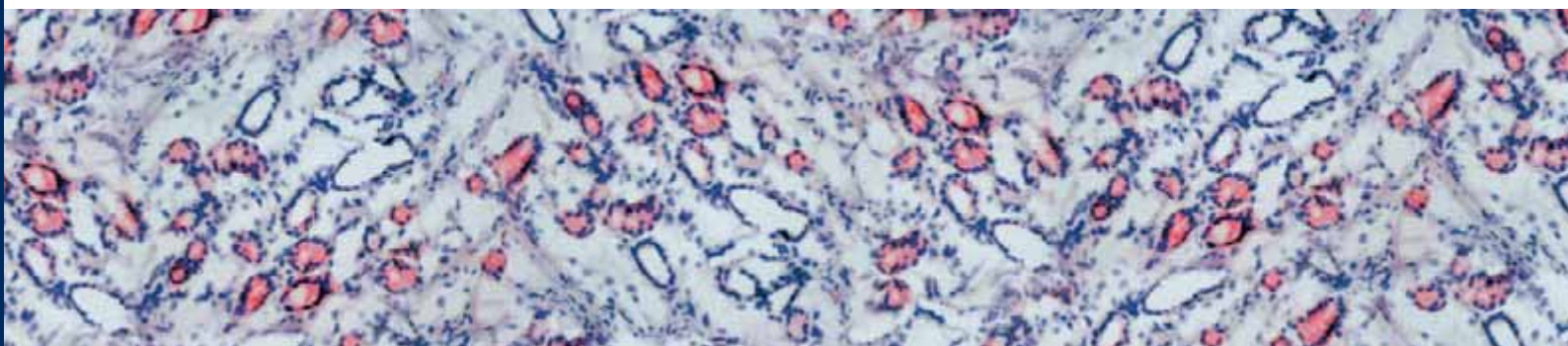




COOPERATIVE RESEARCH CENTRE FOR **ASTHMA**



# ANNUAL REPORT

2003/2004



Established and supported under the Australian  
Government's Cooperative Research Centres Program

# Mission Statement

## MISSION STATEMENT

The Cooperative Research Centre for Asthma aims to reduce the burden of asthma on the Australian community.

# Objectives

## OBJECTIVES

To improve the quality of life of people with asthma and their families by increased understanding of the mechanisms, genetics and diagnosis of asthma.

To determine the most effective ways of treating asthma and evaluate the economics of the treatment programs.

To provide a high quality training environment for younger scientists and to disseminate knowledge to the Australian community.

To develop and commercialise technologies arising out of the centre's projects.

FRONT COVER: Immunohistochemical staining of human upper airway tissue.

Picture by CRCA PhD student Bennett Shum.

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# Partners

## PARTNERS

Woolcock Institute of Medical Research

Monash University

The Garvan Institute of Medical Research

University of Sydney

University of Western Australia

New South Wales Health

AstraZeneca

GlaxoSmithKline

# Report

## CHAIRMAN'S REPORT

The 2003/2004 financial year saw the CRC for Asthma (CRCA) maintain its position as a key player in asthma research in Australia. The tempo of the research program has accelerated and it is pleasing to observe the growing body of scientific knowledge and intellectual property that has been generated by the research groups in Sydney, Melbourne and Perth. The education program is also progressing well and the CRCA is now providing support to a number of exceptional postgraduate students. It is gratifying to note that the latex vaccine research program is moving into the preclinical stages and that planning is underway with Monash University to capitalise on this commercial opportunity.

The Fifth Year Review confirmed the excellent progress that has been made since the inception of the CRCA in 1999. This independent review found that the scientific programs were of high quality, that milestones were being met, and that the leaders placed great emphasis on the exploitation of platform technologies and the achievement of synergistic benefits from collaborative interaction between the research nodes. The reviewers also noted that the overall management of the CRCA was of a very high standard. I would like to congratulate the CEO, Mr Philip Bert, and the executive team for this outstanding outcome.

The members of the CRCA have lodged a submission for a second term of funding under the 9th CRC Selection Round. In the event that this bid is successful, the Board will play an active role in overseeing the transition to the new CRC. The results of this application will not be known until the end of 2004.

Dr Emery Severin resigned as Chairman when he moved to the USA in July 2004. I would like to thank Dr Severin for his contribution to the CRCA and wish him well in the future. I would also like to express my gratitude to Mr Martin Hoffman and Professor Nick Saunders who retired from the Board during the year. I welcome Professor Michael Berndt to the Board and look forward to his contributions in the years ahead.



Dr Arthur Emmett  
Chairman



Dr Arthur Emmett



# Report

## CHIEF EXECUTIVE OFFICER'S REPORT

The CRCA has continued to make significant progress on a number of fronts during the fifth year of operation. All research programs are producing significant outcomes as exemplified by the high rate of publication and increasing number of patent applications.

