



Austin Biomedical Alliance Research Report 2001 | 02
Turning Science into Health

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Front Cover:
Rushika Perera (left) and Anna Marinic,
PhD students, Ludwig Institute for Cancer
Research, Tumour Targeting Program.

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The Austin Biomedical Alliance aims to be acknowledged as a world class medical and health research organisation.

The research groups at the Austin Campus, Repatriation Campus and Royal Talbot Rehabilitation Centre over which the Austin Biomedical Alliance forms an 'umbrella' organisation, are conducting leading edge research into areas such as neuroscience, cancer, immunology and vaccines.

Our vision is "Turning Science into Health" through close collaboration and sharing of services and the development of strategic partnerships.

The research activities at the ABmA encompass biomedical, clinical and public health research – bridging the interface between the laboratory and the clinic.

01: Executive Summary

The Austin Biomedical Alliance (ABmA), a newly formed research and development enterprise, represents a unique collaboration of expertise, technologies and intellectual capital. Located at the Austin and Repatriation Medical Centre (A&RMC), this Alliance integrates and consolidates the activities of 7 independent research groups and the Austin Hospital Medical Research Foundation (AHMRF) with a vision of 'Turning Science into Health'.

The 'partners' within the ABmA are:

- Austin & Repatriation Medical Centre
- The University of Melbourne
- Austin Research Institute
- Ludwig Institute for Cancer Research
- National Stroke Research Institute
- Brain Research Institute including Epilepsy Research Institute
- Institute for Breathing and Sleep
- Parent Infant Research Institute.

The ABmA is growing rapidly:

- Annual revenue of over \$25 million of competitive research grants
- 20% growth in funding over the past 3 years
- Over 700 researchers and support staff – 30% increase in 3 years
- Over 100 post-graduate trainee researchers
- Expanded linkages with hospitals and institutes globally, national and international academic collaborations, multinational pharmaceutical companies, industry, funding bodies, and venture capitalists.

Programs

The development of new research areas has been a major strength of the ABmA with new specialities including nursing and allied health. The research activities at the ABmA encompass biomedical, clinical and public health research – bridging the interface between the laboratory and the clinic.

Research interests are across 5 significant research programs:

- 1) **Neurosciences** – stroke, epilepsy, neuroimaging, psychology and psychiatry
- 2) **Transplantation, immunity and infections** – liver transplantation, renal, autoimmune diseases
- 3) **Metabolic medicine** – diabetes, osteoporosis, digestive diseases, endocrinology and male health and new drug development
- 4) **Cancer** – new treatments based on emerging scientific knowledge, immunotherapy, vaccines, tumour targeting
- 5) **Respiratory & cardiovascular medicine** – airways disease, sleep disorders, hypertension, coronary disease and heart failure.

Platforms

Researchers have access to shared resources and platform technologies in these basic and clinical research programs.

Platforms include:

- Molecular genetics
- Animal models of disease
- Imaging facilities (3Tesla Magnetic Resonance Imaging, Positron Emission Tomography)
- Protein Science
- Structural biology and biological modelling
- Clinical Trials – pharmacology, cancer, neurosciences.

Key Achievements

Advances in basic research that have translated into clinical and commercial outcomes, include:

- Pioneering work on the treatment of hypertension over the last 30 years including recognition of the role of Angiotensin Converting Enzyme (ACE) in hypertension and diabetes
- Major contribution over a number of years to a better understanding of clinical aspects of the acute stroke process
- First gene for epilepsy discovered and key involvement in the discovery of five of nine known genes for epilepsy by the Austin group
- Pioneering work on the development of humanised antibodies against tumour cell antigens and tumour stroma and the development of early diagnostic tests for cancer
- Pioneered in the early 90's the 'piggy back' liver transplantation technique, now widely used around the world and the paediatric and cut down liver transplant
- Discovery of crucial mechanisms in dendritic cells which regulate and enhance immune function
- Development of new ways to treat infection, through novel vaccines
- Development of screening programs for sleep disorders.

Future Directions

Future directions focus on our linkages, intellectual property, commercialisation and training capabilities. Based on our location servicing a catchment of 1.5million people, with assured access to patients (71,000 inpatient episodes and 130,000 outpatient attendances annually), the concept of "bench to bedside" research is where ABmA is focussing its research programs.

The Austin Biomedical Alliance Precinct is a strategic research alliance bringing together all biomedical, clinical and public health research of 7 independent research groups at the Austin and Repatriation Medical Centre.

02: Chairman's and CEO's Report

On behalf of the Austin Biomedical Alliance (ABmA), it gives us great pleasure to present this annual report to you. This is the first research report from the Austin Biomedical Alliance and details the exciting and extensive research that has been conducted by all of the Alliance partners.

This report highlights the ABmA's vision of "Turning Science into Health" through the close collaboration and sharing of services between Research Institutes, the Austin and Repatriation Medical Centre and the University of Melbourne to meet the aim of translating research into better health outcomes. The combination of biomedical, clinical and public health research undertaken collectively by the Alliance provides the bridging interface between the laboratory and the clinic.

In order to foster ongoing collaborative efforts and to take advantage of the unique consortium of expertise, technologies and intellectual capital that makes up the ABmA all researchers will best be served by being housed in a single enhanced biomedical research facility. The redevelopment at the Austin site provides an excellent opportunity to consolidate all of the research activities being undertaken on the hospital site and create a world class research facility. This is a key aim of all partners in the Alliance over the coming years.

The Victorian State Government has committed \$15 million dollars to the Teaching, Training and Research component of the redevelopment, subject to matched funding being available from other sources. A component of these funds has already been allocated to Education facilities for students in the new Austin hospital building. Both the University of Melbourne and La Trobe University have contributed funding to this project. A proposal for a new research facility is under development but is subject to attracting additional investment.

This report outlines the goals and research activities of the ABmA through the five key programs and platform technologies. Also included are the significant achievements across each program and in each platform technology. Future research directions and challenges are also addressed.

It is rewarding to note the many awards presented to ABmA researchers across A&RMC Departments and University of Melbourne Departments as well as in the Research Institutes. Partners of the ABmA have also been successful in attracting over \$25 million in revenue each year through the competitive grants process.

The ongoing commitment by the ABmA to conducting and fostering world class research will result in another exciting year ahead for all.



A handwritten signature in blue ink that reads "Geoffrey Donnan".

Professor Geoffrey Donnan
Chairman
Austin Biomedical Alliance



A handwritten signature in blue ink that reads "J. Williams".

Jennifer Williams
Chief Executive Officer
Austin and Repatriation Medical Centre

December 2002

03: Austin Biomedical Alliance – A Vision for the 21st Century

The Austin Biomedical Alliance was established in recognition of the need to further multidisciplinary scientific research and progression to timely commercial advantage, together with the need for a critical mass of intellectual capacity, physical resources and access to specialist research facilities including platform technologies.

The Alliance members seek to achieve, enable and support high quality research, the development of active linkages with users of research, maintenance of the breadth and depth of research strengths, the fostering of collaborative projects and the attraction and retention of leading edge scientists.

The Alliance has formulated a vision, mission statement and goals to underpin its development over the next five years.

Vision

The Austin Biomedical Alliance aims to be acknowledged as a world class medical and health research organisation. The research groups at the Austin Campus, Repatriation Campus and Royal Talbot Rehabilitation Centre over which the Austin Biomedical Alliance forms an 'umbrella' organisation, are conducting leading edge research into areas such as neuroscience, cancer, immunology and vaccines.

By supporting and promoting close collaboration and sharing of services between the research institutes, hospital and University of Melbourne, and with the development of strategic partnerships, the Alliance aims to translate research into better health outcomes for Australians and the world, thereby achieving its vision of 'Turning Science into Health'.

Values of the Austin Biomedical Alliance

The Alliance is committed to:

Integrity

Adopting high ethical and professional standards in medical research and in the communication of research findings.

Community

Actively collaborating and co-operating to ensure the achievement of synergy in research and application outcomes.

Knowledge

For the ultimate benefit of our patients and the community as a whole:

- Utilising and harnessing the potential of the best technologies and information in pursuit of new understanding across a wide spectrum of basic and applied biomedical knowledge, and
- Adoption of a global perspective in endeavours to challenge the existing boundaries of medical and health science.

Empathy

Create an environment in which the expectations, needs and feelings of all with whom we work and for whom we care are understood and addressed.

Quality

Developing, applying and continually improving research processes to produce and maintain robust, reliable health outcomes that go beyond the expectations of individual patients and the broader community.

Accountability

Adopting and promoting equity and openness in all administrative, financial and decision-making functions of our Alliance Executive, to all partners in our Alliance

- Providing equitable access to appropriate, shared research facilities and resources
- Managing all shared services, facilities and resources in a cost-effective, efficient manner.

Mission Statement

The mission of the Austin Biomedical Alliance is to 'undertake innovative research through collaborative networks to continuously improve health outcomes'.

In achieving its vision and mission, the Alliance will focus on a number of principal themes that will also contribute towards Victoria's vision 'to be recognised as one of the world's top five biotechnology locations for the vibrancy of its industry and quality of its research'.

The principal themes of the Alliance are to:

1. Develop our research directions
2. Enhance our research infrastructure
3. Enhance our skill base
4. Strengthen our commercial capabilities
5. Build and enhance our reputation and profile
6. Ensure our financial sustainability.

Education and Training

Education and training are central to two important principles underpinning this vision:

- Recognition of the importance of teaching in every clinical discipline and hospital department as an integral component of best practice clinical care
- Recognition that high quality, innovative education underpins the Alliance's ability to attract and retain the highest calibre of students, staff, clinical leaders and researchers essential for excellence in clinical care and research.

Goals

To achieve the goals outlined below, the Alliance will work with researchers, clinicians, key agencies, government, industry, venture capitalists, "angels" and the community. The goals, which focus on excellence in research, teaching and education, place emphasis on the benefits from enhanced local and international collaborative links and on wider social and economic benefits.

