Australian Synchrotron Development Plan
Project Submission Form

Section A: Summary and Proponent Details

Project Title

Macromolecular Crystallography Expansion Project.

Spokesperson

Name	Tom Caradoc-Davies
Institution	Australian Synchrotron
Email	Tom.caradoc-davies@synchrotron.org.au
Phone	04 3430 7453

Executive Summary (approx. 100 words)

The Macromolecular Crystallography Expansion Project has four strategic objectives to extend the capabilities of the existing crystallographic infrastructure at the Australian Synchrotron (AS) in order to meet key areas of growth and development in the crystallographic community. These strategic objectives are:
1) To increase the capabilities, capacity and performance of the MX beamlines at the AS.
2) To facilitate crystallography of membrane proteins, protein complexes and other challenging proteins.
3) To enable drug design by fragment-based screening.
4) To support synchrotron-based small-molecule crystallography (SMX).

In order to meet these strategic objectives five building projects are proposed:
a) upgrade the existing high-throughput beamline (MX1) to greatly increase its capabilities, throughput and improve its functionality for the SMX community.
b) upgrade the end-station and focusing optics of the existing microfocus beamline (MX2) to enhance flux, beam stability, performance and functionality for the SMX community.
c) a comprehensive lab upgrade to produce a working structural biology lab at the AS with a set of fragment libraries for users and staff to use for screening experiments in conjunction with crystallization facilities such as C3 and Monash.
d) to build a new macromolecular characterisation beamline on a bending magnet capable of simultaneous CD and SAXS measurement on the same sample.
e) to build a new high performance macromolecular crystallography beamline (MX3) on a 3m in-vacuum undulator source and 5x5 micron focus for determination of structures from weakly diffracting micro crystals of large macromolecules and naturally occurring crystals.

The CD/SAXS and MX3 projects are covered in detail in separate proposals and this project will describe the upgrades to the existing MX beamlines and building of a structural biology laboratory.

Other proponents (add more rows if necessary)

Name	Institution	Email address
Dr. Helen Blanchard	Griffith University	h.blanchard@griffith.edu.au
Prof Charlie Bond	University of Western Australia	Charles.Bond@uwa.edu.au
Dr Nathan Cowieson	Australian Synchrotron	Nathan.cowieson@synchrotron.org.au
Prof Geoffrey B Jameson	Massey University	G.B.Jameson@massey.ac.nz
Dr Marc Kvansakul	WEHI	[kvansakul@wehi.EDU.AU]
Dr Mike Lawrence	WEHI	lawrence@wehi.edu.au
Assoc Prof Peter Metcalf	University of Auckland	peter.metcalf@auckland.ac.nz
Dr Janet Newman	CSIRO	Janet.newman@csiro.au
Dr Tom Peat	CSIRO	Tom.peat@csiro.au
Dr Alan Riboldi-Tunnicliffe	Australian Synchrotron	Alan.RT@synchrotron.org.au
Dr Peter Turner	University of Sydney	p.turner@chem.usyd.edu.au
Prof Alice Vrielink	University of Western Australia	alice.vrielink@uwa.edu.au
Assoc Prof Matthew Wilce	Monash University	matthew.wilce@med.monash.edu.au

Section B: Detailed Description

B1: Description of Proposed Beamline/Development Project

Outline of the Macromolecular Crystallography Expansion Project

On behalf of the Australasian Crystallographic Community, representing protein, macromolecular and small-molecule crystallography, we present this proposal for the Macromolecular Crystallography Expansion Project

The Macromolecular Crystallography Expansion Project has four strategic objectives to extend the capabilities of the existing crystallographic infrastructure at the Australian Synchrotron (AS) in order to meet key areas of growth and development in the crystallographic community. These strategic objectives are:
1) To increase the capabilities, capacity and performance of the MX beamlines at the AS.
2) To facilitate crystallography of membrane proteins, protein complexes and other challenging proteins.
3) To enable drug design by fragment-based screening.
4) To support synchrotron-based small-molecule crystallography (SMX).