The highlight of the year was the successful Fifth Year Review of the performance of the CRCA. The review was carried out in two stages. The first stage was a study undertaken by a team of independent health economists to investigate the economic value associated with the outputs of the Research and Commercialisation Programs. The reviewers found that the CRCA's programs represented a balanced portfolio in terms of risk/return profiles and project lead times. They concluded that early benefits are being achieved from the public good projects and that the commercially focused therapeutic projects have longer lead times but have the potential to generate sizable revenues in the future. The second stage was an independent review of the Research and Education Programs. The reviewers found that the research was of high quality and that the milestones were being achieved. They went on to note that the leaders placed great emphasis upon the exploitation of platform technologies and the achievement of synergistic benefits from collaborative interaction between scientists and clinicians.

Significant effort was devoted to the planning and submission of a bid for a second term of funding under the Ninth CRC Selection Round. The new guidelines and selection criteria placed strong emphasis on commercial and economic outcomes for new CRCs and a competitive commercially focussed preliminary proposal was submitted in March 2004. This proposal was reviewed by the CRC Committee and an invitation was received to lodge a full application. The full application was lodged in July and the successful applicants will

be announced in December. If the bid is successful the CRCA will receive an additional seven years of funding, if not funding will cease in September 2006 as provided for in the original grant.

The Research Program is proceeding apace with key milestones being met. The Immunomodulation Program continues to make good progress and it is planned to commence preclinical work on a latex allergen vaccine in late 2004. The patenting program is moving through the national phase and a business plan is being developed in conjunction with Monash University to commercialise this latex based intellectual property together with grass allergen intellectual property owned by the University.

In the last 12 months the Garvan research group have made solid progress in validating a number of candidate genes, most notably the fatty acid binding protein aP2. Animal model experiments have been successful and we are very encouraged by these findings which suggest that the inhibition of the activity of aP2 may be an effective therapeutic strategy for asthma. The team at Sir Charles Gairdner Hospital in Perth have now completed genetic association studies on polymorphisms in the genes of the leukotriene biosynthetic pathway. They have shown an association between a polymorphism in the LTC<sub>4</sub> synthase gene and asthma, and this work was published as the Editor's Choice in the May edition of the Journal of Allergy and Clinical Immunology. A sophisticated spirometry software package has been developed by the physiologists based at the Woolcock Institute. This package is undergoing testing and market validation prior to being commercialised in early 2005. The Childhood Asthma Prevention Study is proceeding smoothly and the results of the three year assessments have been published. The five year assessments will be completed by the middle of 2005.

Good progress has also been made in the Education Program and the CRCA has provided support to twenty two PhD Scholars. These scholarships were awarded on a competitive basis and they have been designed to enrich the academic experience of this select group of students. A highlight of the year was the symposium on behavioural aspects of asthma that was held in conjunction with the International World Conference of the International Primary Care Respiratory Group that was held in Melbourne in early 2004. The success of the Education Program would not have been possible without the leadership provided by Dr Christine Jenkins.

The fourth CRCA conference was held in Wollongong in November 2003. Once again this meeting provided an invaluable opportunity to strengthen the cooperative linkages between the stakeholders and to promote scientific interaction within the CRCA. It also provided an opportunity to devise strategic platforms for the proposed second term CRCA.

The academic and industrial partners have continued to provide high levels of support to the activities of the CRCA. This is exemplified by the contributions that have been made to the various governance committees as well as the whole-hearted commitment shown by the partners on the project working groups. Professors Robyn O'Hehir, Philip Thompson, Charles Mackay and Norbert Berend continue to provide strong scientific direction and the accomplishments of the past year would not have been possible without their ongoing commitment. I would also like to thank Professor Sue Serjeantson, the CRC Visitor, who has provided valuable support and advice over the past year.

Dr Emery Severin retired as Chairman of the Board at the end of June 2004. Dr Severin played an important role in guiding the CRCA through the

mid term strategic review and in positioning the CRCA for a successful Fifth Year Review. I would like to express my appreciation for his guidance and support over the past two years. Dr Arthur Emmett was appointed Chairman in August 2004 and I am looking forward to working with him in the years ahead.



Mr Philip Bert  
Chief Executive Officer



Mr Philip Bert



# Review

## FIFTH YEAR REVIEW

### INDEPENDENT REVIEWS OF THE CRCA FOR ASTHMA

Two separate reviews were commissioned to assess the performance of the CRCA. The first was a formal review of the scientific performance of the CRCA and the second was an independent assessment of the economic outputs.