- To create an educational precinct that is a vibrant place of learning, accessible to all undergraduate and postgraduate students and to staff in all disciplines
- To provide the highest quality clinical and research education resulting in excellence in clinical care and research, high ethical standards and enhanced clinical risk management throughout the organisation
- To attract and retain the highest calibre of students and staff to enhance Alliance's clinical and research skill base
- To achieve a local, national and international reputation as a centre of excellence in education and training with extensive national and international linkages
- To achieve sustainability through an optimal funding model and efficient use of resources.

Research activities

The research activities of the Austin Biomedical Alliance encompass biomedical, clinical and public health research – bridging the interface between the laboratory and the clinic. These research activities are across 5 significant research programs with a focus of 'bench to bedside' research.

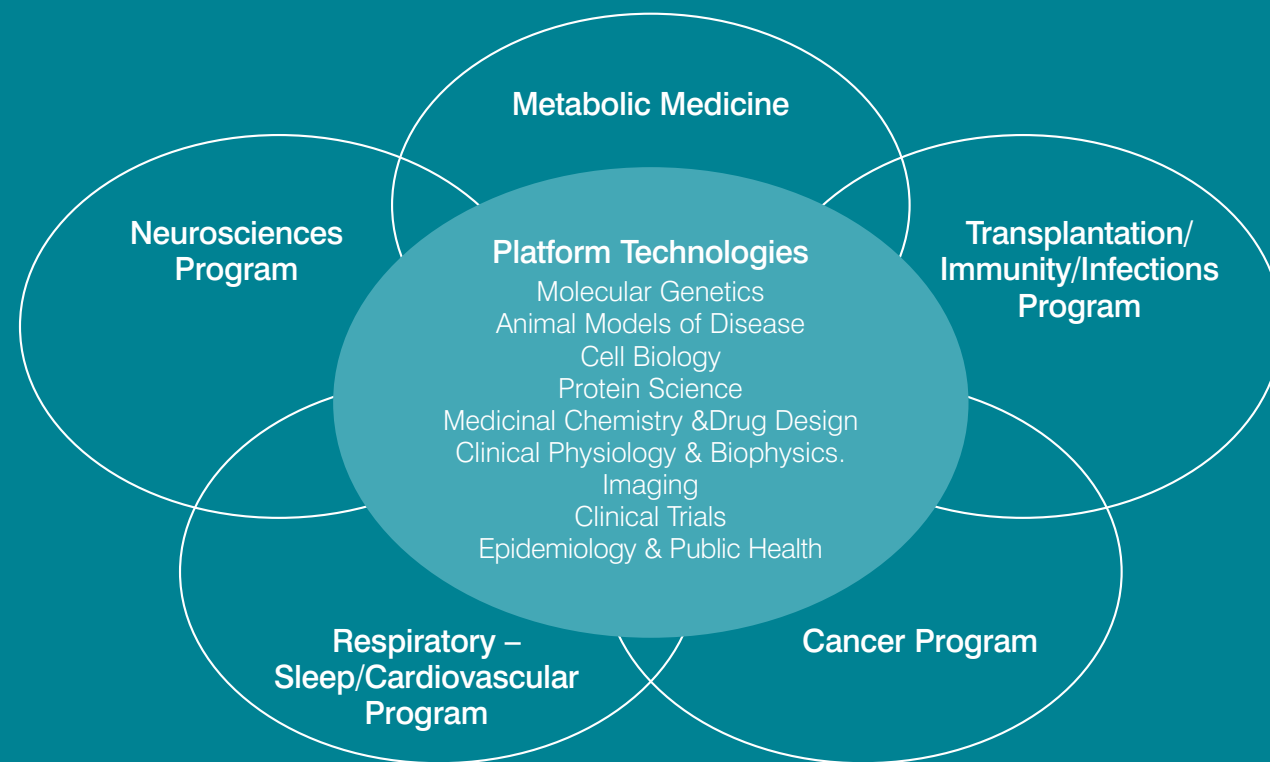


Figure 1: Programs & Platform Technologies

Research Programs

1. Neurosciences – stroke, epilepsy and neuro-imaging
2. Transplantation, Immunity and Infections – liver transplantation, renal, auto immune diseases
3. Metabolic Medicine – diabetes, osteoporosis, digestive diseases, endocrinology and male health, and new drug development.
4. Cancer – new treatments based on emerging scientific knowledge, immunotherapy, vaccines, tumour targeting
5. Respiratory & cardiovascular medicine – airways disease, sleep disorders, hypertension, coronary disease and heart failure

A number of platform technologies are available as outlined in figure 1.

Austin Biomedical Alliance – A Vision for the 21st Century

The “Glue” holding the Austin Biomedical Alliance together is collaboration, intellectual property (IP) and intellectual capital.

The Alliance is a new form of research precinct, where a group of common platform technologies are used to address a wide variety of clinical problems. By its patient-focussed nature, investigators may use the platform technologies at one or multiple points in the pathway from scientific concept to product marketing. The Austin Biomedical Alliance, therefore, is researching the diseases and health concerns of a representative Australian community. Using the platform technologies as a base and involving a broad range of clinicians and scientists, the focus of the Alliance is in five major areas or programs. By doing so, each program is highly competitive at an international level.

The Austin Biomedical Alliance is actively attempting to expand the number of its already substantial commercial and academic partnerships. The location in an acute teaching hospital setting, with the active co-operation of scientists and medical staff, gives added advantage and expanded opportunities to achieve the future directions based around the concept of “Bench to Bedside” research.

Research Collaborations and Linkages

There is a strong spirit of internal collaboration within the Austin Biomedical Alliance. The mechanism of these linkages involves existing collaborative research projects as well as cross-program strategic alliances for the development of future projects. This is underpinned by shared platform technologies, particularly imaging, bio-informatics and cell biological techniques. Some of the linkages between programs have particular strength and are worth emphasising.

Examples are:

- Neurosciences/Cancer – the development of new radioligands to identify forms of brain cancer. Shared common platform technologies of PET and MR allow further development of these initiatives
- Cancer/Transplantation/Immunity/Infections – shared platforms of protein and monoclonal antibody production, cell biology and bioinformatics underpins a commonality of approaches to the basic biology of autoimmunity and basic mechanisms of renal, infectious and chronic inflammatory bowel disease
- Metabolic medicine/Transplantation/Immunity/Infections – the Austin Biomedical Alliance has one of the strongest transplantation programs in Australia. This involves the liver transplantation unit and renal transplantation. Shared approaches to immunosuppression, rejection and technical aspects of transplantation techniques are mutually beneficial.

Many other collaborative linkages exist in sharing platform technologies and intellectual interest in solving problems involving overlapping disease mechanisms. Such internal linkages are either horizontally or vertically integrated – the latter embracing the shared vision of “Turning Science into Health”.

The members of the Alliance have developed numerous external linkages, nationally and internationally as summarised in Section 10.

1. Neurosciences Program

The strengths of the neurosciences program reside in the areas of stroke, epilepsy, neuroimaging, psychology and psychiatry.

Significant achievements of the program include:

Stroke

- Establishment of the Australian Stroke Trials Network (ASTN) within which a large number of clinical trials have already been conducted
- Australia’s largest stroke incidence study, the North East Melbourne Stroke Incidence Study (NEMESIS) continues
- New risk factor for stroke discovered (aortic arch atheroma)
- Influential in establishing thrombolysis as therapy for acute ischaemic stroke
- Developed embolic detection as a surrogate marker for ischaemic stroke post-carotid endarterectomy
- Mechanisms involved in the control of voluntary movement by the nervous system, and its recovery following injury

The genetics revolution has provided a wealth of detailed scientific insights which are now being developed into new therapies that will directly benefit patients.

Austin Biomedical Alliance – A Vision for the 21st Century

- The spatial distribution of the ischaemic penumbra following stroke – Insights provided by mapping methodology
- Specific growth factors have been shown to be responsible for regeneration after brain injury
- Automated identification of strokes – Development of a potential clinical/ research tool.

Epilepsy

- In–depth research into the causes and consequences of epilepsy, using neuroimaging, family studies, and genetic analysis
- New epilepsy syndromes described
- First gene for epilepsy discovered
- Five of the nine known genes for epilepsy discovered by the Austin group
- Identified a genetic mutation responsible for 2 common forms of childhood epilepsy.

Neuroimaging

- Pioneering work on the use of ¹⁸F–Fluoromisonidazole (FMISO) to image those parts of the brain after stroke that are likely to recover (penumbra)
- The use of single photon emission computed tomography (SPECT) was proven to be of use in identifying the origin of seizures
- New software developments for MR imaging
- Implementation of a new technique which allows labelling of physiologically–identified neurons (juxtacellular neuronal labelling)
- Interaction between cholinergic and dopaminergic systems in the living human brain revealed by PET.

Psychology and Psychiatry

- Evaluation of Australian Centre for Post–traumatic Mental Health (ACPMH) – accredited PTSD programs
- The National Depression Initiative Victorian component – Antenatal Support following Depression – Enhancing the Parent–Infant Relationship
- A Randomised, Controlled Evaluation of Sertraline, Cognitive Behaviour Therapy and Combined Therapy for Postnatal Depression
- Premature Infants: Early Intervention for Mothers, Fathers and their Infants.
- Helping Depressed Mothers and their Infants (The H.U.G.S. Program and Intuitive Mothering)
- Developing antenatal intervention based on theoretical models of parenting risk
- Effectiveness of Antenatal Education Classes for Reducing the Occurrence and Severity of Postnatal Depression.

General Neurosciences

- Made major contributions to elucidation of brain pathway involved in cardiovascular reflexes
- Involvement of the perirhinal cortex in verbal memory
- Verbal memory representation in TLE: evidence of brain plasticity
- Clinical studies for the effective treatment and management of Alzheimers Disease, Vascular Dementia and Mild Cognitive Impairment
- Dementia with Lewy Bodies (DLB) and improved diagnosis by a specific SPECT technique
- Assessing the impact of Dementia on Driving Ability.

