of the Standing Committee of the National People's Congress, People's Republic of China. Professor Lu has received numerous prestigious awards including a Knight Commander's Cross (Badge and Star) from the Federal President of Germany in 2000.

KOSEF Visit APF

Dr Oh-Kab Kwon, Chairman and CEO of the Korea Science and Engineering Foundation (KOSEF) and Byung-Whan Ho, Director of International Programs visited the APF on Thursday 7 December, coinciding with the State visit by the President of the Republic of Korea, Mr Roh Moo-hyun. For more information on KOSEF:

http://www.kosef.re.kr/english_new/

In an important new move to strengthen scientific research linkages between Australia and the Republic of Korea, the key scientific bodies of both nations have signed a letter of intent with a main focus on early-career scientists and improved information exchange. Recognising the mutual benefit of scientific and technological interchange, the Australia-Korea Foundation, the Australian Academy of Science, the Australian Academy of Technological Sciences and Engineering and KOSEF have used the signing to ratify their commitment to encourage and facilitate an innovative new program in both countries.

L-R: Dr Stuart Read, Dr Byung-Whan Ho, Dr Oh-Kab Kwon and Dr Ed Bertram.

Japanese Centre of Research Network for Infectious Diseases visits ANU

Dr Yoshiyuki Nagai (second from right, front row) and Japanese colleagues visit the APF.

By invitation of the National Centre of Biosecurity, Dr Yoshiyuki Nagai, Director of the Center of Research Network for Infectious Diseases and a team of researchers from Japan visited the ANU for discussions on similar interests in the Asia-pacific region around infectious disease research and biosecurity. The team spent time at the APF with Ed Bertram, Head of Scientific Programs and CEO Steve Winslade.

AUSTRALIAN PHENOMICS NETWORK

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The APF is a Major National Research Facility that is openly accessible to all Australian and International Researchers, both academic and commercial.

The APF is dedicated to providing the national and international academic and commercial scientific community access to genome scale collections of mice with informative point mutations.

Our mission is to:

- provide access to state-of-the-art facilities, technologies, resources and expertise for analysing connections between mammalian genes and physiological processes,
- foster interdisciplinary linkages between the mammalian genome and phenome, and promote invention and uptake of new genome-phenome analysis tools by Australian and International research and industry in health, agriculture, the environment and biotechnology.

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