#### SCIENTIFIC REVIEW

This review followed the Stage 1 procedures and terms of reference as laid out in the *Fifth Year Review Guidelines (May 2002)*. Professor Donald Campbell, Director Monash Institute of Health Services Research chaired the review committee. The CRCA Board nominated Professor Campbell to chair the review, as he was a member of the original interview panel in 1998 as well as an independent member of the Second Year Review panel in 2001. As such he was well placed to provide an historical perspective to the deliberations and final report. The other members of the panel were Professor Graham Le Gros, Research Director, Malaghan Institute, Wellington, NZ and Professor Richard Henry, Deputy Dean, Faculty of Medicine, University of New South Wales. The findings of the Scientific Review are as follows:

#### **The quality and significance of the research**

The major successes of the CRCA reflect highly focused research efforts which took advantage of platform technologies and relentlessly pursued programs which ensured the achievement of project milestones and research objectives. This is particularly the case for the Immunomodulation Program which has been a major success for the CRCA. The success of this program in bringing basic research discoveries through to a commercially and clinically viable phase of development is a reflection of the excellent strategic vision, focus and commitment to the

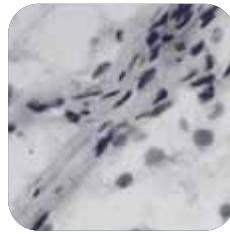
goals of the CRCA. Major outcomes of the Genomics and Proteomics Program have been the identification of two novel candidate asthma genes which have high therapeutic targeting potential for the pharmaceutical industry, and the establishment of an extensive asthma genetic database that will feature strongly in the future gene discovery process. The broad ranging program devoted to Pathophysiology and Diagnosis using the forced oscillation technique has made impressive progress. The next step for this program will be to determine the diagnostic utility of the forced oscillation technique. The Asthma Management and Prevention Program with its absence of fundamental platforms for exploitation and the greatest number of component projects required a greater degree of strategic research management in order to achieve the benefits of synergistic collaboration.

#### **Achievement of research milestones**

The research activity was timely in its achievement of milestones. A high level of productivity has been reflected in the level of publication of research reports in peer reviewed academic journals and in the patent applications. A high number of research developments with potential for commercial exploitation are being actively pursued. The platforms established in health economic evaluation and the various cohorts being studied have potential to produce a public benefit in informing the development of public policy and changing current asthma management practice.

#### **The research capabilities of key researchers and their commitment to the CRCA**

The formation and maturation of teams of researchers from a broad range of disciplines to produce successful cross-disciplinary research requires strategic management, particularly in ensuring that the clinician researcher time commitments match that of individual program leaders who are exploiting platform technologies.



The extent to which projects have been successfully integrated into programs that have achieved the objectives of the CRCA reflect the strategic research management capability of the research leadership of the CRCA. Major emerging collaborative efforts and highly developed research training activities within projects are the hallmarks of the successful research programs within the CRCA.

### Major recommendations

That the Genotypes Project be further integrated with the other projects within the CRCA to contribute to the training of individuals in research which links the clinical and genetic manifestations of asthmatic disease.

*CRCA Board Response: Agreed. Avenues for further integration have been factored into future research plans.*

That the Diagnostic Devices Project should place increased emphasis on determining the clinical relevance of frequency oscillation techniques.

*Response: Agreed. This will be the major research focus for the next two years and validation studies are already underway.*

That the projects within the Asthma Management and Prevention Program be further integrated to exploit potential synergies.

*Response: A number of these long-term projects are nearing completion and it will not be feasible to integrate them further at this late stage.*

That the research training program would benefit from a more focused strategic management approach across the whole of the CRCA.

*Response: Agreed. A more strategic framework will be developed should the CRC be successful in obtaining a second round of funding.*