Future directions are based around the concept of “Bench to Bedside” research, particularly in the areas of development of new neuroprotectants for stroke and therapies for epilepsies, and particularly with commercial partners. Through its nodal linkages with Neurosciences Victoria (NSV) strong commercial links have already been established with CSL and Schering AG.

2. Cancer and Cancer Biology Program

The genetics revolution has provided a wealth of detailed scientific insights which are now being developed into new therapies that will directly benefit patients. These include drugs which can block the molecular mechanisms which drive cancer.

The Cancer Program undertakes research which bridges the interface between the laboratory and the clinic. Its mission is to develop new treatments based on emerging scientific knowledge. This is achieved by co–ordinating and drawing on expertise from the hospital’s clinical and research community, as well as wide–reaching collaborations within the intramural program of the Ludwig Institute for Cancer Research (LICR) and with industry. The joint Ludwig A&RMC program was established in order to provide an optimal environment for the crucial interface between patient care and basic and clinical research into novel cancer therapies.

The major focus of this research has been immunotherapy, where insights into the relationship between the immune system and cancer have given rise to an exciting range of new treatments aimed at eradicating cancer by immune mechanisms. This research is currently being tested in clinical trials and is showing great promise. This is a major focus of the LICR and the Austin Research Institute.

The program includes the:

- **Medical Oncology Unit** – a joint clinical unit of A&RMC and the Ludwig Institute
- **Tumour Targeting Program** which performs basic research and tumour targeting strategies with recombinant antibodies and signalling molecules for diagnostic and therapeutic applications
- **Cancer vaccines** which uses newly discovered molecules as targets for anti–cancer immune responses
- **Biological Production Facility** – which manufactures biological agents, to high quality standards, for clinical trials
- **Immunohistochemistry and Tissue banking** laboratory program to analyse tumours prior to, and during, treatment with new anti–cancer therapies
- **Growth factors program** from the University Departments of Medicine and Surgery determining the role of peptide growth factors in cancer initiation and progression.

Significant achievements of the cancer program include:

- The development of a novel chimeric antibody for treatment of malignant melanoma
- Pioneering work on the development of humanised antibodies against tumour cell antigens and tumour stroma
- The discovery of unique therapeutic molecules against the EGF–Receptor which have anti–cancer effects
- Clinical evaluation of new cancer vaccine strategies against melanoma and other tumours
- Discovery of crucial mechanisms in dendritic cells which regulate and enhance immune function
- Pioneering work on the role of positron emission tomography (PET) in the staging and therapeutic monitoring of cancer through molecular imaging
- Research into the immunisation of cancer patients, with the aim of producing effective immunotherapies to assist in cancer treatment
- Use of molecular biology techniques to study prostate cancer progression and metastasis
- Identifying links between benign prostatic hypertrophy and the renin–angiotensin system
- Establishment of autoradiographic techniques to allow the study of AT2–receptor expression in human tumours grown in athymic nude mice

- Elucidation of the role of AT2–receptors and its putative interacting protein (ATIP) in human tumour cell growth
- Utilisation of immunohistochemistry of tumour antigens as applied to the application of tumour targeting by Positron Emission Tomography. This basic work supports tumour imaging in the Ludwig Institute immunotherapy trials of several common cancers
- Minimal residual disease in melanoma detected by Quantitative Real Time PCR using the NY–ESO1 and tyrosinase genes (used to monitor remission in clinical trials of melanoma immunotherapy)
- The ongoing development of Intensity Modulated Radiotherapy
- Participation in clinical studies examining the efficacy of radiotherapy for cancer treatment
- Identification of the components of the renin–angiotensin system (RAS) in the human prostate at protein and mRNA level
- Presence of angiotensin AT₁ and AT₄ receptors in the human prostate
- Over–expression of angiotensin–converting enzyme (ACE) in the human prostate in benign prostatic hyperplasia (BPH)
- Over–expression of renin in the human prostate in BPH
- Over–expression of the peptide angiotensin II in the human prostate in BPH
- Down–regulation of angiotensin AT₁ and AT₄ receptors in the human prostate in BPH

In achieving its vision and mission, the Alliance will focus on a number of principal themes that will also contribute towards Victoria's vision 'to be recognised as one of the world's top five biotechnology locations for the vibrancy of its industry and quality of its research'.

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- Angiotensin II enhances local sympathetic activity in the rat prostate
- Development of BPH in the prostate of the transgenic m(Ren-2)27 rat in which the local RAS is over expressed
- Over-expression of IGFBP-6 inhibits growth of skeletal muscle tumours in vitro and in vivo
- IGF-II inhibits the protective effects of butyrate, a fermentation product of dietary fibre, in colon cancer cells
- Establishment of a microarray facility to evaluate the genetic profiles of different dendritic cell subsets and cancer cell types.

Future directions of the Cancer Program include continuing the translational research of the Cancer Research Programs, with an emphasis on developing therapies based on cancer biology and LICR discoveries. The world-wide LICR cancer research programs provide a unique resource for allowing rapid development and translation of novel anti-cancer therapies to the clinic.

The Cancer Biology Program is examining the role of a number of growth factors in the initiation and maintenance of a variety of gastrointestinal and neural cancers. Studies range from neoplastic cells, animal models to resected tumours from the human. The unifying hypothesis is that these factors are major contributors to the development of cancer.

Some of the major achievements include:

- Identification of specific growth factors such as gastrin, bombesin and IGF in tumours
- Demonstration that removal of these factors slows the development of these cancers in cell and animal models.

Future directions will include the development of specific antagonists to these growth factors and whether measurement of these factors in the circulation will be helpful as an early diagnostic test.

3. Metabolic Medicine Program

Metabolic Medicine includes research into diseases such as diabetes, osteoporosis, kidney and digestive diseases and endocrine disorders including male health and imbalances of metabolites. This research involves a full range of experimental strategies from basic science through physiology to applied research to clinical trials. The Metabolic Medicine Program aims to develop coherent interacting strategies to understand diagnosis and develop therapies for these diseases.

Significant achievements of the program include:

Diabetes

- Pioneering work on the causes and prevention of the complications of diabetes
- Developing new treatments for diabetes
- Significant progress in explaining why hypertension and diabetes are related, as well as identifying an important new mechanism that causes proteinuria
- Recognition of the importance of growth regulatory proteins in common diseases such as diabetes and cancer
- Advanced glycation end products cause proximal tubular cells to transdifferentiate into myofibroblasts which may lead to fibrosis and kidney damage
- Increased diabetes-associated atherosclerosis in a new mouse model
- Prevention of diabetic renal disease with new glycation blockers
- Effective blockade of diabetic nephropathy with combination therapy
- New growth factors and hormones are associated with diabetic renal disease and atherosclerosis
- The characterisation of amylin as a growth factor important for pancreatic beta cell and renal proximal tubular cell integrity: important implications for the onset of diabetes and complications.

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Osteoporosis

- World class studies on how to diagnose osteoporosis and predict who may develop this disease
- Testing of drugs for the treatment of osteoporosis
- The identification of a putative novel calcium transport system involved in calcium homeostasis: implications for osteoporosis.

Endocrine disorders

- Understanding genetic influences on the male reproductive system and prostate cancer
- Identification of hormone receptors in the thyroid and the brain
- Identification of eye muscle antigens in Graves' Ophthalmopathy
- The widespread expression of calcitonin receptors during foetal and tissue development: key cells in organogenesis and a role in tumourigenesis.

Renal disease

- Identification of new signalling pathways in the kidney that control salt excretion
- Isolation of heparanase as a new therapeutic target in kidney disease
- Elucidation of the role of dietary vitamins in renal disease
- New model of renal disease in mice with lipid abnormalities
- The renin–angiotensin system in other forms of renal disease
- Central site for Beginning and Ending Supportive Therapy (B.E.S.T) Kidney Epidemiological Study.

Digestive diseases

- Regulatory roles for mammalian bombesin in the reproductive and gastrointestinal tracts
- Demonstration of the critical importance of the gut hormone gastrin for gastrointestinal functions of the new-born
- Control of expression and secretion of gastric regulatory peptides
- Demonstration that precursors of gastrin are biologically active acting through novel receptors
- Establish that patients with peptic ulcer disease have an increased proportion of gastrin precursors in the circulation.

Metabolite imbalance

- First experimental use of super high-flux membranes in the world
- First controlled human study of high-volume hemofiltration in sepsis
- Major site for Saline versus Albumin Fluid Evaluation (S.A.F.E.) study.

There is a very close interaction between the relevant clinical units treating these diseases and the research teams studying their aetiology. This breadth is a major strength of the metabolic medicine program.

Future directions include an expansion of studies of male hormones and male health, ongoing and continuing expansion of studies of the treatment of osteoporosis and the identification of novel mechanisms in diabetic vascular disease. Expansion of studies of the gastrointestinal system and renal disease will also occur.

4. Transplantation/ Immunology/Infectious Disease Program

An important feature of the Austin Biomedical Alliance is its integrated programs of immunology, transplantation and infectious disease.

This program is focussed on the:

- Development of new ways to treat infection, through novel vaccines
- Treatment of transplant rejection, by new and highly selective means of manipulating the immune system
- Overcoming organ shortage, by engineering animals as organ donors for human recipients
- Developing new anti-cancer vaccines and treatments
- Autoimmune diseases by specifically designing and developing new drugs.

The unique transplantation groups within the Austin Biomedical Alliance includes Victoria's only, and Australia's most successful, liver transplant unit, which has performed over 320 transplants since its inception in 1988. Interactions with research groups, attempting to understand mechanisms of rejection and alternatives to human organs include selective immunosuppression to prevent transplant rejection and engineering of animals to allow organ donation from animals to humans.

