

# ARC Centre of Excellence in Structural and Functional Microbial Genomics

In 2002 the Australian Research Council (ARC) introduced the Centres of Excellence scheme. The overall aim was to draw together accomplished researchers to attack broader problems than could not be addressed under the project grant system. As a consequence, Ben Adler, Julian Rood, John Davies and Ross Coppel from the Department of Microbiology at Monash University got together with Phillip Nagley, Rod Devenish, James Whisstock and Jamie Rossjohn from Biochemistry and Molecular Biology at Monash to develop a Centre proposal based on researching bacterial pathogens of clear agricultural significance.

The initial proposal involving these eight Monash chief investigators (CIs) focused on the idea of establishing a Centre addressing bacterial (rather than viral) veterinary pathogens. The proposal took a multi-disciplinary approach based on molecular biology and genetics, coupled with structural biology and studies of host-pathogen interactions. This would provide a unique organisation in Australia, and one of only a handful worldwide, capable of addressing issues of national and international significance in advanced molecular aspects of bacterial veterinary pathogenesis. Whilst all the CIs were

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to be based at Monash (presented as a strength, rather than a weakness, in view of the diverse expertise and interests of the CIs), there were explicit links to collaborators at the Universities of Sydney and Queensland, as well as projects with CSIRO Animal Health, CSL (at it was then known), the Victorian Bioinformatics Consortium and the biotechnology company Cytopia.

The name of the Centre, Structural and Functional Microbial Genomics, encapsulated the ongoing work on whole bacterial genome sequencing, microarray analysis to generate transcriptional profiles in bacteria, structural biology and the expertise in eukaryotic cell biology that underpinned robust approaches to studying host-pathogen interactions.

Alongside a series of programmes of research on individual organisms and particular animal or fowl diseases, the Centre embodied a novel 'generic pipeline' (Figure 1) which was to express in high throughput hundreds of genes encoding candidate outer surface proteins from various bacterial pathogens to generate pure protein products. This pipeline builds on data generated from genomic, proteomic and transcriptomic data. This in turn feeds into protein production followed by structural analysis, ultimately leading to vaccine development, identification of new drug targets and development of a rational drug design approach to lead to novel anti-microbial reagents. Another explicit endpoint is, of course, the acquisition of valuable and unique biological knowledge.

Unfortunately, we were not successful after the first round of interviews, and we gave up thoughts of a Centre to return to our respective project grant-based research. Then, in mid-2003, virtually out of the blue, ARC contacted Monash with an offer of a Centre based on the CIs pooling their ARC project grant funds plus a premium for 5 years to enable the setting up of an ARC Centre for Structural and Functional Microbial Genomics.



Chief Investigators of the ARC Centre of Excellence in Structural and Functional Microbial Genomics. L-R (front row): James Whisstock, Ben Adler (Director), Phillip Nagley (Deputy Director), Julian Rood & Jamie Rossjohn; (back row): Ian Smith, Ross Coppel, John Davies & Rod Devenish.



Figure 1. The generic high throughput microbial pipeline; details are explained in the text.

ARC solemnly advised us that the word “excellent” must not be used in the rubric of the Centre, so we became a “Centre of Very-Goodness” – nonetheless, the implementation of our strategies would be consistent with standards of excellence under the directorship of Ben Adler.

The funding from 2003 facilitated collaborative research programmes and, significantly, enabled the successful establishment of the protein production pipeline. This development was important, not only for its technological outcomes and wide application, but also for the concept of generic programmes not ‘owned’ by individual CIs, thus constituting the essence of a real Centre.

In 2004, ARC announced another round of Centres of Excellence, and this time we were successful, with the inclusion of Ian Smith as CI bringing a strong proteomics theme into the Centre’s programmes. The ARC Centre of Excellence in Structural and Functional Microbial Genomics commenced operations on 1 July 2005, its mission being:

*To conduct integrated research that will elucidate key aspects of microbial pathogens and the hosts they infect. The research will encompass genomic analyses, development of modern veterinary vaccines, identification of antimicrobial targets and development of antimicrobial agents.*

The Centre’s current research programmes on a variety of topics in microbial molecular biology and mammalian cell biology, each linked into studies on host-pathogen interactions, are underpinned by a series of integrated core technologies, which together form the high throughput microbial pipeline.

Some of the core components were already in place at Monash University, including extensive bioinformatics expertise, microarray technology and an x-ray crystallography facility. But as a direct consequence of the ARC Centre of Excellence funding, the Victorian State government has provided funds for salaries for skilled personnel to drive the pipeline as well as generating crucial proteomic infrastructure, including advanced

mass spectrometric instrumentation. The resulting proteomic information complements the data generated from the genomic and transcriptomic efforts already established within the Centre, in addition to supporting the protein expression and structural biology components of the microbial pipeline. Thus, the Centre is now equipped with state of the art equipment using cutting-edge technologies in genomics, microarray analysis, animal infection models and protein production, including the world’s largest parallel protein purification workstation, and next year will have direct on-site access to the Australian Synchrotron. Taken together, these core capabilities allow the Centre to undertake a unique approach to the study of microbial pathogens and, therefore, to make more rapid and more significant

contributions to the fundamental advancement of knowledge within this field of research.

In conclusion, funding through the ARC Centre of Excellence scheme, along with substantial cash support from the Victorian State government and Monash University, has allowed a group of scientists with a diverse but highly complementary range of skills and expertise to come together to undertake a fully integrated, broad-based, multi-disciplinary approach to address the complex biological questions surrounding microbial pathogens and their interactions with host cells. This research will lead to advances in fundamental knowledge, the identification of new drug targets, and the development of new vaccines against important agricultural microbial pathogens.



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## **The ARC Centre of Excellence in Structural and Functional Microbial Genomics**

The objectives of the Centre are:

- To develop vaccines against microbial pathogens.
- To identify and validate genes essential for microbial survival.
- To facilitate the development of novel antimicrobial agents.
- To elucidate host-pathogen interactions.
- To train a new generation of multi-skilled researchers.

By taking this integrated approach, it will now be possible to identify a gene of interest from bioinformatic analysis, use genetic analysis to determine its biological function, purify and characterise the gene product by proteomics and study its biochemical behaviour, develop a structural model and finally determine how it interacts with its ligands and co-factors. All of these studies will be carried out within a cohesive and focussed research team, providing a depth of analysis and discovery not possible outside the Centre’s collaborative research environment.

Outcomes from the Centre will include:

- The advancement of fundamental knowledge of the functional biology of micro-organisms.
- A detailed understanding of relevant aspects of host-pathogen interactions.
- The development of new technologies for the control and treatment of microbial diseases of economic and social importance to Australia