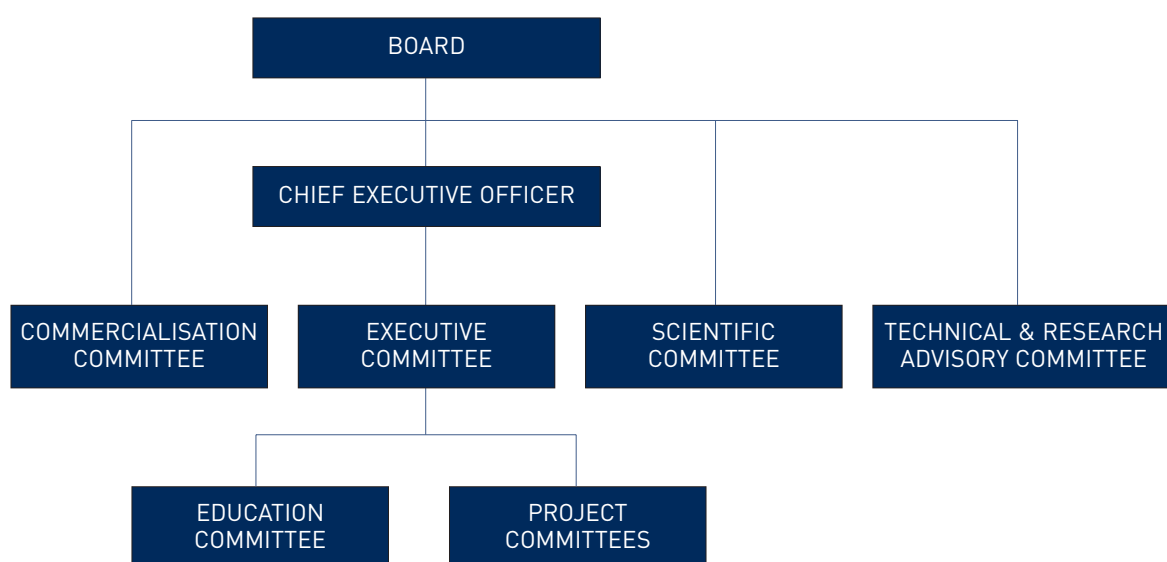
## ASSESSMENT OF ECONOMIC PERFORMANCE

Specialist independent health economic consultants, Health Outcomes International, were engaged to undertake a study into the actual and potential economic value associated with the CRCA's research activities. The findings of this study were that successful commercialisation of latex allergen vaccines in the healthcare worker market alone would generate \$6m in royalties in the first five years, that asthma diagnostics could generate \$10m in royalties and the higher risk asthma drug targets could generate \$150m. The consultants also concluded that the potential fiscal savings to Australian governments from the Childhood Asthma Prevention Study would be approximately \$9m over five years once this work had been completed and the findings disseminated. The Evidence Based Guidelines project would result in lower drug usage that would, on conservative calculation, save the Pharmaceutical Benefits Scheme \$15m over five years. It was noted that the benefits from this project are already being realised, as findings have been included in national guidelines.

# Structure

## STRUCTURE AND MANAGEMENT

The CRCA was established in October 1999 as a company limited by guarantee. The CRCA is a joint venture between two medical research institutes, three universities, two pharmaceutical companies and the New South Wales Department of Health. It brings together some of Australia's leading asthma research groups working out of Sydney, Melbourne, Newcastle and Perth.



## BOARD OF DIRECTORS

The Board is responsible for setting strategic goals and monitoring the performance and management of the CRCA. The Board met four times during the year. Professor Nick Saunders and Mr Martin Hoffman resigned as directors during the year and Professor Michael Berndt has joined the Board. Dr Emery Severin, the Chairman, resigned in July 2004 and has been replaced by Dr Arthur Emmett.

Dr Arthur Emmett	Chair
Professor Michael Berndt	Monash University
Mr Philip Bert	Chief Executive Officer
Professor David Burke	University of Sydney
Professor Lou Landau	University of WA
Mr Mervyn Michell	Woolcock Institute
Ms Julie Nutting	Industry Representative

## EXECUTIVE COMMITTEE

The role of the Executive Committee is to coordinate the research and education programs of the CRCA. The committee is chaired by the Chief Executive Officer and includes senior research leaders.

Mr Philip Bert	CEO (Chair)
Professor Norbert Berend	Woolcock Institute
Professor Charles Mackay	Garvan Institute
Professor Robyn O'Hehir	Monash University
A/Professor Philip Thompson	University of WA

# Structure

## TECHNICAL & RESEARCH ADVISORY COMMITTEE (TARAC)

This committee is responsible for overseeing the research programs and plays a key role in setting research priorities and allocating resources. TARAC meets annually and is chaired by the Chief Executive Officer with representation from all the academic and industry partners. Asthma Foundations of Australia (the peak consumer organisation) and the National Asthma Council are also represented. The committee reviews the overall research performance and considers individual project research plans. TARAC also reviews project budgets and provides recommendations to the Board.

Mr Philip Bert	CEO (Chair)
Professor Norbert Berend	Woolcock Institute
Mr Michael Cassar	Asthma Foundations of Australia
Dr Carlo Maccarrone	GlaxoSmithKline
Professor Stephen Leeder	University of Sydney
Professor Charles Mackay	Garvan Institute
Dr George Moore	AstraZeneca
Professor Robyn O'Hehir	Monash University
A/Professor Philip Thompson	University of WA
Ms Kristine Whorlow	National Asthma Council

## COMMERCIALISATION COMMITTEE

The Commercialisation Committee is responsible for overseeing the management of intellectual property and negotiation of the commercial and licensing arrangements of the CRCA.

Dr Arthur Emmett	Chair
Mr Philip Bert	CEO
Ms Julie Nutting	Director
Dr Gregory Pearce	Independent

## EDUCATION COMMITTEE

The Education Committee is chaired by Dr Christine Jenkins of the Woolcock Institute of Medical Research. This Committee sets policy for the Education Program and prioritises the implementation of the projects. The Committee also oversees the CRCA scholarship program. Dr Mary-Anne Kedda resigned from the committee in September, and was replaced by Dr Bernadette Bradley of the University of Western Australia. A/Professor Jennifer Rolland resigned from the committee in December, and was replaced by A/Professor Jo Douglass. Mr Michael Cassar of Asthma Foundations of Australia joined the committee in January.