The development of new approaches to the treatment of autoimmune diseases, such as rheumatoid arthritis, lupus, inflammation of the kidney and other organs, as well as

treatment of allergy, is a major area of investigation, particularly understanding the processes and developing new treatments for these conditions. This area has linkages into rheumatology, haematology and the understanding of inflammatory processes in cardiovascular, respiratory, kidney, liver and vascular disease.

The development of novel approaches to vaccine production is a key component of the basic R&D across a spectrum of vaccine approaches, including anti-viral, anti-bacterial immunity, and mucosal immunity (relevant to diseases such as AIDS and other sexually transmitted diseases, gastrointestinal – including cholera, rota virus, diarrhoea, tuberculosis and periodontal disease as well as anti-parasite immunity, especially in relation to malaria).

Significant achievements of the program include:

Transplantation

- Pioneered transplantation of hepatitis B patients
- Pioneered in the early 90's the 'piggy back' liver transplantation technique, now widely used around the world and the paediatric and cut down liver transplant
- Our development of a new anti HBV prophylactic treatment has totally prevented post-transplant recurrence of HBV. This therapy is now widely used around the world
- Hepato-pulmonary syndrome in end stage liver failure and post liver transplantation

- One of the top 3 laboratories in the world in the area of xenotransplantation and organ transplant research
 - Identification and cloning of the protein CD46 (Cluster Development 46 – membrane co-factor protein) (which will help to prevent rejection of pig tissue when introduced to humans)
 - World first in identifying and engineering to make animal organs more "human-like".

Immunology

- Pioneered monoclonal antibody technology for diagnosis and treatment of disease
- The development of a vaccine which can protect against lethal malaria after a single dose, and can clear large tumours in mice
- X-ray crystallography and molecular modelling to describe for the first time the proteins of white blood cells, called Fc receptors (FcR), that bind antibodies and trigger inflammation
- Identification of novel antigens in head and neck squamous cell carcinoma and hepatoma which elicit immune responses in tumour patients and are over-expressed in cancer
- Establishment of new methods for the quantitation of T-cells which recognise tumour antigens, which will improve the measurement of responses following cancer immunotherapy
- Investigating the role of laryngeal involvement in rheumatoid arthritis.

Infectious disease

- Identification of the gene responsible for vancomycin resistance in vancomycin-resistant enterococci (vanB)
- Identification that faecal colonisation with VRE occurs in the healthy Australian population at a rate of 0.2%, suggesting that the emergence of VRE is a complex, multi-faceted issue
- Clinical trials to identify the real level of VRE contamination by these patients during Outpatient, Radiology and Dialysis visits to help develop improved patient management guidelines
- Identification of the first case of MRSA with reduced susceptibility to Vancomycin (hVISA) in Australia
- A large epidemiological study of MRSA colonisation at A&RMC has been conducted as well as a series of interventions aimed at reducing the load of MRSA.

Cancer vaccines

- Novel methodologies developed to generate 'magic bullets' – anti-cancer drugs and toxins coupled with tumour seeking monoclonal antibodies
- Assessment of vaccines for cancers of the breast, lung, colon, ovary and pancreas clinical trials
- Establishment of quantitative molecular methods (quantitative real-time PCR) to measure the mRNA of tumour antigens
- Establishment of a pilot facility of the production of human DC for application as cancer vaccines.

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– A Vision for the 21st Century

Future directions include:

- Research in xenograft using harvested organs which is important to augment the shortage of organ donors. By using the pig and new techniques in cloning and genetic engineering the hurdle of rejection may become a reality. Studies are underway examining transgenic mice which reduce the galactose sugar (to which antibodies react) and determine the effects of various modifications on organ and cell transplantation. These studies will be the prelude to the production of pigs whose organs could be used for successful human transplantation
- Research of liver dialysis and artificial liver support is also under way, some of this research has been incorporated into clinical practice
- Drug development to reduce hepatitis B recurrence and transplant rejection
- Focussing on research that will contribute in the understanding of the most important mechanisms of resistance to infectious diseases and destructive inflammation in autoimmune disease. Acquiring knowledge that will enable the development of effective and highly specific therapeutic approaches to the treatment of disease and a better understanding of the functioning of the immune system.

5. Respiratory/Sleep Health & Cardiovascular Program

A broad range of research programs, education and public health advocacy are provided by the Institute for Breathing and Sleep and the Departments of Respiratory and Sleep Disorders Medicine and Thoracic Surgery at the A&RMC precinct. These are under-pinned by the platform technologies of:

- Respiratory and sleep physiology in which A&RMC has had an international reputation for more than 4 decades
- Respiratory pharmacology
- Epidemiology, and
- Cellular biology and cytogenetics of lung cancer.

There are active research programs in airways disease (asthma and COPD), in lung cancer, in sleep disordered breathing and respiratory failure, and in the clinical measurement of respiration and sleep in health and disease.

Significant achievements of the program include:

Respiratory and sleep:

- Studies into morbidity and treatment of mild obstructive sleep apnoea
- Links between hypertension and sleep disorder breathing
- Finding of an increased prevalence of sleep disordered breathing in transport workers and in spinal cord injured patients

- Development of screening programs for sleep disorders in industry
- Discovery of a specific abnormality on the short arm of chromosome 9 in non-small cell lung cancer
- Establishment of the Victorian Respiratory Support service as a statewide service for research and management of respiratory failure requiring ventilatory support
- The identification of a 10% prevalence of obstructive sleep apnoea in Australian transport workers
- The effective reduction in CPAP treatment pressure requirement following weight loss in severely obese patients with obstructive sleep apnoea
- Severe gastro-oesophageal reflux is associated with impaired respiratory gas exchange
- The identification of an 80% incidence of obstructive sleep apnoea in patients with acute quadriplegia.

Cardiovascular (ischaemic heart disease, hypertension, heart failure, and cardiac rehabilitation and secondary prevention)

- Novel treatments for hypertension and heart failure, treatments that are now used in patient care
- Pioneering work on the treatment of hypertension over the last 30 years including recognition of the role of Angiotensin Converting Enzyme (ACE) in hypertension and diabetes
- Pioneering work on a range of novel centrally acting agents, calcium antagonists and other vasodilators

The physical environment of A&RMC will change dramatically with the \$325M redevelopment of the hospital, and the Austin Biomedical Alliance wants to enhance the research environment in parallel.

An overarching philosophy will be to continue to focus on the mechanisms of diseases that are common and important in our society.

Austin Biomedical Alliance – A Vision for the 21st Century

- Strong track record in heart failure particularly with links with depression and the value of exercise training
- National guidelines for the management of heart failure
- Telephone guidance on risk factor modification after myocardial infarction and coronary artery surgery
- The benefits of treatment for hypertension in those over the age of 80
- Multicentre randomised trials assessing new treatments for unstable angina, myocardial infarction, hypertension and heart failure
- Ongoing evaluation of the fate and longevity of arterial grafts, particularly the radial artery in coronary artery surgery
- Evaluation of left ventricular reconstruction, mitral valve repair and ventricular containment in the treatment of heart failure
- Evaluation follow-up of radio frequency coagulation in the treatment of atrial arrhythmias
- Causes and treatment of venous leg ulcers in the elderly
- The comparison of Stentless Porcine Valve with the currently available heart valves
- Physiology and Pharmacology of Third generation by-pass grafts
- Evaluation of cardiomyoplasty
- Apoptosis in the pathogenesis of cardiovascular disease. Heart failure patients can safely undertake muscle strengthening exercises with marked improvements in their strength and endurance
- Functional capacity of heart failure patients is associated with the ACE gene
- Heart failure patients do not have impaired skeletal muscle mitochondrial oxidative capacity as previously thought
- Prosthetic external ventricular containment and ventricular reduction surgery can be safely undertaken in coronary artery bypass patients with enlarged, impaired left ventricles
- The morphology of radial arteries can be assessed non-invasively prior to their use as coronary artery bypass conduits
- Intravenous phosphodiesterase inhibitors have revolutionised our ability to undertake cardiac surgery on patients with poor LV function
- The Cardiac Depression Scale (developed at the A&RMC as a quality of life measure) has been translated into multiple languages and is being used in the USA, Europe, Canada, Japan, Thailand and other countries.

Future directions on investigations into the mechanisms of upper airways dysfunction in sleep disordered breathing and into the morbidity and management of patients at the milder end of the spectrum will be extended. The clinical pharmacology of asthma and airways disease will continue to be another research focus. More recently cellular biological basic research has been developed in lung cancer as have epidemiologic studies of sleep disordered breathing, airways disease and lung cancer which will continue. We will continue to define the biological mechanisms of cardiac disease with the emphasis on assessment of therapeutic approaches. The work into the links between depression and the risk of cardiac disease is continuing, and new studies will assess the effectiveness of guidelines in the management of heart failure, and define more precisely cardiac disease in patients with diabetes.

Future challenges

The Alliance will continue to promote partnerships and work collaboratively with many different partners, including the academic community, research community, industry, government agencies and funding bodies, and other institutions.

The most important element in the success of the Austin Biomedical Alliance will be its ability to recruit and retain scientific and medical staff. Staff who can identify clinical problems and address them in novel ways, leading to the development of strong intellectual property. Elements that will be strengthened include the bond between scientists and clinicians, and nurturing individuals whose careers straddle both of these areas.

In order for this interaction to take place, both physical and cultural changes are required.

The Austin Biomedical Alliance will look to:

- Enhance the physical facilities for its researchers
- Establish relationships with organisations such as the Australian Pharmaceutical Co-operative to move ideas to product development initially but in the long term to a technology park

- New ways for the interaction of scientists and clinicians employed by different entities within the Alliance will be developed so as to maximise interaction
- Develop an environment that can attract Venture Capital, which is crucial to the commercial development of the precinct. Co-location of Pharmaceutical companies, both large and small, as well as start-up companies is a major priority
- Adopt a pro-active approach, establish a secretariat that will attempt to attract suitable companies, and identify investors.

