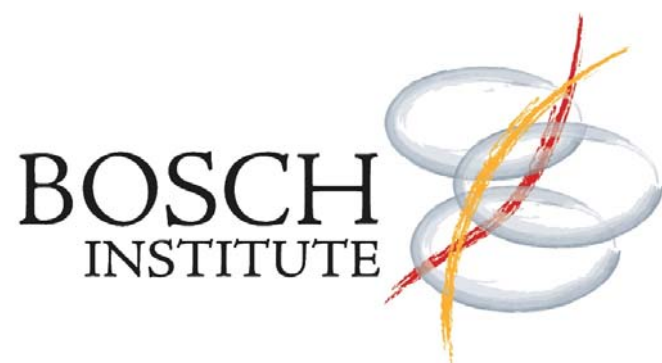


**The Bosch Institute
Brief update
July – September 2007**



Bosch research team discovers binocular vision gene



Atomu Sawatari, Catherine Leamey and Sam Merlin (l to r)

Dr Catherine Leamey heads the Developmental Neurobiology Laboratory of the Bosch Institute. In collaboration with her colleagues from the Massachusetts Institute of Technology (MIT) and the Max-Planck institute for Biochemistry in Germany, Dr Leamey's team have identified an important gene responsible for binocular vision. The researchers previously discovered *Ten_m3* in a screen to identify genes that are important in establishing appropriate patterns of neural connectivity in the developing visual system. They have now shown that *Ten_m3* is critical for the brain to meld images from the two eyes into one useful picture in the brain. This discovery may lead to new treatments for sensory disorders in which people experience the strange phenomena of seeing better with one eye covered. This is important for humans who normally see a single in depth view of visual space that integrates signals from both eyes; this process is disrupted in people with visual disorders such as strabismic amblyopia, for example.

The developing nervous system needs to overcome many problems to enable us to perceive the world appropriately.

Understanding how projections from the two eyes are integrated in the brain has fascinated researchers for decades. Dr Leamey commented "The work is exciting because it is the first discovery of a molecule which specifically regulates the alignment of the projections from the two eyes. The importance of this for visual function was elegantly demonstrated by the behavioural experiments performed by PhD student Sam Merlin. These showed that mice lacking *Ten_m3* perform behavioural tasks that require patterned vision as if they were blind. If projections from one eye are blocked, however, the mice were able to perform the tasks normally. The rescue of visual function was astonishing and tells us immediately that it is the mismatch of projections from the eyes in the *Ten_m3* mutants that underlies their visual deficits. The findings are also supported by our anatomical data". The full report was published in the Sept. 4 issue of Public Library of Science (PLoS) Biology.

Dr Leamey commenced this project while she was undertaking her Postdoctoral period at MIT in the laboratory Professor Mriganka Sur. The project continues to be an ongoing international collaboration, but much of the work is now undertaken in her laboratory within the Bosch Institute. Current PhD students Sam Merlin and Kelly Glendining as well as previous Honours students Paul Lattouf and Natasha Demel and collaborator Atomu Sawatari, also of the Bosch Institute, all contributed to the work.

This work was funded by the National Health and Medical Research Council, The National Institutes of Health and the Simons Foundation.

Information related to these studies can be found at this website:

<http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.0050241>

Bosch CJ Martin Fellow



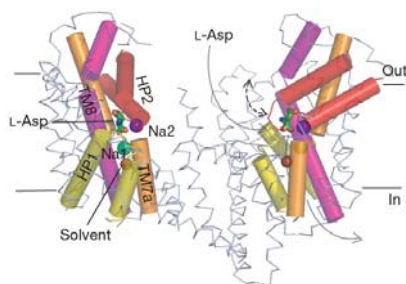
Dr Renae Ryan is a CJ Martin Fellow in the Bosch Institute. Dr Ryan completed her PhD in the Discipline of Pharmacology under the supervision of Associate Professor Rob Vandenberg, head of the Molecular Pharmacology Laboratory within the Bosch Institute.