Dr Christine Jenkins	Woolcock Institute (Chair)
Mr Philip Bert	CEO
Dr Bernadette Bradley	University of WA
Mr Michael Cassar	Asthma Foundations of Australia
A/Professor Jo Douglass	Monash University/Alfred Hospital
Ms Adrienne James	Lung Health Promotion Unit/Alfred Hospital
Dr Carlo Maccarrone	GlaxoSmithKline
Ms Jodi Roper	Education Manager

## SCIENTIFIC COMMITTEE

The Scientific Committee provides the Board with strategic scientific advice, comments on the scientific quality of the work of the CRCA and provides guidance on new avenues for research. Professor Richard Ruffin of Adelaide University, Professor Robin Taylor of University of Otago and Dr Simon Foote of the Walter and Elisa Hall Institute are independent members.

Professor Norbert Berend	Woolcock Institute
Mr Philip Bert	CEO
Dr Simon Foote	Walter and Elisa Hall Institute
Professor Charles Mackay	Garvan Institute
Professor Robyn O'Hehir	Monash University
Professor Richard Ruffin	Adelaide University
Professor Robin Taylor	University of Otago
A/Professor Philip Thompson	University of WA

# Commercialisation

## COMMERCIALISATION

The research program of the CRCA covers a wide range of disciplines from immunology, genetics and physiology through to economics and epidemiology. While a number of projects have distinct commercial outcomes, others have been commissioned to provide public benefit. Outcomes from this latter group will have significant economic ramifications in the form of more effective policy setting, the prevention of asthma, and the lowering of expenditure on asthma medication.

The Immunomodulation research group based at Monash University has continued to make good progress on developing intellectual property based on the clinically important latex proteins Hev b5 and Hev b6. This work is aimed at the development of therapeutic and diagnostic products that will be useful in the treatment of latex allergy in health care workers. The Hev b5 intellectual property jointly developed by Monash University and the CRCA is moving through the national phase of the patenting process and the Hev b6 intellectual property has also entered the national phase. The research program is also proceeding well and work on preclinical studies will commence in late 2004. Monash University researchers have developed a significant intellectual property position in the area of Rye and Bermuda grass allergens. This technology is complementary to the latex work of the CRCA, and an agreement has been reached with Monash to work cooperatively on the commercialisation of these technologies. This cooperative approach will generate significant synergies. It is proposed to establish a jointly owned spinout company in 2005 and a business plan is being developed at present.

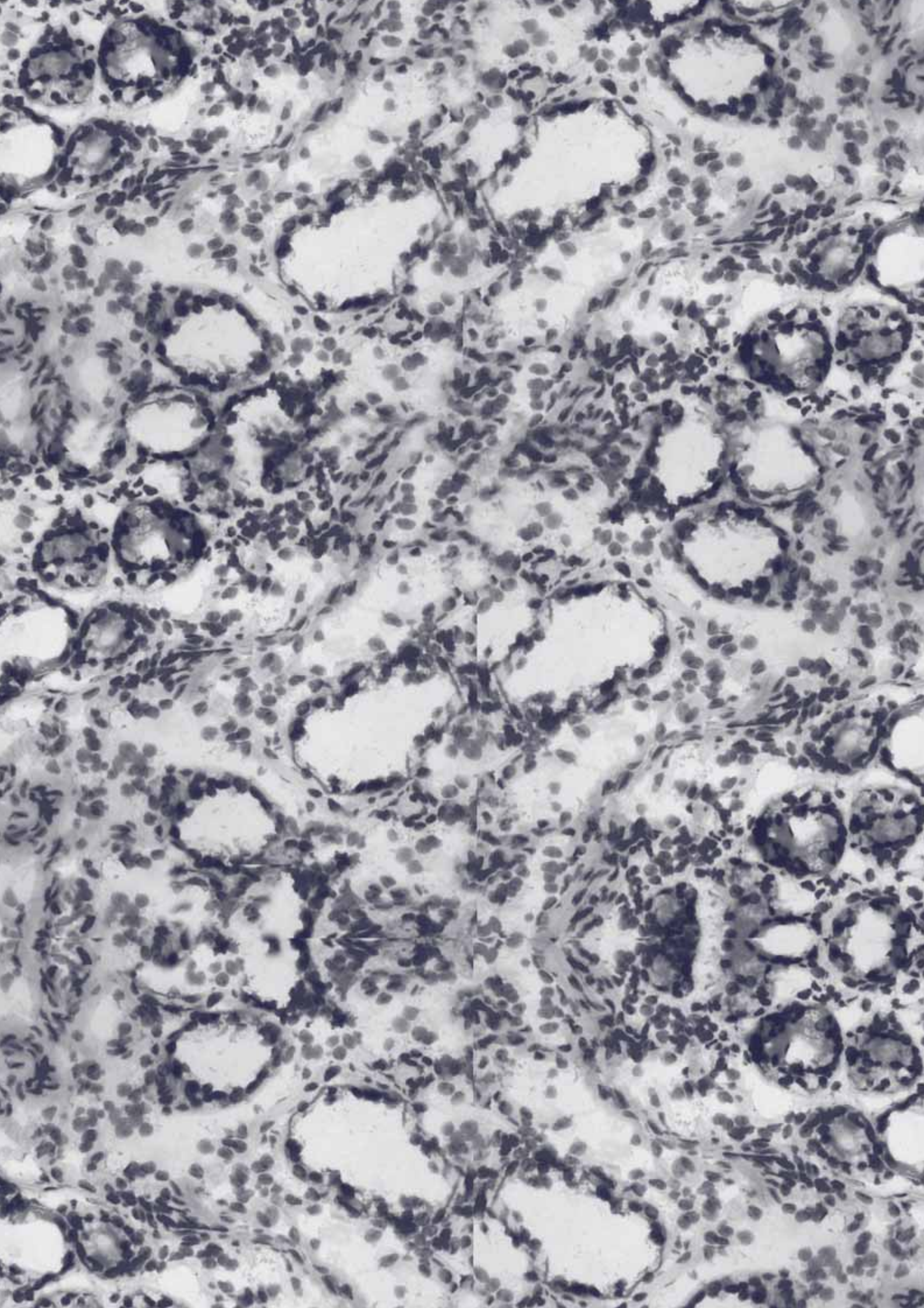
CRCA researchers at the Garvan Institute have utilised advanced microarray technologies to identify novel gene targets that are implicated in the pathogenesis of asthma. This research program has now reached the stage where a number of such targets are being generated. The first of these targets, a gene known as aP2, has been protected by way of a PCT. The significance of this target has been confirmed by a knock-out