The physical environment of A&RMC will change dramatically with the \$325M redevelopment of the hospital, and the Austin Biomedical Alliance wants to enhance the research environment in parallel.

The programs and the structure of the Alliance outlined earlier and further described below reflect areas of intellectual commonality, research interests and strengths. By establishing the Alliance we have provided the critical mass to co-locate activity and resources necessary to compete for national and international funds. This has also provided the structures able to attract and retain high quality

scientists to the A&RMC. Future investments will continue to build on the research excellence of the Austin, ensuring that internationally competitive individuals are recruited. An overarching philosophy will be to continue to focus on the mechanisms of diseases that are common and important in our society. Through this co-ordinated strategic approach we will continue to make further progress.

The vast storehouse of information uncovered by the Human Genome Project is continuing to reveal potential new therapeutic targets in diseases such as epilepsy, dementia, hypertension, diabetes, cancer, gastrointestinal and respiratory disorders.

04: Platform Technologies

The Alliance's strategic initiative has addressed the need for a critical mass of intellectual capacity and physical resources, and access to specialist research facilities including platform technologies. Key platform technologies contributing to current research achievements are:

1. Molecular Genetics
2. Animal Models of Disease
3. Cell Biology
4. Protein Science
 - Monoclonal Antibody Production
 - Protein Production
 - Peptide Biology
 - Structural Biology and Molecular Modelling
5. Medicinal Chemistry and Drug Design
6. Clinical Physiology and Biophysics.
7. Imaging and Positron Emission Tomography (PET) and 3Tesla Magnetic Resonance Imaging (MRI)
8. Clinical Trials and Drug Evaluation
9. Epidemiology and Public Health.

1. Molecular Genetics

Molecular and clinical genetics will be major features of medical research in the new millennium. Standard gene cloning and gene analysis technologies are in widespread use within the Austin Biomedical Alliance, and underpin many basic and clinical studies.

Access to real time polymerase chain reaction (PCR), messenger ribonucleic acid (mRNA) expression, in-situ hybridization and gene expression using micro-arrays is available. In addition, gene identification by subtraction hybridisation or expression cloning strategies are also in use. The analysis of mutation and disease processes is undertaken by collaboration with the Australian Genome Research facility (AGRF) and with Grant Sutherland in South Australia.

2. Animal Models of Disease

The Austin Biomedical Alliance has a well-established skill base in identifying therapeutic targets gained from basic and clinical research, and expertise in using the techniques of functional genomics. The vast storehouse of information uncovered by the Human Genome Project is continuing to reveal potential new therapeutic targets in diseases such as epilepsy, dementia, hypertension, diabetes, cancer, gastrointestinal and respiratory disorders. At the A&RMC there is a long tradition of developing and using animal models of disease.

The main area in which models have been created include chemical induction of:

- Cancer
- Diabetes
- Epilepsy, and
- Surgical induction of heart failure, renal failure and liver disease.

Many models mimicking the initiation and progression of lung, breast, colon and other types of cancers have been developed. Naturally occurring models of disease such as the spontaneously hypertensive rat and the obese rat are also used. More recently the roles of particular genes are examined by targeted mutagenesis or over-expression.

Our use of these animal models range from:

- Examining the basic mechanisms of disease
- Identifying therapeutic targets
- Determining the efficacy of potential treatments
- Quantifying the pharmacokinetics and toxicology of lead compounds.

The cutting edge approach to animal model development is now dependent on transgenic systems. The ability to introduce and delete specific genes in a tissue and time specific manner will allow rigorous design of a new level of animal model systems. Expertise and experience in the important area of research is available at A&RMC.

Platform Technologies

The Austin Biomedical Alliance has successfully produced transgenic animals and knock out animals, eg for analysis of inflammation and immunological processes, and has the capability for embryonic freezing and embryo stem cell work.

Transgenic models are in use or being developed in the study of the following areas:

- Diabetes and obesity
- Muscle disease (skeletal and cardiac)
- Bone disease (osteoporosis)
- Normal Immunity
- Autoimmunity and inflammation
- Transplantation – allo and xeno
- Infection
- Cancer
- Functions of male hormones.

3. Cell Biology

Genetic and biochemical processes determine cellular behaviour and the co-ordination of cells determines how the tissues and organs function. Cell biology is therefore essential to research into health and disease. It underlies research into fields as diverse as degenerative disorders, wound healing, cancer and immunology.

Cell biologists at the Austin Biomedical Alliance study the proliferation and differentiation of different cell lineages from stem and progenitor cells through to those which are fully differentiated and function

as fully mature cells. These studies include phenotypic and functional changes through the developmental processes as well as interactions with other cells, migration, adhesion, differentiation and death.

Using an impressive array of clinical and laboratory resources, scientists at the Austin Biomedical Alliance are applying their skills to a wide range of important clinical problems for example: understanding how cancer cells grow and spread in the body, or developing better ways of targeting immune attack against cancer cells.

4. Protein Science

Monoclonal Antibody Production

The development of monoclonal antibodies in Australia, for basic scientific use and for diagnostic and clinical therapeutic use, has been a major contribution of the Austin Biomedical Alliance, and especially the ARI; most recently, with the development of a monoclonal antibody Good Manufacturing Practice (GMP) facility at the Ludwig Institute. Monoclonal antibodies have revolutionised many aspects of research and the development of new therapeutics. The Austin Research Institute has pioneered many of these with clinical trials undertaken using antibody or drug-antibody conjugates, and more recently whole humanised antibodies in the Ludwig clinical trials program. The application of these antibodies in defining cell

surface molecules, in immunohistochemistry, in various aspects of cell biology and in the diagnosis and treatment of cancer, transplant rejection and inflammation have been key developments of the Alliance.

Over 500 monoclonal antibodies have been produced, are in use, or are in storage. Antibodies to hormones, cell surface proteins, intracellular proteins, enzymes, carbohydrate, in humans and animals are being produced in mice and rats, as well as being re-engineered by recombinant means using technologies and skills available within the Austin Biomedical Alliance.

Protein Production

The production of recombinant proteins or natural products forms a fundamental basis of many aspects of research and development. With the description of a number of mammalian genomes drawing to a close, the analysis of the proteins encoded by these genes from human, mouse and rat, as well as those from infectious organisms will be a major focus of future research. Proteins are required for structure – function studies and in-vitro and in-vivo experiments. Clearly, for future research and development (R&D) a protein production capability is essential.

Great advances in vector systems and production systems have made this technology broadly available to research laboratories. The Austin Biomedical Alliance has developed skills in protein production in prokaryotic and eukaryotic systems, in protein purification, tagging and expression. These include E-coli (secreted and inclusion bodies), yeast (*Pischia pastoris*), insect cells (bacculo virus, *drosophila*), mammalian (myeloma, human fibroblasts, rodent fibroblasts, endothelial cells and other cell types), retroviral gene transfer (normal and proliferating cells).

These systems are widespread throughout the Austin Biomedical Alliance, offering great flexibility in the expression of proteins, such as membrane glycoproteins, enzymes, hormones, nuclear factors, immunoglobulins. In addition, know-how in relation to these expression systems, as well as the production of functional fusion proteins, and protein engineering is also available and recombinant proteins in a variety of systems have been, and continue to be, developed.

Peptide Biology

The Human Genome contains around 30,000 genes and these are translated into an estimated 300,000 different peptide and proteins. It is the analysis of these gene products which will provide information on mechanisms of disease, disease markers and therapeutics.

ABmA's expertise includes:

- Identification and quantification of peptides using electrophoresis
- Radioimmunoassay
- Yeast two hybrid assays
- Mass spectrometry
- Chromatography.

Additional skills are in localising peptides, determining biologically relevant modifications, interactions, bioactivities and ultimately function. These activities are a fundamental part of the drug discovery and diagnostic developmental process.

Structural Biology and Molecular Modelling

Structural Biology in its broadest context includes X-ray crystallography, macro molecular homology modelling, nuclear magnetic resonance (NMR) and a variety of protein structure technologies.

The Austin Biomedical Alliance has established X-ray crystallography and homology modelling as key technologies. These combined with structure function analyses of proteins are collectively aimed at understanding protein function, where the function is known, and assisting in function identification for those proteins whose function is unknown. X-ray structures of antigen presenting molecules, membrane proteins involved in inflammation, graft rejection, as well as immunoglobulins and

inflammatory proteins have been successfully determined. Homology models have been built for proteins involved in inflammation, cancer and immunity.

The facilities include:

- Computational capability with Silicone Graphics and Linux workstations fully equipped with commercial and public domain software, including Molecular Sciences packages
- Access to synchrotron beam lines through the Australian Synchrotron Program.

Information about the three-dimensional structure of proteins and protein-ligand complexes is used to design new drugs and to engineer new proteins with desired properties. This approach will optimise the utilisation of the information emerging from the various "Genome Projects" and "Proteomics Projects". In addition, the facility will make use of available genomic and proteomic information in order to find promising drug targets. In a case where no X-ray or NMR structures are available, homology based models of target proteins will be created, which can be iteratively refined in collaboration with experimental groups. This provides a unique expertise in Victoria, combining structural and biological knowledge with that available on existing databases.

Platform Technologies

5. Medicinal Chemistry and Drug Design

The Clinical Pharmacology Unit has a comprehensive range of capabilities including receptor characterisation, development of novel ligands, the identification of new targets and screening for new pharmacological agents.

Together with our affiliate the Victoria Institute of Biotechnology, the ABmA has a comprehensive program in drug design and medicinal chemistry. With the advent of new technologies and new chemistries, especially in relation to new chemistries, the development of a range of new classes of drugs is now possible.

The combination of X-ray crystallographic protein structure, molecular modelling and bioinformatics and new chemistries, using both computer based, virtual chemistry, as well as synthetic organic chemistry is an extremely powerful technology for drug development. A variety of proprietary and public domain computational approaches to drug design, protein structure docking, are available. Silicone Graphics and Linux workstations, a Linux processor for computational chemistry and drug design, virtual library screening are available and form the basis of small chemical entities for subsequent synthesis.

