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Biography

Rob Cappon's research group focuses on the detection, isolation, characterisation, identification and evaluation of novel bioactive metabolites from Australian marine and terrestrial biodiversity. These metabolites span all known biosynthetic structure classes including many molecules new to science, and their study requires the use of sophisticated chromatographic, spectroscopic and chemical technologies. Natural products uncovered during our investigations represent valuable new leads in the search for drugs with application in the fields of human and animal health and crop protection, have potential as molecular probes to better interrogate and understand living systems, and could find application as biological control agents.

Large-scale recombinant protein production and structure-based drug design capabilities at CSIRO

George Lovrecz, Geoff Dumsday & Tim Adams

Email George.Lovrecz@csiro.au
Geoff.Dumsday@csiro.au
Tim.Adams@csiro.au

CSIRO has opened its large-scale Recombinant Protein Production Facilities (RPPF) as part of the National Collaborative Research Infrastructure Scheme (NCRIS).

The new state-of-the-art facility is capable of the optimisation, scale-up, production and purification of recombinant proteins in large quantities: from hundreds of milligrams to kilograms to allow preclinical or even clinical trials.

CSIRO's facility is equipped with a range of cell culture and fermentation equipment to allow the use of a wide range of expression systems and host cells including mammalian, insect and microbial cells:

- Over 30 stirred tank reactors, ranging from 2 to 500L scale to allow rapid optimisation and large-scale protein production.
- Single-use bioreactors with working volumes of up to 25L.
- Roller bottle apparatus, spinner and shaker flasks suitable for scale-up and process development work.
- A wide variety of analytical equipment to follow cell growth, metabolism and characterisation of proteins.
- Downstream and purification equipment suitable for processing large-scale batches of microbial and mammalian cell cultures.

Recent projects have included the production of:

- Monoclonal antibodies.
- Receptor signalling and cytokine proteins.
- Process development and production of bioremediation enzymes for field trials.
- Production of small molecules via microbial biotransformation.
- Process development and production of structural proteins to demonstrate proof of manufacture and for materials testing.
- Process development and production of malaria vaccine candidates.
- A wide range of other bacterial and insect cell proteins.

The RPPF is the largest research laboratory in Australia open for collaborative or fee for service projects providing access to process development, optimisation and protein production at best-practice standards.

The facility is supported by the expert capabilities of various other molecular and cell biology groups to allow cell line development and protein chemistry for rapid purification and characterisation of proteins. Figure 2 provides further details. There is also a

Figure 1. Photo of the equipment at the RPPF, showing some of the microbial fermentation systems. Left: 500L fermenter; Centre: 75L fermenter; Right: 150L fermenter). The fermentation systems offer a high degree of flexibility with a number of operating and control modes. Bacteria, yeast and filamentous fungi can be produced using the fermentation systems and tens of kilograms of wet cell pellet can be produced in a single batch.

direct connection to the Bio21-C3 crystallisation laboratories and to the Australian Synchrotron to allow structural studies.

Fragment-based screening and protein–protein interaction studies are also available to identify suitable candidates for further pharmaceutical research programs.

Both academic and industrial researchers are encouraged to cooperate with the new facility. Flexible collaborative schemes are available along with IP protection if needed.

The facility will accelerate the commercialisation of new products by providing Australian researchers with easy access to state-of-the-art facilities for protein production, process development and optimisation.

This NCRIS subprogram includes nodes in the Australian Capital Territory, New South Wales, Queensland, South Australia and Victoria. The Victorian node of NCRIS is housed in a newly refurbished, dedicated laboratory at Monash University's Centre for Green Chemistry for protein purification and purpose-built pilot scale fermentation laboratories at CSIRO Molecular and Health Technologies, immediately adjacent to Monash University and the Australian Synchrotron.

NCRIS is part of the Australian Government's Backing Australia's Ability initiative, which provides substantial funds to generate ideas, accelerate commercialisation, encourage collaboration, develop and retain skills.

Biography

Dr George Lovrecz is a Senior Principal Research Scientist at CSIRO Molecular and Health Technologies with 25+ years experience in fermentation, specialising in mammalian cell cultures. George provides expertise in the area of large-scale production, optimisation, development and characterisation of recombinant proteins for internal and external research programs. He has played an integral role in the development of a large-scale production system for mammalian cell receptor glycoproteins resulting in the first published 3D structures of hIR and EGF receptor fragments.

Geoff Dumsday is a senior research scientist at CSIRO. His research interests are focused on industrial microbiology, specifically the use of microbial systems for production of useful products ranging from vaccines and enzymes to the production of small molecules from a range of starting materials, particularly biomass.

Tim Adams is a Senior Principal Research Scientist and Program Leader, Molecular and Cell Biology. His research interests encompass the engineering of mammalian cell lines for the production of antibodies, growth factors and other proteins of biomedical interest.

Figure 2. Structure-based drug design at CSIRO.