mouse study and a range of other investigations are underway. A second set of allergic leukocyte targets has also been protected by a US Provisional patent. Information on these developments has been shared with the industry partners who have first rights of offer to commercialise the IP.

Results flowing out of the Asthma Management Program have started to have a significant impact on asthma management practices and the recently commissioned health economic study has quantified these benefits (see Fifth Year Review report). Research groups at Monash University and the John Hunter Hospital in Newcastle have been working on consumer attitudes and asthma education, and the results of these studies have been published in international and local journals. A symposium on this aspect of the CRCA's work was one of the highlights of the prestigious World Conference of the International Primary Care Respiratory Group that was held in Melbourne in early 2004. This symposium was run in collaboration with the National Asthma Council and Asthma Foundations of Australia. The John Hunter team has also published its findings on the optimal dosage of inhaled corticosteroids. These findings were incorporated into guidelines published by the National Asthma Council.

The Monash research group are working with the industry partners on a community care project that will specifically compare those individuals with asthma who purchase beta-2-agonists over the counter with individuals simultaneously purchasing beta-2 agonists with a prescription or on advice from their doctor. The findings of this study will facilitate the development of targeted strategies to improve the health of the large number of people with mild asthma.

A suite of spirometry software developed by clinicians and computer programmers based at the Woolcock Institute is in the process of being validated and market-tested by RJ & VK Bird P/L, a small Victorian based respiratory device company. It is envisaged that a licence to market this product will be negotiated in late 2004.



# Research

## RESEARCH

The Executive Committee actively manages the research program and project progress is reviewed by the Technical and Research Advisory Committee and the Board on a regular basis. The Scientific Committee evaluates the quality of the projects and provides independent advice on the research strategies adopted by the CRCA. Through these processes, areas of opportunity are identified and additional funding is provided to accelerate promising projects. Potential problems are also identified at an early stage and if necessary, action is taken to conserve resources.

## IMMUNOMODULATION & ALLERGY

Approximately 80% of asthmatics are atopic and exposure to allergens can induce an asthma attack in these individuals. Moreover, there is evidence that development of an allergic phenotype precedes the onset of asthma symptoms. Strategies which fully define critical allergens in the allergic immune response with resultant improved diagnostic tests, novel treatment regimens and assays to monitor clinical efficacy will cause a significant reduction in the burden of asthma. The current trend is away from chronic pharmacotherapy towards treatment options that alter the natural history of disease with the possibility of cure. To achieve this goal, the following fundamental questions need to be addressed:

"What are the major allergens of clinical relevance in asthma?"

"What are the factors that regulate the immune response to allergens and how do these differ between normal, atopic and asthmatic subjects; can these factors be exploited to down-regulate the pathogenic response in asthma?"

"What are the most reliable laboratory assays for diagnosing and monitoring efficacy of treatment of allergic asthma?"

"How can immunomodulation with a desensitising vaccine for clinically important allergens best be delivered for effective and safe use in patients with asthma?"

Our research projects are aimed at addressing these questions.

## IMMUNOMODULATION

**Project Leader: Prof Robyn O'Hehir**

**Deputy Leader: A/Prof Jennifer Rolland**

Allergy is a well-recognised and important underlying disease process in asthma. This project aims to develop allergen preparations for immunomodulation of the adverse immune response to allergens for treatment of allergic asthma/rhinitis, and to generate improved diagnostic reagents and a suitable laboratory assay for monitoring efficacy of allergen-specific immunotherapy. Latex allergy is the initial model system. Other allergens of clinical importance for asthma particularly grass pollens will be included in the program should the CRCA receive a second round of funding.