Dr Ryan has recently returned to the Bosch Institute following a 3 year Postdoctoral Fellowship, 1 year in the lab of Eric Gouaux at Columbia University and 2 years at the NIH/NINDS with Joe Mindell.

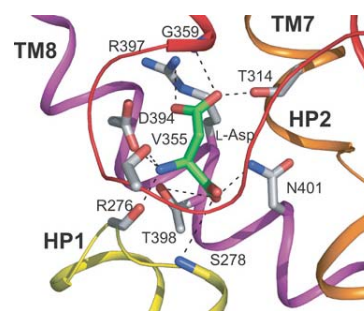
Dr Ryan's research focuses on the structure and function of glutamate transporters. These transporters play an important role in regulating normal neurotransmission in the brain and their dysfunction has been implicated in disease states such as Alzheimer's disease, Motor Neurone Disease and Ischemia following a stroke. Dr. Ryan was involved in determining the crystal structure of a bacterial glutamate transporter which has revealed an atomic level snapshot of this protein. The structure of the bacterial transporter allows us to predict the structure of the human glutamate transporters, the conformational changes that occur during transport and also how drugs bind to and affect these proteins. Her work in this area has been highly successful and has been acknowledged with two articles published in *Nature*¹ and *Nature Structural and Molecular Biology*² earlier this year.

Dr Ryan's CJ Martin Fellowship will continue for a final 2 years and she is looking forward to resuming her research in Associate Professor Vandenberg's Lab. Renae will ultimately seek her own funding and hopes to have her own lab that will focus on the structure and function of membrane proteins by the time the new Arc building is completed.

a



b



a Location of sodium-binding sites on the permeation pathway of aspartate. Two protomers of Glt_{ph} are shown. N-terminal cylinders are in ribbon representation, the TM helices in the C-terminal protein cores are shown as cylinders and bound aspartate is shown in stick representation. HP2 (red) serves as an extracellular gate and opens to afford aspartate access to the binding site. Sodium 2 (purple) serves as a lock on the gate, providing additional energy necessary for its closure. Below the substrate-binding site is sodium 1 (green) and bound solvent (red sphere). The proposed intracellular gate is formed by HP1 (yellow), TM7 (orange) and TM8 (magenta), which are held together by sodium 1. The proposed permeation pathway for the substrate is shown as a grey line and motions of HP2 are shown as a dashed double-headed arrow. **b** View of the aspartate-binding site showing HP1 (yellow), TM7 (orange), HP2 (red) and TM8 (magenta). A remarkable number of polar contacts solvate the highly charged substrate.

1. Boudker O*, Ryan RM*, Yernool D, Shimamoto, K and Gouaux E (2007) Coupling substrate and ion binding to extracellular gate of a sodium-dependent aspartate transporter. *Nature* 445, 387-393. (*equal authorship)

2. Ryan RM and Mindell JA (2007) The uncoupled chloride conductance of a bacterial glutamate transporter homolog. *Nature Structural and Molecular Biology*, 14, 365-71.

Bosch Researcher receives prestigious award



Dr Solomon with Dr Judy Morris, Flinders University (l) and Prof Glenda Halliday, President, ANS (r).

Dr Samuel Solomon heads the Laboratory of Vision and Cognition within the Bosch Institute. In July 2007, at the annual meeting of the Australian Neuroscience Society (held in conjunction with that of the International Brain Research Organisation) in Melbourne, Sam was presented with the AW Campbell award. This prestigious award acknowledges the best contribution to the field by a member of the society in their first five postdoctoral years, and commemorates the eminent Australian neurologist whose "Histological studies on the localisation of cerebral function" in 1905 founded cerebral cytoarchitectonics.

Nature Article

Executive Director of the Bosch institute, Professor Nicholas Hunt and colleague Professor Roland Stocker, head of the Vascular Research Laboratory of the Bosch Institute were invited to submit a "News and Views" article on "Heme moves to center stage in cerebral malaria" in Nature Medicine, Volume 13, Number 6 June 2007.