Drug synthesis using established and novel chemistries to make natural and synthetic products enables the development of a wide range of small chemical entities for screening

in in-vitro and in-vivo systems. As part of the drug synthesis capability, combinatorial chemistry approaches to generate libraries of potential new drugs for screening or for the rapid refinement of rationally designed drugs are being developed.

These capabilities integrate into molecular modelling and X-ray crystallography and form the basis of new drug development, such as the:

- Development of an ultra short acting β_1 specific blocking drug (D140) for intravenous use in coronary care and for anaesthetic practice
- Evaluation of early introduction of β blockade in post myocardial infarction patients using D140
- Generation of CHO cell lines transfected with rat and human β_1 , β_2 and β_3 adrenoceptors for pharmacological testing in place of laboratory animals
- Generation of mutations of the rat β_{1A} -adrenoceptor and their stable expression in mammalian cells in the investigation of important amino acid residues involved in binding of agonists and antagonists and the activation of G-proteins and adenylate cyclase
- CoMFA analysis of human β_1 adrenoceptor binding
- Identification of a novel imidazoline receptor (I_3) localised to neuronal cell bodies in human and rat brain
- Synthesis of I_3 specific ligands including a novel radio-iodinated ligand ^{125}I -0515.

6. Clinical Physiology and Biophysics

Clinical physiology and human biophysical measurement have been strongly developed:

- The respiratory physiology laboratory has been one of the leading Australian facilities for nearly 4 decades
- The sleep physiology laboratory is the largest in Victoria and takes the complex caseload statewide through the Victorian Respiratory Support Service
- The neurophysiology and cardiovascular laboratories (cardiac electrophysiology, echocardiography, cardiac catheter and vascular laboratories) are highly developed and serve a large clinical population.

These laboratories have substantial research components integrated with their large clinical caseloads and are thus significant clinical research centres. Several of these laboratories are statewide reference facilities in biophysical measurement.

The A&RMC clinical physiology laboratories perform a major teaching role through their affiliations with the University of Melbourne, Swinburne University and Victoria University and utilise student placements and post-graduate research positions to develop a career path for young scientists who provide a highly productive research resource. The recent appointment of a Melbourne University Chair in physiotherapy at A&RMC has derived from the very strong base of research in physiotherapy across neuroscience, respiratory, cardiology,

orthopaedics and rheumatology disciplines and the establishment of a limb movement and gate disorders laboratory. Collaborative internal links between these various aspects of clinical physiology are evident in the joint exercise research facilities, and the respiratory neurobiology and VRSS research programs. Along with numerous national and international external academic affiliations, these linkages make A&RMC a leading research centre for biophysical measurement and clinical physiology in Australia.

7. Imaging

The A&RMC Department of Nuclear Medicine and Centre for PET is the largest and most comprehensively equipped in Australia. It contains state-of-the-art imaging equipment including 10MeV cyclotron together with a whole body positron emission tomography (PET) camera and triple and dual head SPECT cameras. A "next generation" GSO crystal based PET camera combined with a CT scanner will be installed in 2002.

The Centre has a track record in research drug development, and in oncology and neuroscience basic research, and offers a drug development package that utilizes PET and SPECT for human biodistribution and dose determination studies. A full range of radionuclides is produced including N-13, O-15, C-11 and F-18. SPECT research with I-123 labelled compounds is also undertaken.

Over 1,500 PET studies are performed annually. The A&RMC pioneered the use of ictal injections of Tc-99m ceretec for assessing cerebral blood flow, a technique that is now used around the world for diagnosing epilepsy.

Magnetic resonance imaging (MRI) facilities are present at the BRI – a 3Tesla GE (General Electric) camera, the only one in the southern hemisphere has been installed. This enables real-time brain activation to be performed as well as chemical shift imaging (CSI) spectroscopy. A 1.5Tesla GE facility is used predominantly for stroke research on the Austin campus.

8. Clinical Trials and Drug Evaluation

There is a longstanding and high quality level of expertise in pre-clinical and clinical trial methodology at A&RMC. Clinical trials are currently undertaken in the ABmA programs including cancer, liver transplantation, neurosciences and sleep disorders.

One of the busiest cancer clinical trials units in Australia is based at the ABmA. The focus is evaluation of new anticancer therapies with a particular emphasis on novel immunotherapies such as the use of monoclonal antibodies and cancer vaccines. Early phase clinical trials with other anticancer agents are also performed, including the use of molecular inhibitors of receptor tyrosine kinases, angiogenesis inhibitors and novel cytotoxic drugs. The clinical priorities include important community

cancers, such as lung, breast and colon. In addition, cancers which are central to our special academic interests include malignant melanoma and hepatocellular carcinoma. These clinical trials are performed as collaborative arrangements with numerous organizations including the Centre for Developmental Cancer Therapeutics, the International Breast Cancer study group, Trans-Tasman Radiation Oncology Group, Australian GI Trials Group and Australia Leukaemia and Lymphoma Study Group. Numerous studies are undertaken in collaboration with industrial partners from the pharmaceutical and biotechnology sectors.

Within the Clinical Pharmacology Unit, phase I development is carried out while phase II safety and efficacy issues are addressed in both the Clinical Pharmacology Unit and Neurosciences. Phase III clinical trials, either investigator driven or commercially linked, are carried out in most clinical departments, particularly the Neurosciences, Hypertension, Endocrinology and Renal. One of Australia's few Drug Evaluation Units for the Therapeutic Goods Administration is contained within the A&RMC. This is the only group contracted by Canberra to provide clinical evaluations of new drug applications. The Unit has considerable experience in drug trial design, pharmacokinetics, phase I, II, III and IV clinical studies and adverse reaction monitoring.

The Liver Transplantation Unit performs multiple drug trials including clinical trials involving drug usage and hepatitis, and intra-operative bleeding.

Platform Technologies

The Neurosciences program contains a number of clinical trial units. Phase II and III trials are conducted. The NSRI will be housing the Australian Neuroscience Trials Network headquarters.

Three of the largest randomised controlled trials in the world in critical/intensive care are conducted at the A&RMC. These include the Saline versus Albumin Fluid Evaluation (SAFE) Study, Beginning & Ending Supportive Therapy (BEST) Kidney Epidemiological Study, and percutaneous tracheostomy. Other achievements include the first controlled study of the Medical Emergency Team in the world and the first experimental use of super high-flux membranes in the world.

Research conducted by the Pharmacy department includes:

- Examination of the need for surface contamination monitoring of preparation areas for antineoplastic agents in cancer treatment centres in Australia
- A comprehensive assessment of the impact of a clinical pharmacy service in the Emergency Department of a metropolitan tertiary referral hospital
- Implementation and assessment of electronic antibiotic approvals and monitoring.
- Implementation and evaluation of Australian consensus warfarin guidelines
- Implementation of a hospital-based community liaison pharmacy service to reduce older patient re-admission to hospital.

9. Epidemiology and Public Health

Within the National Stroke Research Institute, the Division of Epidemiology and Public Health comprises an experienced group of epidemiologists and statisticians with appropriate computer and software facilities. The Division has experience in cohort, case control and incidence of disease studies. Researchers have strong linkages to state and federal government agencies whereby epidemiological and other data is used to shape public health policy.

The NHMRC Health Evaluation Unit is housed on the Repatriation campus of the A&RMC within the Neurosciences Building with strong collaborative associations with members of the Alliance whereby the economic aspects of health evaluation are assessed.

In addition other epidemiological groups within the ABmA are based in the areas of sleep, bone disease and mental health. For example, the largest Australian trial (5,000 women) conducted into community screening and treatment for postnatal depression has been by a member of the Alliance. This randomized controlled trial investigated the effectiveness of early identification and the comparative efficacy of low and high cost intervention.

The Human Genome contains around 30,000 genes and these are translated into an estimated 300,000 different peptide and proteins. It is the analysis of these gene products which will provide information on mechanisms of disease, disease markers and therapeutics.



05: Members of the Austin Biomedical Alliance

Austin & Repatriation Medical Centre

The A&RMC is one of Australia's leading teaching hospitals and medical research centres. With more than 840 beds, we treat approximately 71,000 inpatients and 130,000 outpatients a year from 3 campuses, the Austin campus, the Repatriation campus and the Royal Talbot Rehabilitation Centre. Major research is carried out in the following areas:

- Aged Care Services
- Anaesthesia
- Australian Centre for Posttraumatic Mental Health
- Cardiac Services
- Cardiac Surgery
- Clinical Haematology
- Endocrinology
- Gastroenterology and Hepatology
- Infectious Diseases Department
- Intensive Care
- Laboratory Medicine
- Nephrology
- Neurology and Neurosurgery
- Nuclear Medicine and Centre for PET
- Nursing Services
- Nutrition and Dietetics
- Occupational Therapy
- Pharmacy Department
- Physiotherapy Department
- Psychiatry, Psychology, Clinical and Health Psychology
- Radiation Oncology

- Rheumatology
- Royal Talbot Rehabilitation Centre
- Social Work
- Speech Pathology Department.

University of Melbourne

**Department of Medicine
(Professor Jeffrey Zajac)**

**Department of Clinical Pharmacology and Therapeutics
(Professor William Louis)**

**Department of Psychiatry
(Professor Graham Burrows)**

**Department of Surgery
(Professor Christopher Christophi)**

The A&RMC is one of the three general Clinical Schools for the Faculty of Medicine, Dentistry and Health Sciences of The University of Melbourne. Each clinical school takes approximately seventy medical undergraduate students each year plus undergraduate students in Physiotherapy (30 students) and Clinical Psychology (10 students). In addition to the undergraduate students, there are approximately 95 postgraduate students (either full time or part time) in BSc Honours or postgraduate PhD or MD degrees. There are also postgraduate nursing students. There are approximately 230 clinical, teaching and research staff employed by the University located at the A&RMC.