For our vaccine development, we have pursued two strategies, one based on T cell epitope peptides and one based on the generation of recombinant mutant latex allergens. The dominant T cell epitope peptides have been shown to be non-IgE reactive and thus suitable candidates for a Hev b5 vaccine. For the cysteine-rich Hev b6.01, hypoallergenic mutants were developed by site-directed mutagenesis of selected cysteine residues within the Hev b6.02 domain. Peptides corresponding to the Hev b6.02 domain of two of the Hev b6.01 mutants were also synthesized.



These mutants and peptide variants showed markedly decreased or ablated binding of IgE from latex-allergic patient sera by immunoblotting and ELISA. Whole blood basophil activation testing confirmed markedly decreased activation with successive cysteine substitutions of the mutants and complete abrogation with a particular Hev b6.02 peptide. Retention of T cell reactivity is crucial for effective specific immunotherapy and all mutants and peptide variants maintained their latex specific T-cell reactivity.

Our results suggest that the T cell epitope based peptide approach is more likely to result in a feasible and efficacious vaccine candidate for clinical evaluation. The dominant Hev b5 T cell epitope peptides together with a particular Hev b6.02 peptide are strong candidates for inclusion in a latex immunotherapy preparation.

After extensive optimisation of immunisation protocols (mice strains, routes, doses and timing of immunisation, adjuvants, antigens) and assay systems, (ELISpots, ELISA, T cell proliferation etc) we established a mouse model of allergic asthma for the latex allergens. Immunised mice exhibit the hallmarks of an allergic Th2-type response, comparable with those for a control ovalbumin allergy model with allergen-specific CD4+ T cell proliferation, serum allergen-specific IgE (IL-4, IL-13), an eosinophilic infiltrate in the lung (IL-5), mucus hypersecretion by airway epithelial cells (IL-13) and IL-5 secretion in the bronchoalveolar fluid. Limited experiments have also demonstrated heightened airway resistance consistent with the asthma trait. We are now exploring different immunomodulatory regimens using our hypoallergenic latex peptides and mutant proteins.

Flow cytometric analysis of intracellular cytokines of allergen-stimulated T cells has been optimized and established using our in vitro model system. Identification of the CD4+CD25+ IL-10 producing regulatory T cell subset was optimized for a house dust mite immunotherapy trial. These cytokine assays will be evaluated for reliable monitoring of clinical efficacy in subsequent trials of our latex allergy vaccines.

Several of these achievements have been patent protected and a number of publications have resulted in international journals.

# Research

## GENOMICS & PROTEOMICS

Asthma is a complex condition, resulting from an interaction between genetic and environmental factors. Defining the genetic and molecular basis of asthma will give insight into the pathophysiology of the condition and help us to understand why some people get asthma, why there are different asthma subtypes, why asthma severities vary and how genetics influences treatment responses.

By combining the state-of-the-art genomics facilities of the Garvan Institute with the extensive DNA banks at the West Australian node, the CRCA is very well placed to identify novel genes in asthma, to discover new drug targets and to better define and classify the various subtypes of clinical asthma at both the phenotypic and genetic level. This information will be used to develop new drug therapies targeting specific gene products, and to optimise the treatment of individual asthma patients. The program also aims to explore the pharmacogenetics of asthma and to develop innovative ways of directing asthma therapies to those patients most likely to benefit from those therapies.

## MOLECULAR BASIS OF ASTHMA

**Project Leader: Prof Charles Mackay**

**Deputy Leader: Dr Michael Rolph**

Recent advances in genomics, and particularly the sequencing of the human genome, have revolutionised research into the molecular and genetic basis of human disease. Most genes in the human genome have now been identified, and the availability of this information is providing an enormous boost to research. Medical researchers are now in a position to apply these advances to disease gene discovery, and already the genomic revolution has fostered some major breakthroughs.

Our research aims to identify new genes that participate in the pathogenesis of allergic inflammation and asthma. By doing so, we expect to identify therapeutic and diagnostic targets for these diseases. The initial phase of the research involved extensive use of microarray technology to 'profile' gene activity in every inflammatory cell type known to be important in asthma. We believe we have one of the most extensive and diverse inflammatory microarray datasets worldwide (the 'immune transcriptome'), and this resource will be of ongoing value for directing gene discovery efforts. During the year we submitted a provisional patent covering the most promising genes that we have extracted from the immune transcriptome.

In the last 12 months we have made major steps forward in validating a number of our candidate genes, especially the fatty acid binding proteins aP2 and mal1. Using an animal model, we now have unequivocal data demonstrating the key role of aP2 and mal1 in allergic airway inflammation. We are very encouraged by this finding which suggests that inhibiting the activity of aP2 and mal1 may be an effective therapeutic strategy for asthma.

A number of other microarray-derived candidate genes have been under intense investigation in our laboratory during the last year. One such gene is a novel GTP-binding protein that we hypothesise to be involved in leukocyte migration and cytokine release. A knockout mouse strain for this gene has now been developed. The analysis of these mice should give us a clear indication of the potential of this gene as a therapeutic target for asthma.