In order to meet these strategic objectives five building projects are proposed:
a) upgrade the existing high-throughput beamline (MX1) to greatly increase its capabilities, throughput and improve its functionality for the SMX community.
b) upgrade the end-station and focusing optics of the existing microfocus beamline (MX2) to enhance flux, beam stability, performance and functionality for the SMX community.
c) Creation of a comprehensive laboratory to support drug design by fragment-based screening , to interface with crystallization facilities such as C3 and Monash and MX beamlines.
d) to build a new macromolecular characterisation beamline on a bending magnet capable of simultaneous CD and SAXS measurement on the same sample.
e) to build a new high performance macromolecular crystallography beamline (MX3) on a 3m in-vacuum undulator source and 5x5 micron focus for determination of structures from weakly diffracting micro crystals of large macromolecules.

The Macromolecular Crystallography Expansion Project proposal has been conceived as part of a concerted approach to providing a world-class structural biology facility, along with the proposals for a new high performance macromolecular crystallography (MX3) beamline, a CD/SAXS beamline, upgrades to the existing beamlines (MX1 and MX2) and a new structural biology laboratory at the AS.

The CD/SAXS and MX3 beamline projects are covered in detail in separate proposals and this project will describe the upgrades to the existing MX beamlines and building of a structural biology laboratory.

1. MX1 beamline upgrade

Currently requests for beamtime on MX1 at the Australian Synchrotron saturate the available capacity. It is anticipated that demand will soon outstrip supply due to:

- Expansion in the Australian and New Zealand crystallographic community, e.g. new laboratories now being established at La Trobe University and in Adelaide.
- The increasing use of robotics in macromolecular crystallization. This will increase the success rate of crystallization thus increasing the demand for beamtime.
- The growing demand for beam time on MX1 due to the establishment of Fragment Based Drug Discovery projects and other projects requiring high-throughput crystallography facilities.
- The growing use of MX1 by the small-molecule crystallography community

Proposed Upgrade

The MX1 beamline upgrade will substantially improve the beamlines capabilities and allow for a more than 300% increase in screening capacity. The proposed improvements are:

1. Installation of a double multilayer monochomator (DMM) inside the existing MX1 monochromator vessel.
2. Installation of a pixel-array detector such as a Pilatus 2M.
3. High-speed sample loading robot
4. Mini-Kappa goniometer head
5. Endstation improvements and ancillary equipment

1. DMM

A DMM will produce around 50 times the existing flux of MX1 and allow for faster exposures and shutter-less data collection. Currently MX1 is flux-limited, with relatively long average exposure times (5-10 seconds per image). The DMM would allow for almost all samples to be screened with 1 second (or less) exposures, significantly reducing the time required for collection of a full set of data. The new monochromator will be able to switch modes between the DMM and DCM (double crystal monochromator) to allow for anomalous dispersion experiments such as MAD and SAD to be carried out as they cannot be easily performed using the DMM. The increased flux from the DMM is required to make shutter-less data collection using a pixel-array detector (see below) viable as the flux from the existing DCM is too low to allow for significant increases in throughput using this technique.

2. Pixel-array detector

A pixel array detector (such as a Pilatus 2M) will offer significant improvements to both the MX and SMX communities. Firstly, it can be operated at 30 Hz and would allow for shutter-less data collection. In this mode the sample is rotated at a constant velocity while the detector reads out continuously. In a standard data collection each image requires the rotation axis to be accelerated to a velocity which remains constant during the exposure (gated by the experimental shutter). The synchronization of the shutter and rotation axis is critical for data quality and controlling each image produces over 1.2 seconds of "dead-time" per image. In shutter-less mode this "dead-time" is almost zero (3ms) and a single dataset of 180 degrees rotation can be collected in 60 seconds with a 3 degree per second rotation rate. A dataset collected in standard mode with 1 second exposures would take 6.6 minutes.

Secondly, the dynamic range of a pixel-array detector is several orders of magnitude greater than that of conventional CCD detectors. This has significant benefits for both the MX and SMX communities as both types of data usually suffer from overloaded reflections on CCD detectors. The ability to collect very intense reflections without overloading the detector will make collection of synchrotron SMX data far easier and allow for strongly diffracting samples (such as inorganic complexes) to be studied. MX users often collect low and high resolution passes from the same crystal in order to measure the strong low-angle reflections and high resolution weak reflections. A pixel-array detector will allow both types of reflections to be collected in a single pass which removes the time taken to collect multiple passes and the need to scale multiple sets of data together.

