Monash receives Grand Challenges Explorations funding

Monash University announced that it will receive Phase II funding through Grand Challenges Explorations, an initiative created by the Bill & Melinda Gates Foundation that enables individuals worldwide to test bold ideas to address persistent health and development challenges. Dr Fasseli Coulibaly, from the Dept of Biochemistry and Molecular Biology, will continue to pursue an innovative global health and development research project, titled MicroCubes as vaccines for the developing world.

“We have developed a new crystal-based vaccine carrier and we plan to establish whether these MicroCubes are a potent and ultra-stable way to deliver vaccines. If so, it would make it suitable for use in remote areas where adequate refrigeration facilities are not always available,” Dr Coulibaly said.

From 2009 to 2012 Dr Coulibaly was awarded two Phase I grants for the MicroCube program. Grand Challenges Explorations (GCE) Phase I recognizes individuals worldwide who are taking innovative approaches to some of the world’s toughest and persistent global health and development challenges. GCE invests in the early stages of bold ideas that have real potential to solve the problems people in the developing world face every day. Phase II recognizes those ideas that have made significant progress toward implementation.

Dr Coulibaly’s project is one of four Phase II Grand Challenges Explorations grant awardees announced this week.

In previous Gates Foundation funded studies, Dr Coulibaly has engineered a vaccine where the HIV Gag protein has been embedded into these MicroCubes and showed that this vaccine stimulates strong immune responses in preclinical studies.

“To assess the suitability of MicroCubes as a generic vaccine platform, we will work on a flu vaccine and compare it to existing vaccines. Given the fantastic tools available for research on influenza virus, it will then be easy to translate preclinical studies to knowing what is going to happen in humans,” Dr Coulibaly said.

“Together with my collaborators Associate Professor Rosemary Ffrench and Professor Lorena Brown from the Burnet Institute and University of Melbourne, respectively, we’re hoping to establish in this Phase II project that MicroCubes have unique properties that also warrant their development as a vaccine vector targeting infectious diseases with the highest burden in developing countries: malaria, TB and HIV.”

Courtesy Vicki Burkitt, Communications and Projects Officer

Left:
Artistic representation of poxvirus IV-like particles based on X-ray crystallography and cryoEM data.

Please visit Dr Coulibaly’s Structural Virology Laboratory webpage to see more images:
www.med.monash.edu.au/biochem/staff/coulibaly.html

Right:
Structure of the IBDV infectious particle.
Researchers unveil new strategy in an age-old evolutionary arms race

_A team from the Department has uncovered a new strategy employed by viruses to deceive the mammalian immune system. The findings, published in Nature Immunology reveal the latest viral "immunoevasion" tactic and how natural killer immune cells have countered this._

_Natural killer (NK) cells form part of the innate immune system and monitor the body for cells that lack the expression of "self" MHC markers, which are normally expressed on the cell surface but are down regulated during cancer and viral infections. To avoid detection by NK cells, a number of viruses express MHC-like molecules that act as decoy receptors. The team, led by Dr Richard Berry, determined the structure of a cytomegalovirus MHC mimic, m157, bound to a mouse Ly49 NK receptor. Surprisingly, the m157 molecule targeted the helical stalk region of the receptor._

_The mode of interaction was analogous to "a Welsh rugby player 'tackling the legs' of an Englishman", Rossjohn said._

_This breakthrough has the potential to unlock new areas of research. Dr Berry explained, "Receptor stalks are generally considered as innocuous regions that simply serve to link the functional domain to the cell membrane. Our finding suggests that rationally developing ligands to bind to receptor stalk regions may constitute a general mechanism of receptor activation."_
Lab Head Profile: A/Prof Ashley Buckle, NHMRC Senior Research Fellow

In 1988, during the third year of my Chemistry undergraduate degree, I spent a year in a pharmaceutical lab and joined the Advanced Drug Delivery Unit at Ciba-Geigy UK (later to become Novartis). This was my first experience of real research and I was lucky because the whole unit operated like a research institution, with divisions for biochemistry, immunology etc., doing exciting, even blue-sky research. I became interested in protein structure and function and saw a glimpse of the brave new world of protein engineering emerge. Intrigued, I took a night class in protein engineering at Birkbeck College, London, taught by Janet Thornton, a pioneer of structural bioinformatics (now director of the European Bioinformatics Institute). There I learnt that one person in particular, Alan Fersht, was pioneering the engineering of proteins at Imperial and setting up a new lab in Cambridge. So after my final exams in 1990 I telephoned Alan to ask if I could come and do a PhD in his lab. At the interview, I was worried that my undergrad marks weren’t good enough, so as soon as I walked into his office I have him a printout of a computer program I had written the year before that displayed protein structures as ribbons. This was pre-WWW so in order to obtain a protein to display I had written to Janet Thornton requesting coordinates of 6 structures from the PDB (there were only 365 in the PDB in 1989, there are 91,000 today). She sent me the coordinates as hardcopy – so I spent months typing them into my Sinclair QL microcomputer. Luckily this distracted Alan from my poor marks, so he offered me a PhD. If I was interested in protein structure, he told me, I needed to become a crystallographer. I nodded, having no idea what that was! Three months into the PhD having spent days collecting diffraction data on film at Daresbury synchrotron and weeks laboriously imaging them I really thought I had made a big mistake. But after I got my first look at the electron density I was hooked.