Austin Research Institute

Director: Professor Mark Hogarth

Since its foundation in 1991, in the grounds of the Austin Campus of the A&RMC, the Austin Research Institute (ARI) has earned a reputation as one of Australia's leading medical research facilities. The ARI has a world recognised team of 100 researchers dedicated to combating cancer and finding ways to treat many common diseases by using the most recent advances in genetic engineering and immunology.

Ludwig Institute for Cancer Research

Director: Professor Tony Burgess

The Ludwig Institute for Cancer Research (LICR) is a worldwide network of ten branches in seven countries dedicated to basic and clinical cancer research. The program at the A&RMC was established to develop creative new therapies for cancer and is jointly supported by the LICR and the A&RMC.

National Stroke Research Institute

Director: Professor Geoffrey Donnan

NSRI conducts predominantly clinical research in the field of stroke in epidemiology and neuro-imaging using MRI and Positron Emission Tomography (PET), ultrasonography (including emboli detection) and clinical trials of therapy (thrombolytic agents, neuroprotective agents) and laboratory based research. The NSRI acts as a national focus for stroke research with collaborative centres in a number of states and internationally

Brain Research Institute (including the Epilepsy Research Institute)

**Director: Professor Graeme Jackson
Scientific Director: Professor Sam Berkovic**

The Brain Research Institute (BRI) was established at the Austin and Repatriation Medical Centre, in 1996. It supports collaboration between specialities in order to develop a better understanding of how a healthy or diseased brain functions. It is an affiliated institution of The University of Melbourne and an administering institution of the National Health and Medical Research Council. BRI, employs over 40 researchers full time and part time and 25 visiting honorary staff. Staff include neurophysiologists, paediatric and adult neurologists, physicists, radiographers, radiologists and scientists from Australia and overseas.

Institute for Breathing and Sleep

Director: Professor Rob Pierce

The Institute for Breathing and Sleep (IBAS) is an incorporated not-for-profit organisation designed to facilitate and co-ordinate research, education and public advocacy in respiratory and sleep health. IBAS developed from the programs of research based at the Department of Respiratory Medicine and the Sleep Disorders Service at the A&RMC and the University of Melbourne.

Parent Infant Research Institute

Director: Professor Jeannette Milgrom

The Parent-Infant Research Institute (PIRI) was established in 2000 as a separate body to oversee and to build on the clinical and research work undertaken through the Infant Clinic, Department of Clinical and Health Psychology, Austin & Repatriation Medical Centre. PIRI was incorporated in March 2001 with an advisory board chaired by Mr Garry Evans and aims to become the pre-eminent body conducting research into parent-infant difficulties including prematurity, risk screening, and early intervention following postnatal depression.

Above from left:
Professor Jeffrey Zajac
Professor Christopher Christophi
Professor Mark Hogarth
Professor Geoffrey Donnan
Professor Graeme Jackson
Professor Sam Berkovic
Professor Rob Pierce
Professor Jeannette Milgrom

Not shown:
Professor William Louis
Professor Graham Burrows
Professor Tony Burgess

The Alliance is an avenue for increased co-operation between the various parties, allowing greater sharing in certain services and benefits from the funding opportunities available to a centralised cluster of research.

06: Governance of the Austin Biomedical Alliance

The role of the Austin Biomedical Alliance is to support and enhance the activities of the members. The central stakeholder being the A&RMC, the Alliance will initially encompass the hospital and the seven independent research groups located on A&RMC campuses and the University of Melbourne. The Alliance is an avenue for increased co-operation between the various parties, allowing greater sharing in certain services and benefits from the funding opportunities available to a centralised cluster of research.

Each Alliance member has signed a Memorandum of Understanding for an unincorporated joint venture. The structure of the Alliance consists of the Board, a Research Strategy Advisory Committee, a Marketing and Corporate Relations Committee, a Facility Management Committee, and a Commercial and Business Development Committee. The Executive Director will work closely with the Board, the Committees and the research community. This organisational structure is being currently implemented to undertake the research, fundraising, marketing, and other operational activities of the Austin Biomedical Alliance.

The Board will oversee the strategic plan implementation and develop a set of agreements between the parties on which the Memorandum of Understanding is based. The Board composition includes the hospital, researchers and industry. The majority of the Board members will initially have a research

background. However, the composition of the Board will shift towards a predominance of business and industry Board members as appropriate individuals are identified.

The Research Strategy Advisory Committee will advise the Board on the strategic direction of the research programs. The Research Strategy Advisory Committee will play a pro-active role in identifying and promoting research collaborations within the Alliance and external collaborators. Terms of Reference will be developed that encompass:

- Adherence to criteria for 'intellectual property'
- Consultation and recommendations on the focus of future research strategy(ies)
- Strengthening of existing excellence in research
- Review and monitoring of the structure, content and activity of research.

The Marketing and Corporate Relations Committee will advise the Board on marketing and fundraising strategies. The terms of reference of this committee encompass:

- Developing the Austin Biomedical Alliance's strategic marketing and fundraising plan
- Determining viable fundraising projects
- Facilitating industry and community support
- Promoting effective communication with industry and community
- Providing personal support to marketing and fundraising activities.

Members of the Marketing and Corporate Relations Committee will include business, media, advertising and general community representatives who are leaders in their field.

The Facility Management Committee will advise the Board on major projects and establish facility management principles.

The Commercial and Business Development Committee will identify opportunities and assist to link researchers with funding agencies or commercial groups.

The Executive Director will be responsible for implementing the policies of the Board, liaising with key stakeholders and promoting the research activities of the Alliance.

07: Awards

Anaesthetics Department

- Florence Marjorie Hughes Research Award, 2002. Post–Operative Creatinine Changes In Patients With Pre–Existing Renal Impairment After Low–Flow Isoflurane Or Sevoflurane: A Randomised Clinical Trial.

ARI

- Professor Ian McKenzie, Austin Hospital Medical Research Foundation “Distinguished Scientist Award” for 2001
- Ms Dodie Pouniotis, Dr Laurence LeWinn Foundation Post Graduate Research Scholarship
- Mr Owen Proudfoot, La Trobe University Scholarship
- Ms Anita Gamvrellis, 1st Class Honours, Melbourne University; RMIT University Scholarship
- Dr John Kanellis, was a NHMRC Biomedical Research Scholar and is currently a CJ Martin Fellow at Baylor College of Medicine, Houston, Texas, USA. He has also received a grant from the Don and Lorraine Jacquot Foundation
- Dr Vasso Apostolopoulos, DSTO Career Development Award, from the Australian Academy of Science
- Dr Peck Szee Tan, Immunology Group of Victoria, Postgraduate Award, Immunology Group of Victoria (ASI), 9th Annual Mt Buffalo Conference
- Annemiek Van Spriel, KWF fellowship for fundamental and (pre)–clinical research Dutch Cancer Association, NOW talent fellowship

- Greg Moseley, Postdoctoral fellowship, Royal Society, UK
- Dr Pei Xiang Xing, Austin Biomedical Alliance Research Award, 2001.

BRI

- Epilepsy Association of NSW Travel Award 1999 – Regula Briellmann
- Austhos Travelling Scholarship 2000 – Regula Briellmann
- Professor S.F Berkovic. Glaxo Smith Kline Award for Research Excellence (Epilepsy), 2002.

Department of Clinical and Health Psychology

Australian Rotary Health Research Fund Ian Scott Fellowship, awarded to C. De Paola with Professor J. Milgrom as mentor and collaborator. 2000–2001. Developing a Risk Screening Tool for High Risk Families of Infants.

Clinical Pharmacology

- Dr Simon Louis: Inserm/NHMRC Overseas Fellowship
- Dr Diem Dinh: CJ Martin Overseas Fellowship
- Professor William Louis: Elected Vice President – International Society of Cardiovascular Pharmacotherapy (ISCP)
- Professor William Louis: Hellenic Distinction Award (2000).

Infectious disease

- Paul D.R. Johnson, Winner, GlaxoWellcome Agents for Change Award, 1999
- M. Lindsay Grayson, Inaugural visiting Fellow, Malaysian Infectious Diseases Society, Kuala Lumpur, and Sabah, Malaysia, 2000.

Intensive Care Unit

- Baxter Award for Best Paper in Basic Science, ANZICS Annual Scientific Meeting, Melbourne, October 1996
- American Society of Critical Care Medicine, Presidential Citation for Outstanding Contribution to the Society (1996)
- Hewlett–Packard Award for Best Paper in Clinical Medicine, ANZICS Annual Scientific Meeting, Hobart, October 1997
- Best Nursing Paper, ANZICS Annual Scientific Meeting, Adelaide 1999.

Renal Unit

- Dr Vicki Levidiotis, Young Investigator Award of the Australian and New Zealand Society of Nephrology, 2001 for project “Heparanase in glomerulonephritis”
- Dr Vicki Levidiotis, Amgen Fellow of the Australian Kidney Foundation
- Vicki Levidiotis, Ludwig Institute Scholarship (2001 Austin & Repatriation Hospital Research Week)
- Dr Peter Mount, Royal Australasian College of Physicians Quality Assurance Prize in 2001 for the project “Clinical Benefits of a Quality Assurance Project of Infection Rates of Haemodialysis Access Catheters”
- Scott Fraser, Dora Lush Postgraduate Research Scholarship from the NHMRC.

Nutrition

- Best poster presentation at DAA national conference 2001 Dianne Reidlinger Veterans Initiative
- Best poster presentation at A&RMC Research Week, Nutrition Department, 2000
- Investigators Award for non–medical research A&RMC Research Week, Karen Manley 1999 Can Dialysis Patients Take Control of Their Own Results.