Carrick Award

Dr Hilary Lloyd is a Senior Lecturer in Pharmacology. In July 2007 Hilary was one of 10 recipients of a Carrick Institute's "Discipline Based Initiative Scheme". The \$94,368 grant will fund the project "Ensuring Quality Graduates of Pharmacology". Hilary's role will be joint project co-ordinator alongside leader, Dr James Ziogas, Melbourne University.

Prize Lecture

Professor David Allen was awarded the Prize Lecture of the Australian and UK Physiological Societies. He was the guest of the UK Physiological Society and presented his lecture entitled 'Of muscle damage in mice and men; role of stretch-activated channels and reactive oxygen species' at nine different institutions around the UK in September 2007. He also gave the 2007 Basic Science Lecture at the Cardiac Society of Australia and New Zealand in Christchurch in Aug 2007.



Major Equipment Grants



Des Richardson centre with his colleagues in his lab.

The Bosch Institute has been successful with two applications to the Faculty of Medicine Major Equipment Grants Scheme totalling \$80,000. These funds will be used to purchase equipment for the molecular biology core facilities in both the Anderson Stuart and Blackburn buildings. These grants were supported by 30 senior researchers in the Bosch Institute.

Chief investigator Professor Des Richardson said "These funds are of great value to grow our core facilities". He further added that "This was a good example of the benefits of researchers working in a cohesive manner to attract vital funding and grow capacity in biomedical research within the Bosch Institute and the University of Sydney". Des also commended Molecular Biology Officer Dr Donna Lai for her invaluable support with the grant applications.

Bosch Visiting Scholar



Dr Hajime Yuasa from Kochi University, Japan, arrived in September to spend one year on study leave in Professor Nick Hunt's Laboratory. Dr Yuasa is an expert on the enzyme indoleamine dioxygenase (IDO). Recently, Dr Helen Ball in Professor Hunt's laboratory identified a gene that makes a protein that has some properties similar to IDO. They called this protein "IDO-2" and their paper reporting this discovery (Ball HJ et al. Gene 396, 203 - 213, 2007) has provoked a lot of interest from scientists in the USA. The IDO-1 and IDO-2 genes arose by a "gene duplication" event more than 300 million years ago according to the work of Dr Ball and Dr Lars Jermiin from the School of Biological Sciences.

Dr Yuasa will work with the Hunt Laboratory to investigate the evolution of IDO-like proteins and to identify the roles in human beings of the newly-discovered IDO-2.

TamPap Pty Ltd

Following on from the story on cervical cancer in the last Bosch Brief Update, it was Brian Morris who patented the first use of PCR for HPV detection. Subsequently, the purchase of this patent by Polartech has led to the commercialization of the self-sampling kit.

Travelling Fellowship for Bosch Young Investigator



Mel Barron, Katie Dixon and Tara Brennan are PhD students in the Mason Lab, photo taken at the Bosch Young Investigators Harbour Cruise Welcome.

Katie Dixon is undertaking her PhD in Vitamin D and protection from sun damage under the supervision of Professor Rebecca Mason, Head of the Bone & Skin Laboratory, Bosch Institute. Katie was successful in securing a travelling fellowship from the Education and Training Committee of the European Society for Photobiology to attend the European Photobiology Society meeting in Bath, UK at the beginning of September.



Male Circumcision

On Monday 27 August Professor Brian Morris presented a live interview on 60 Minutes discussing his opinion of circumcision. Professor Morris is Head of the Basic & Clinical Genomics Laboratory in the Bosch Institute and is an advocate for male circumcision. Professor Morris also chaired the session "Male Circumcision: The Cutting Edge of HIV Prevention" at the International AIDS Society conference held in late July.

DATES FOR YOUR DIARY:

Thursday 1 November 2007, 3.45 – 5.45pm

Official Opening of the New Bosch Advanced Microscopy Facility, Anderson Stuart Building – RSVP essential

Wed 21 November 2007, 1.00 – 2.00pm

Bosch Biannual Members Meeting Room N248 Anderson Stuart, F13

Friday 14 December 2007

Bosch Young Investigators Symposium, Eastern Avenue Complex, F19

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