

Co-operative Research Centres

The CRC for Cellular Growth Factors

Since 1991 we have been collaborating with CSIRO Health Sciences and Nutrition, the Ludwig Institute and AMRAD in the CRC for Cellular Growth Factors (CRC-CGF). The CRC-CGF is now a major international centre of research and is advancing its aim to develop novel therapeutics based on its expertise in cellular growth factors.

One of the CRC-CGF's major scientific discoveries is the SOCS family of intracellular proteins, which modulate growth factor signal transduction. SOCS1 and SOCS3 have recently become the subject of a major international deal negotiated by AMRAD. In February 2001 AMRAD announced an exclusive research and development collaboration and licence agreement with the newly-created international pharmaceutical company GlaxoSmithKline (GSK). This arrangement highlights the level of interest in molecules regulating signal transduction and the ability of the CRC-CGF to attract international backing from leading pharmaceutical companies. Combining AMRAD's

proprietary SOCS technology platform with the drug discovery and genomics strengths of GSK will increase the chances of developing new treatments for cancer and infectious diseases.

In another deal arising from CRC-CGF research, a joint venture with Advanced Micro Devices (AMD), has enabled the acquisition of one of the world's fastest high-performance computers dedicated to the design of new drugs. Known as *Caduceus*, the new computer enables potential new drugs to be rapidly identified and evaluated. Based on a technique developed for NASA known as a Beowulf cluster, the computer comprises powerful AMD Athlon™ processors donated by AMD and achieves a speed comparable to the peak performance of Australia's fastest commercially available supercomputers, but at a fraction of the cost. *Caduceus*, so named because the shape of the computer cluster resembles the staff of Hermes in Greek mythology, was designed and constructed by CRC-CGF PhD student, Kim Branson.



Kim Branson with his supercomputer. Photo: Eamon Gallagher/Courtesy of The Age.

The CRC for Vaccine Technology

Our partners in the CRC for Vaccine Technology are the Queensland Institute for Medical Research (the host institution), The University of Melbourne, CSIRO, CSL Limited, Monash University and the Australian Red Cross Service. An important milestone completed this year from the work of Andrew Lew's group was a trial conducted to ascertain the optimum dose and safety of a targeted measles DNA vaccine in animal models (hCTLA4-g3-MTH). A dose escalation study was performed and response was observed in 5/9 animals. This work was done in collaboration with other CRC members including Mary Tachedjian, Biserka Horvatic, Jan Tennent, and Marion Andrew from CSIRO. Gene gun vaccination with the CTLA-4 targeted vaccine significantly enhanced the speed and magnitude of the IgG antibody responses compared to the control.

Bill Heath's team is investigating how killer T cell armies destroy virus-infected cells and PhD student, Justine Mintern, has demonstrated an important role for expression of the transcription factor cRel in dendritic cells generating killer T cells.

Irene Caminischi and Ken Shortman have been identifying new genes expressed by dendritic cells. Caminischi has identified two novel genes encoding proteins expressed on the surface of dendritic cells and is currently investigating their function.

Brendan Crabb and his colleagues are characterising virulence determinants in *Equine rhinitis* viruses, important causes of respiratory diseases in horses. This work has made important progress toward the development of vaccines for use in horses. Additionally, his group is analysing functional and immunological aspects of important vaccine candidates

identified in *Plasmodium falciparum*, which causes the most severe form of human malaria.

CRC for the Discovery of Genes for Common Human Diseases

We have now completed four successful years of the CRC. Our partners are the Queensland Institute of Medical Research (QIMR), the University of Queensland's Institute for Molecular BioSciences, the Murdoch Children's Research Institute and the CRC host institution ExGenix Corporation, which became Cerylid Corporation during the year.

In the first couple of years of its existence the CRC focussed on planning and developing a wide range of projects furthering its aims. At the end of the second year the portfolio of projects being supported by the CRC was pared down to a smaller number, with the aim of devoting increased resources to the major ones. WEHI is primarily responsible for two of these: the multiple sclerosis project and the identification of the insulin-dependent diabetes susceptibility locus *idd11* in mice. We are also involved to a much smaller extent in the QIMR-based study mapping genes for endometriosis and in a smaller human diabetes study.

Two years after this focussing of resources, the CRC's major projects have matured greatly, and data collection is nearing completion in the two especially large ones on endometriosis and multiple sclerosis. Progress on the *iddm11*, human diabetes and multiple sclerosis studies is summarised elsewhere in this report, see page 66.

An important part of the CRC's mission is the professional development of participants in the Centre. Another is its ethics-focussed education program for the end-users of genetic research: schools, professional, community and industry groups.

Postgraduate students and research scientists from WEHI benefit greatly from their participation in the CRC's annual retreats and scientific meetings, while WEHI has been the venue for Victorian State finals of Genethics competition.



Mr Lindsay Tanner MP, centre, with Professor Don Metcalf, left, and Dr Doug Hilton, Director, CRC for Cellular Growth Factors.