3. High-speed robot

The DMM and pixel array detector will significantly reduce the time required to collect a complete dataset. Without upgrade the existing SAM robot, which takes 55 seconds to swap samples, will become the rate limiting step in fragment screening. Modified SAM robots utilizing a double-tong design have been implemented in beamlines at the Photon Factory and this design allows for samples to be exchanged in less than 6 seconds. Implementation of a high-speed robot similar to this will greatly increase the screening capacity of the beamline for all robotic users.

4. Mini-Kappa goniometer head

The existing MX goniometer heads allow a sample to be rotated around a single-axis. Kappa geometry is required for several experimental cases such as SMX users who need to conduct several data collections at different crystal orientations in order to collect complete data and MX users who need to collect friedel pairs on the same image for difficult MAD/SAD phasing experiments. A commercial mini-kappa head such as that available from MAATEL would be required due to the low sphere of confusion (3µ) and existing kappa-head control and alignment software such as STAC. The STAC control system would be required for a kappa-goniometer in order to allow users to have an integrated gui for sample alignment and most importantly a collision map to prevent damage to beamline components by the movement of the kappa head.

5. Endstation improvements and ancillary equipment

The following upgrades to the endstation hardware are required in order to better meet the needs of the MX and SMX communities:

- improved crystal visualization (cameras, lenses, lighting)
- equipment for high-speed sample centering (needed for high-speed screening).
- modifications to detector mount to allow for smaller crystal-detector distance for high resolution data collection (essential for many SMX experiments)
- deployment of two-theta movement for detector
- upgrades to A-frame in order to allow both CCD and pixel-array detector to be mounted on the detector cage
- programmable temperature control of cryojet to allow for SMX phase transition studies
- purchase and installation of a high-pressure diamond anvil cell for the SMX community
- Single crystal microspectrophotomer to allow for measurement of spectral features of single crystals.
- on-line Raman spectrophotometer for monitoring crystal damage, checking for inclusion of soaked ligands and in-crystal secondary structure determination. As a Raman spec operates in a scattering mode, difficulties with transmission through crystals and X-ray beams are circumvented.

2. MX2 beamline upgrade

Proposed Upgrade

The MX2 beamline upgrade will substantially improve the beamlines performance and stability. The proposed improvements are:

1. Installation of a large pixel-array detector such as a Pilatus 6M
2. Installation of a new vertical focusing mirror (VFM) subtrate
3. Mini-Kappa goniometer head
4. Installation of equipment for in-plate microcrystal screening
5. Endstation upgrades and ancillary equipment

1. Large pixel-array detector

A large pixel-array detector (such as Pilatus 6M or equivalent) will significantly improve the data quality from the MX2 beamline for both the MX and SMX communities. The large dynamic range and high sensitivity of this detector will allow for faster data collection (single fine-phi sliced pass rather than traditional HR and LR passes). The lower detector readout noise will reduce systematic error from finely phi-sliced data. For data collected from very large assemblies where reflections are close together on the surface of the detector the very small point-spread function (1 pixel) will allow for collection of higher resolution data than a conventional CCD detector. A pixel-array detector will also provide the ability to conduct shutter-less data collection. The larger detector area allows for the measurement of higher angle reflections at the same detector distance. A cluster for real-time data integration is required and solutions are supplied with the detector by the vendor

2. Replacement VFM substrate

A replacement VFM mirror substrate will improve the focal size of the beam, increase the flux-density of the collimated beam at the sample and allow for faster user-controlled changes in the beam size. This will allow for higher quality data to be collected on smaller samples.

3. Mini-Kappa goniometer head

A mini-kappa goniometer head is required for SMX users of the MX2 beamline and will be rigged so as the kappa and phi goniometer posts can be quickly and easily exchanged by beamline staff. As with MX1 a commercial mini-kappa such as that sold by MAATEL would be preferable due to the existing high-quality alignment and collision prevention software available.

4. In-plate screening equipment

This upgrade will provide a new capability for in-plate screening of micro-crystals. This is intended to provide information to users as to which micro-crystal forms diffract but is not intended for in-plate data collection. A significant problem in the growth of crystals suitable for X-ray analysis is the determination of which "hits" in a crystal screen (that are often micro crystals a few microns in size) are best to optimize. Purified protein is usually in short supply and the crystals grown in screening experiments are usually too small for conventional X-ray analysis. In-tray screening on the MX2 beamline will be a significant asset to the MX community as it will provide key information as the diffraction qualities of crystal hits. The in-tray program will require close coordination with Australian crystallization facilities so that they can offer in-tray screening to their users. The plates may either be mounted on a modified holder on the goniometer or held in a modified gripper by the SAM robot (we need to carry out further testing to see if the robot is capable of this). Other equipment such as cameras, barcode scanners and a tray storage enclosure will be required.