For the 3 years of my PhD I studied the small ribonuclease barnase, a model protein for stability and folding studies. This yielded the first ever high-resolution understanding of the response of a protein structure to an engineered mutation, allowing an interpretation of the thermodynamic properties of a mutant protein in a structural context. This was followed by the structure of a barnase-DNA complex, giving a comprehensive model of ribonuclease action and an enzyme-transition state complex. In the final year of my PhD I determined the crystal structure of the complex between barnase and its protein inhibitor barstar. This work was extremely rewarding and is still the favoured benchmark for theoreticians studying protein associations. My PhD involved 3 years of training in X-ray crystallography at the Laboratory of Molecular Biology (LMB) in Cambridge – the birthplace of structural biology. I was incredibly fortunate to be in an environment with many Nobel Prize winners still active (Max Perutz would regularly come into the model building rooms to chat and see what we were working on).

As soon as my thesis was awarded in early 1994 I took up an MRC postdoctoral fellowship in Alan’s lab, investigating the role of molecular chaperones in protein folding. I solved the crystal structure of the GroEL minichaperone which gave the first detailed structural model of GroEL-substrate interactions. These were exciting times to be in the LMB – John Walker was awarded the Nobel Prize for the ATPase structure (1997) and Greg Winter’s lab and spin-out company CAT were producing the humanised monoclonals that are now blockbuster drugs.

Cambridge is incredibly seductive – it took me 13 years to escape! In 2003 I decided to relocate to Monash as a Research Fellow. I was fortunate to work alongside Steve Bottomley, James Whisstock and Rob Pike and was supported by an NHMRC program grant in protease biology. This funding and the support of the department was incredibly important for me at that stage. The environment was perfect, with lots of great science so it was easy to setup exciting collaborations. I spent 4 years developing a new research program in structural biology and also new directions in computational biology. All the support paid off - in 2007 I was awarded an NMHRC Senior Research Fellowship and established my independent research group.

Ten years down the track my research is still focused on protein structure and folding, but the emphasis has steadily shifted from static, crystallographic structures, to a more dynamic view of proteins and how they move and change shape. Using molecular dynamics simulations, X-ray crystallography and a range of biophysical techniques, we try to understand the role of conformational change and flexibility in protein function. We approach this from two directions: first using simulation and bioinformatics to provide experimentally testable predictions, and second to provide a theoretical framework for interpreting existing experimental data. We study a broad range of systems, including the dynamics of pMHC-TCR interactions, serpin misfolding and disease, PolyQ-mediated aggregation, disorder in disease-causing mutations, and the structural basis for autoantibody-antigen engagement. Computational biology needs significant supercomputing: I am fortunate that we have first-rate computing resources and we have access to some of the most powerful supercomputers in the world at the Victorian Life Sciences Computation Initiative (VLSCI).

OHS MATTERS

1. Liquid Nitrogen Dispensing Incident at LN2 Facility in 77G

A message from Jeff Wright (Manager of LN2 facility in 77G)

1. Observation - Someone had altered the sensitivity of the temperature cut-off. The thermocouple in the back corner of the weigh scale is intended to cut off when it detects liquid nitrogen. It had been altered to -100 degrees C. I have restored it to -30 degrees. It will result in more false shut-offs from the stream of vapour nitrogen cooling the room but should also give greater sensitivity.

2. The system is not designed for the small volumes that users are trying to dispense. The scale is in whole numbers or whole kilograms but people are trying to dispense 0.5 kg of liquid N2. Apart from being extremely wasteful it is beyond the accuracy of the system and will lead to overfilling. If the system is not seeing the weight change then there is no shut off.

3. The weighbridge scale doesn’t tare. It needs to be turned off/on to zero. This seems to be a fault in that scale. Again, it means if not done properly the system loses its zero and will overfill small amounts.

The solution seems to be to put a minimum fill volume to the system. I would suggest a 3 kg minimum fill volume.

2. Procedure for Training staff/students on any X-ray/sealed radiation source (Including the X-ray Generator, Saxxs instrument and animal imagers)

I have verbally recommended in the past that if anyone needs to train anyone in the X-ray Generator or Saxxs rooms, that it is very important that the Trainer and the Trainees ARE wearing their own personal radiation badges when inside the rooms.

Even though the instruments may be OFF at the time of training, it is a requirement under WorkSafe (Victorian legislation) that all those entering such areas must wear their personal radiation badges at all times when inside. This is a highly restricted area and all those who manage these rooms should be following the correct guidelines when training new users/visitors/collaborators.

All ‘new’ users (first time users of the equipment here in Biochem) of the Saxx and X-ray generator rooms must fill in a form obtained from the Radiation Officer (Irene Hatzinisiriou), who will issue them their own personal radiation badge BEFORE they enter the room for training or for anything else.

Please follow this ‘training procedure’:

2. Send a request for a personal radiation badge to the Radiation Officer (Irene Hatzinisiriou).
3. A form is signed by the supervisor and user, then badge handed over thereafter.
4. Training request to be sent to Matthew Wilce or other registered trainer.
5. Sign document for completion of training (copy of training records to be kept by both the Manager and the user). These records MUST be kept for 50 years here on campus.
6. Then given access via id swipe card system (Matthew Wilce).

3. Phenol Chloroform use in the labs

• must use only in a ducted fume hood
• all users to be trained and read a risk assessment before using
• all users know where the Burns Module for Phenol/Chloroform skin exposure is located (on top of the first aid kits)
• DO NOT USE WATER if skin is exposed to Phenol/Chloroform

4. RE Lab inspection results from Chemical Audit in Nov 2012

Can now be located on the V drive for all to see!
V:\biochem\Admin-OHSE

5. Safety Manuals and BioSafety Manuals

New updated copies can be picked up from 76G, just outside the Imaging Facility in 76G58.

Every group should have a copy of both manuals showing in all lab areas.

There is a flow chart for what to do in an Emergency, it is imperative that all read this and are clear as to what to do, who to contact and what forms need to be filled out.