NSRI

- Dr. Peter Batchelor, Istvan Tork Prize, Australian Neuroscience Society 1999
- Dr. Christopher C. Levi, Runner–up, Robert Siekert Young Investigator Award, American Heart Association, 1999
- Dr. Christopher C. Levi, Finalist, Young Investigator Award, Australian Association of Neurologists, 1999
- Dr. Romesh Markus, Young Investigator Award, National Stroke Foundation, 1999
- Dr. Alison Baird, The Michael Pessin Award, American Heart Association, 1999
- Dr. Amy Brodtmann, Australian Young Investigator Award for the XI International Congress of EMG and Clinical Neurophysiology 1999
- 1999. Romesh Markus, PhD student, Peter Bladin Young Investigator Award, Stroke Society of Australia, Statistical parametric mapping of the ischemic penumbra
- 2000. Romesh Markus, PhD student, International Scholarship, American Academy of Neurology, Statistical parametric mapping of the ischemic penumbra
- 2000. Romesh Markus, PhD student, Best Abstract, European Stroke Society ASM, Statistical parametric mapping of the ischemic penumbra
- Dr. Romesh Markus, Top 20 Abstract Award, European Stroke Council 2000
- Dr. Romesh Markus, Top International Abstract, American Academy of Neurology 2000

- Dr. Julie Bernhardt, et al. Best Paper, Sixth International Australian Physiotherapy Association Congress. APA Sixth International Congress. May, Canberra, 2000
- Dr. Velandai Srikanth, Bristol–Myers Squibb Young Investigator’s Award, Australian Society of Geriatric Medicine Annual Scientific Meeting , Cairns, Queensland, 2000
- Dr. Amy Brodtmann, RIKEN Neurosciences Institute Summer School Scholarship (Plan B), Tokyo Japan, June–July, 2001
- Dr. Peter Wright, Young Investigator Award, Stroke Society of Australasia, New Zealand, September 2001
- 2001. Peter Wright, PhD student, Peter Bladin Young Investigator Award, Stroke Society of Australia, Mapping the ischemic penumbra with MRI
- Dr. Velandai Srikanth, Peter Bladin Young Investigator’s Award for the Stroke Society of Australasia, Auckland, New Zealand, September 2001
- Dr. Anne Abbott, Finalist – New Investigator Award, Stroke Society of Australasia Annual Scientific Meeting, Auckland NZ 2001
- Dr. Velandai Srikanth, Young Investigator Award, National Stroke Foundation 2002
- Dr. Julie Bernhardt, The Peter Bladin Young Investigator Award, Stroke Society of Australasia 2002.

Awards

Pathology

- Dr. Volker Gürtler, 1999 ARMC Research Week travelling scholarship for work in RNA spacer analysis.

Pharmacy

- SHPA GlaxoSmithKline Medal of Merit. Graeme Vernon. August 2001, for contribution to Hospital Pharmacy in Australia
- National Clinical Pharmacy Renal Grant (\$5000). Francine Tanner. August 2000. National preceptorship at another Australian Hospital
- SHPA William Mercer Young Achiever Award. Margaret Carroll. August 2000. Recognition of contribution of young pharmacists in Victoria
- Myer Foundation Community Services International Residency Grant. (\$7,500). Rohan Elliott. September 2000. Development of Clinical Pharmacy in India
- Board Certified Pharmacotherapy Specialist (BCPS), Board of Pharmaceutical Specialties, Washington DC, USA. Alice Chow. October 1999
- 1999 Board Certified Nuclear Pharmacist (BCNP), Board of Pharmaceutical Specialties, Washington DC, USA. Gordon Chan. October 1999.

Royal Talbot

- A&RMC Research Week 2001 – Investigators Award in Non-Medical Research (Wayne Dite).

Department of Medicine

- Mr Stephen Headey, Novartis Junior Investigator Award of the Endocrine Society of Australia 2001. IGF binding determinants of IGF1BP-6
- 1999 – Eric Susman Prize, Royal Australasian College of Physicians to Prof Mark Cooper, for Most Outstanding Contribution to any Branch of Internal Medicine
- European Society of Hypertension Travel Award (2001), Dr Maurice E. Fabiani
- 1999 David Weintrob, PhD student, Glaxo Young Investigator Award, American Epilepsy Society. Metabolic correlates of verbal memory
- 1999. David Weintrob, PhD student, TOP Scholar, Epilepsy Society of Australia, Metabolic correlates of verbal memory
- 2001. David Weintrob, PhD student, TOP Scholar, Epilepsy Society of Australia, Functional activation studies of verbal memory in TLE
- 2002. Professor Sam Berkovic, Glaxo Smith Kline Award for Research Excellence (Epilepsy)
- 2002. Professor Ego Seeman, Frederick C Bartter Award of the American Society of Bone and Mineral Research (Osteoporosis)
- 2002. Professor George Jerums, Kellion Award of the Australian Diabetes Society (Diabetes).

Department of Surgery

- 2002 Oneel Patel Best Biomedical Poster Award ARMC Research Week
- 2002 Adrienne Paterson Gastroenterology Society of Australia International Travel Award.

08: Grants

Researchers of the Alliance have secured funding from National and International Funding Bodies in the order of \$25 million. Included are a number of NHMRC Program and Clinical Centre of Excellence grants. This reflects 160 different projects for the 1999 – 2002 period.

In addition the Austin Hospital Medical Research Foundation supports research conducted by the Alliance (~\$300,000 per year).

Funding bodies include the NHMRC, NHF, ARC, JDRF, NIH (see Section 11).

A full listing of grants funded can be accessed on the ABmA website <http://www.armc.org.au/Pages/abma.htm>

09: Publications

Research generated by investigators of the Alliance has been published in 118 Book chapters and 948 Journal articles.

Articles have been published in journals including Nature, New England Journal of Medicine, Lancet.

A full listing of research publications can be accessed on the ABmA website <http://www.armc.org.au/Pages/abma.htm>

The combination of biomedical, clinical and public health research undertaken collectively by the Alliance provides the bridging interface between the laboratory and the clinic.

10: Collaborations

International Academic Collaborations

USA/Canada

Cornell University
Dalhousie University
Duke University
Harvard University
Massachusetts General Hospital
McGill University
Memorial University
Stanford University
University of California
University of Iowa
University of Minnesota
University of Pittsburgh
University of Texas
Washington State University

Asia

Beijing Medical University
Gumma University
Hallym University
Peking University
Shanghai University

UK/Europe

Bonn University
Cochim Institute
Freiburg University
Heidelberg University
Institute of Neurology
Karolinska Institute
Lausanne University
Liverpool University
Medical Research Council (UK)
Montpellier University
Oxford University
Paris University
University of Galway
University of Geneva
University of Lund
University of Zurich

International

Ludwig Institute for Cancer Research

National Academic Collaborations

Adelaide University
CSIRO
Flinders University
LaTrobe University
Monash University
Queensland University
RMIT
Swinburne
Sydney University
University of Melbourne
University of New South Wales
Victoria University of Technology

Austin Biomedical Alliance members have received funding from a range of National and International bodies including Pharmaceutical companies, Biotechnology companies, Business/Venture Capitalists and other Research Institutes.

11: Funding Bodies

Austin Biomedical Alliance members have received funding from a range of National and International bodies including Pharmaceutical companies, Biotechnology companies, Business/Venture Capitalists and other Research Institutes. Funding bodies are listed in alphabetical order below.

Amgen
 AMRAD
 Amylin Pharmaceuticals
 Anti Cancer Council
 Arthritis Foundation
 Astra Zeneca
 Austhos
 Australian Kidney Foundation
 Aventis
 Bionomics BHP Community Trust
 Boehringer Ingelheim
 Bristol Myers Squibb
 Centenary Institute
 Centre for Early Human Development
 Compumedics
 CpG Inc
 CRC for Vaccine Technology
 CSIRO
 CSL
 Dana Faber Cancer Institute
 Diabetes Australia
 Garvan Institute
 Gilead Sciences
 Glaxo Smith Kline

Hammersmith Hospital
 Hanson Cancer Centre
 Helen MacPherson Schutt Trust
 Higeta Shoyu
 Hoechst Marion Roussell
 Howard Florey Institute
 Ian Potter Foundation
 Ilexus Pty Ltd
 Immunex Corporation
 Institute of Experimental Endocrinology
 Jackson Laboratory
 Jansen Cilag
 Johnson & Johnson Research
 Juvenile Diabetes Research Foundation
 Kirin Breweries
 Krakenhause Nordwest Cancer
 Kyowa Hakko Kogyo
 Lilly
 Mater Medical Research Institute
 Mayo Clinic
 MedStart
 Melbourne Uni Innovation
 Memorial Sloan-Kettering
 Mental Health Research Institute
 Montreal Neurology Institute
 Motor Neurone Foundation
 Murdoch Children's Research Inst
 National Health & Medical Research Council
 National Heart Foundation
 National Institute of Allergy & ID
 National Institute of Health
 National Institute of Musculoskeletal Disease

National Jewish Medical & Research Center
 Novartis
 Pfizer
 Pharmacia
 Prima Ltd
 ProteinExpress
 Qld Institute of Medical Research
 Rebecca Cooper Foundation
 ResMed
 Roche
 Royal Children's Hospital
 Royal Marsden Hospital/Institute of Cancer Research
 Royal Perth Hospital
 Sanofi-Synthelabo
 Schering AG (Berlin)
 Schering Plough
 Scripps Research Institute
 Servier (France)
 Servier
 St. Vincent's Research Institute
 The Dunlop Foundation
 Victorian Institute of Biotechnology
 Viertel Foundation
 WA Institute of Medical Research
 Walter & Eliza Hall Institute
 Wellcome Foundation
 Wyeth

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Austin campus

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PO Box 5555
Heidelberg Vic Australia 3084
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Facsimile: 03 9496 4779

Repatriation campus

300 Waterdale Road
PO Box 5444
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Telephone: 03 9496 5000
Facsimile: 03 9496 2541

Royal Talbot Rehabilitation Centre

1 Yarra Boulevard
Kew Vic Australia 3101
Telephone: 03 9496 4500
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