It is envisioned that once in-tray screening is operational regular beamtime (2-4 hours a week) will be allocated for screening of trays in conjunction with crystallization facilities so that users can get rapid feedback on the qualities of their samples. We will work with participating crystallization facilities to arrange for plate transport, storage and screening so that users can request that their crystals are tested but do not need to apply for beamtime or arrange for shipping of their samples.

5. Endstation upgrades and ancillary equipment

The following upgrades to the endstation hardware are required in order to better meet the needs of the MX and SMX communities:

- improved crystal visualization (cameras, lenses, lighting)
- a thermal stability circuit is required to keep the temperature of the goniometer/slit box stands constant as fluctuation in the hutch temperature affects the stability of the system.
- Vibration dampening via a redesign of the goniometer and slit box bases
- Exhaust system for the cryojet dewar and robot dewar as they significantly cool the hutch when they are filled with liquid nitrogen.
- Beamline modifications to be able to mount the in-line Raman spec
- modifications to the existing detector mount in order to allow for a lower minimum crystal-detector distance for high resolution data collection (essential for many SMX experiments)
- deployment of two-theta movement for the detector
- upgrades to A-frame in order to allow both CCD and pixel-array detector to be mounted on the detector cage
- programmable temperature control of cryojet to allow for SMX phase transition studies

3. Structural biology lab

Drug design by fragment-based screening is an emerging technology for developing drug-like inhibitors from crystallographic information. The method has been adopted by several laboratories within Australia and will become increasingly widely used within the next five years. Fragment-based screening requires large amounts of beamtime and a high level of technical expertise in automation. Substantially automated processes are required for growing, soaking and collecting data in order to attain reproducibility. The proposed laboratory and beamline facilities will support synchrotron staff and users in developing a world-class center for fragment screening. This center will bring together expertise in screening and medicinal chemistry to assist users to progress from solving a biologically interesting structure to developing a promising lead compound. The lab upgrade is also required to facilitate in-plate

screening on the MX2 beamline as there is currently no crystal growth or tray storage facility at the AS.

Staff research program

Fragment-based screening is a very recent and cutting-edge technology requiring a significant investment in methods development. The proposed structural biology laboratory facilities and staff based research program are targeted towards developing fragment-based screening methods and facilities at the AS and supporting user experiments in this area.

In achieving this aim it is essential that MX staff at the AS remain active in their research and keep current with modern techniques. The staff research program will target proteins shown to be essential for bacterial virulence and survival. These data will aid in understanding these processes at the molecular level and will provide a framework for the development of methods for combating bacterial infections and, in the long term, remedying the diseases they cause.

Proposed Upgrade

A comprehensive lab upgrade is required to produce a working structural biology lab at the AS. The proposed improvements are:

1. Fit-out of space inside the AS with equipment, consumables and fine chemicals to produce a functioning lab.
2. A set of fragment libraries for users and staff to use for screening experiments in conjunction with crystallization facilities such as C3 and Monash.
3. Improved beamline facilities for data processing.
4. Facilities for users to safely conduct heavy-atom soaks at the AS.
5. Ancillary equipment for temporary installation on the beamlines such as beamline spectrophotometers.
6. Xenon chamber for sample derivatisation
7. Cassette loading kits for loan to new users.
8. Other ancillary equipment identified as being needed for user experiments

1. Lab set-up

The construction of new buildings on the AS site under the IEF program will make laboratory space available inside the facility. This project proposes to create a complete structural biology lab at the AS. Such a laboratory would include facilities for the cloning of genes of interest, growing of bacterial and mammalian cells and the purification, crystallization and analysis of proteins.

Key equipment would include:

- Autoclave
- Lab benches
- FPLC equipment including columns and peristaltic pumps
- Shaker incubators
- Laminar flow hood
- Fume hoods
- Refrigerated centrifuges (floor standing, benchtop and micro)
- Refrigerated cabinets for crystal growth and protein purification
- Gel electrophoresis and blotting equipment
- Molecular biology equipment such as PCR machines
- Waterbaths
- Crystal growth room
- Balances
- Spectrophotometers including a nano-drop
- MQ and RO water plants
- Glass and plastic ware
- Dewars
- Cassettes and loading kits
- Microscopes
- Ice-maker
- pH and conductivity meters
- Drying cabinet
- Freezers (both -80 and -20 degrees)
- Linux workstations for structure determination

This lab would allow staff and visitors access to complete laboratory facilities. These lab facilities will allow AS staff to conduct their own research and nucleate research at the facility in structural biology. Such facilities are essential to allow the development of cutting-edge research at the AS and to keep the beamlines current with developments in the field. These lab facilities will also be of use for preparation and study of samples for staff and users of other beamlines such as SAXS/WAXS and CD/SAXS.

2. Fragment libraries

The laboratory will require stocks of commonly used fragment libraries (such as Maybridge, Chembridge, Enamine etc) in order to allow staff and users to conduct screening experiments. These library stocks will be shared with crystallization facilities and collaborating research groups in order to facilitate fragment-based screening and drug-design.

3. Improved data processing facilities

One of the assets of the MX beamlines is the crystallography expertise of staff. During users beamtime it is often difficult to process all data and solve difficult structures. It is proposed that a

space adjacent to the structural biology lab be fitted out with linux workstations for structure determination and that these facilities are made available to users both during and after their experiments. In this way staff can assist users with difficult crystallographic problems and the facility will offer a "crystal club" where every fortnight at a scheduled time users can bring their difficult datasets (or come along to learn) and work with staff at the data processing facility. This will help to teach the new generation of crystallographers the fundamentals of crystallography as increasingly powerful software can become a "black-box" for tractable datasets.

4. Facilities for on-site heavy atom soaks

One of the standard techniques for generation of experimental phases is the use of heavy atom derivatives. There is currently no dedicated area at the AS for users to carry out heavy atom soaking experiments. It is proposed to set up a separate room in the structural biology lab with a comprehensive range of heavy atom solutions, disposable bench guards, microscope, balance, fume hood, dewars etc so that all steps from opening the tray to freezing the derivative crystal can be conducted inside the single room. Users will only be permitted to take frozen crystals from the HA soaking room to the beamline to reduce the risk of contamination. Prior to use users will be trained on HA soaking procedure and after the soaking experiments will be supervised during cleanup and removal of the disposable bench coating. This facility should also help to train new crystallographers as to the potential dangers of HA salts, how to conduct soaks safely and effectively and allow for the determination of more new crystal structures.

5. Ancillary equipment for both lab and beamlines

Equipment that is temporarily installed on beamlines (such as in-line spectrophotometers) will be set up in the structural biology lab so that users can conduct preliminary experiments using this equipment prior to their beamtime. This will allow users to make the most productive use of their beamtime as standards and control regimes can be prepared ahead of time.

6. Xenon chamber

In addition to the use of a pressurised Xe environment to provide phasing to X-ray structure determination, it can be used to probe the interaction of proteins with molecular oxygen. Recent studies on a number of different enzymes have shown the presence of molecular channels as conduits to allow access of small gaseous molecules such as dioxygen to enter active sites in a controlled manner. Structural studies to probe the mechanism of entry and the possibility of channel gating can be pursued using a pressurized Xe cell. In such studies, crystals of the enzyme are subjected to Xenon gas in order to saturate the oxygen binding sites on the molecule and diffraction analysis carried out on the resultant derivatized crystals. Such an approach has been successfully employed for myoglobin, cytoglobin and Ni-Fe hydrogenase providing unique opportunities to study the dynamic role of residues involved in oxygen binding and transport.

7. Cassette loading kits

New users are often able to use the SAM robot as they do not have cassettes or loading kits. A number of cassettes and loading kits will be purchased for loan to new users. Once users are regular users of the beamline they would be expected to purchase their own cassettes.

8. Other ancillary equipment

Equipment identified as being needed by users of the beamlines.

B2: Applications and Potential Outcomes to Australian Scientific Community

The Macromolecular Crystallography Expansion Project proposal has been conceived as part of a concerted approach to providing a world-class structural biology facility, along with the proposals for a new high performance macromolecular crystallography (MX3) beamline and the CD/SAXS beamline. The MX PAC, as representatives of the user community have been involved in the outline of specifications for this proposal.

These facilities will reduce the time required to proceed through the critical checkpoints of structural biology:

- Users of crystallization facilities (such as C3 and Monash) will be able to send the same sample for analysis using the CD/SAXS beamline. The data from the CD/SAXS beamline may provide key information on biophysical characteristics of the sample to improve crystallization
- Promising hits in screening trials will be screened in-tray using the MX2 beamline to determine their diffraction quality
- Together these steps will reduce the time required to produce crystals suitable for X-ray analysis of difficult proteins or those where little material is available
- Micro crystals can be used for structure determination on the MX2 or HPMX (MX3) beamlines depending on the size and diffracting ability of the samples
- Fragment screening can be performed between the AS structural biology lab, crystallization facilities and user labs
- Hundreds of fragment soaked datasets can be collected and analysed in real-time using the MX1 beamline
- Further biological information on solved structures can be produced using the CD/SAXS beamline once the structures have been determined (ligand binding, assembly etc)
- SMX users will be able to carry out world-leading research at the AS beamlines with the new facilities including charge-density analysis, phase transition studies and challenging micro crystal small molecule structures
- The MX capacity of the AS will be significantly increased to cover existing and future demand.

The existing MX beamlines at the AS were constructed to provide the best facilities within the available budget. Given the significant advances in optics, detector and computer technology since the construction of the existing beamlines these upgrades will provide a major increase in capability and performance.

Together the new facilities will create a synergy of capability that will accelerate the pace of crystallographic research in Australasia.

B3: Match to Selection Criteria

Meet the demands of an identified group of researchers for new techniques

The MX and SMX community of the AS have already produced more than half of the facilities total output of refereed publications. This sizeable and highly productive community has a clear need for world-leading facilities. The Macromolecular Crystallography Expansion Project will significantly increase the capacity of the AS to carry out fundamental crystallographic research. It will also push back the boundaries in what is possible to study at the AS. The MX3 beamline will provide a world-leading capability for micro crystallography, the CD/SAXS will be the first simultaneous CD and SAXS instrument ever built and the upgrades to the existing MX beamlines will significantly increase their respective capabilities.

Take advantage of the existing third generation light source

The MX2 and proposed MX3 beamlines both use in-vacuum undulators as sources. Clearly this requires the use of a third generation source.

Will position Australasian scientists at the leading edge of their field

The AS MX and SMX facilities will be transformed from merely good to become truly world-leading. The combination of high throughput (MX1), broad range and capability (MX2), high performance (MX3) and biophysical characterisation (CD/SAXS) along with the facilities to allow users of all four beamlines to carry out on-site preparation will be unique.
The CD/SAXS beamline will be the first instrument of its type in the world and will provide a clear advantage to the Australasian structural biology community.
The MX3 beamline will be at the cutting edge of micro crystal analysis and provide the AS with the sole capability that Australasian crystallographers are currently forced to travel overseas to use. This beamline will push back the frontiers of what is possible to probe with single crystal X-ray diffraction and will allow the determination of structures that are currently unattainable due to crystal size and properties.
The Macromolecular Crystallography Expansion Project is essential in order to provide a clear path for future development of the AS crystallography program.

Can be demonstrated to be feasibly constructed within a 3 year time-frame

All components of the Macromolecular Crystallography Expansion Project can be constructed within three years. The MX3 and CD/SAXS project submissions both describe that the beamlines in question can feasibly be constructed in three years. The upgrades of the existing MX beamlines and lab construction can similarly be completed within three years.

B4: Potential Users

The MX beamlines at the AS currently have the largest user base of any group using the AS. The CD/SAXS beamline will be used by most of the MX community and a range of other users interested in pure CD or SAXS to further increase the user base.

Finally, the MX3 beamline will be expected to have a sizeable international user base once it has been shown to be world-leading. With only three (SLS, ESRF, APS) true microfocus beamlines in existence MX3 will be the only beamline in the southern hemisphere with this capability and will be expected to attract users worldwide.

Commercial use of the MX beamlines is expected to grow from the present rate.

An indicative list of the organisations that would use this facility are listed below.

Australian National University

CSIRO

Flinders University

Griffith University

Latrobe University

Massey University

Monash University

St Vincent's Medical Research Institute

The Walter and Eliza Hall Institute of Medical Research, Melbourne.

University of Auckland

University of Queensland

University of Melbourne

University of New South Wales

University of Sydney

University of Tasmania

University of Western Australia

University of Wollongong

Victor Chang Cardiac Research Institute