Looking to the year ahead we expect to complete the functional analysis of a number of other candidate genes, and to move our lead candidates into commercial development.



## GENOTYPING

**Project Leader: A/Prof Philip Thompson**

**Project Manager: Dr Bernadette Bradley**

One of the primary aims of the Genotyping Project is to characterise genetic polymorphisms in genes which are thought to have a role in asthma, in a large population of carefully phenotyped asthma patients and non-asthmatic controls. One of the asthma phenotypes we are investigating is disease severity and another is aspirin-intolerant asthma (AIA). To date, we have recruited 1751 asthmatics and non-asthmatic controls for our study, and DNA extracted from all of these patients is stored in a DNA database.

We have used molecular techniques such as PCR-RFLP to characterise polymorphisms in genes encoding enzymes in the arachidonic acid-leukotriene and prostaglandin biosynthetic pathways, including 5-lipoxygenase (ALOX5), 5-lipoxygenase activating protein (ALOX5AP), LTC<sub>4</sub> synthase, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). We have also studied polymorphisms in the receptors of these pathways, the kinin B1 and B2 receptors, and the cysteinyl leukotriene receptors.

We have now completed genetic association studies on polymorphisms in the genes of the leukotriene biosynthetic pathway and are close to completing work on the genes in the prostaglandin pathway. We have shown an association between a polymorphism in the LTC<sub>4</sub> synthase gene and asthma, and this work was published as the Editor's Choice in the May edition of the *Journal of Allergy and Clinical Immunology*. We found no associations between polymorphisms in the ALOX5 or ALOX5AP genes and asthma, and are preparing manuscripts describing these studies. Association studies on the COX-1 and COX-2 genes are almost complete with the first manuscript describing this work accepted by the *Journal of Clinical and*

*Experimental Allergy*. Three more manuscripts are in preparation. Our research on the kinin B1 and B2 receptors is complete and we are also preparing publications to describe this work. Our work continues studying mutations in the cysteinyl leukotriene receptors.

We have also used a new, high throughput genotyping technique called MALDI-TOF (matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry), using the Sequenom platform, through the Australian Genome Research Facility (AGRF) in Brisbane, to characterise several polymorphisms the ADAM33 gene. The ADAM33 gene has previously been shown to be associated with asthma in a British and American population, but we find no such associations with our population. We have submitted a manuscript describing our findings to an international journal.

Our future research will be carried out using a new high throughput genotyping technology, commercial chemo-fluorescent Taqman assays in 384-well format that will allow us to genotype a polymorphism in our entire population in just one day. This will dramatically increase our genotyping capacity and be used to study polymorphisms in the genes for prostaglandin synthesis and their associated prostaglandin receptors.

# Research

## GENE EXPRESSION AND PROTEOMICS

**Project Leader: A/Prof Philip Thompson**

**Deputy Leaders: Dr Neil Misso and Prof Peter Gibson**

During the past year work has continued on characterising the phenotype of asthmatic patients by the measurement of biomarkers in body fluids such as induced sputum. We completed a study in which the concentrations of cysteinyl leukotrienes, prostaglandin E<sub>2</sub> and isoprostane were measured in induced sputum supernatants from mild, moderate and severe asthmatic patients. This work has been extended into a collaborative project between the Perth (UWA) and Newcastle (John Hunter Hospital) nodes of the CRCA.

It is increasingly recognised that improved phenotype characterisation is required in order to understand mechanisms, improve diagnosis and inform treatment decisions in asthma. Recent studies show clear benefits when asthma management is based on measurement of markers of airway inflammation in induced sputum. Therefore the aim of this project is to identify candidate immunochemical or biochemical markers in induced sputum of asthmatic patients and in particular, markers that will permit discrimination between patients with eosinophilic or non-eosinophilic forms of airway inflammation. Potential markers of eosinophilic asthma include interleukin-5, RANTES, cysteinyl leukotrienes (cysLT), cysLT receptors, isoprostanes and nitric oxide metabolites, while potential markers of non-eosinophilic asthma include IL-8, the chemokine receptors (CXCR1, CXCR2), neutrophil elastase, leukotriene B<sub>4</sub> and matrix metalloproteinase-9.

These markers will be measured in induced sputum of patients with asthma and their validity for the phenotypic classification of asthma will be evaluated. In addition we plan to assess mRNA expression for the leukotriene synthetic enzymes and receptors, chemokines and chemokine receptors, in peripheral blood leukocytes and induced sputum cells of patients with different asthma phenotypes. The ultimate goal of this work is to develop a diagnostic test based on the expression of specific biomarkers and/or genes that can be used to aid in diagnosis and treatment decisions for patients with asthma.

Assays for a number of markers and techniques for RNA extraction and quantitative assessment of gene expression have been established. We are currently performing induced sputum challenges on asthmatic patients with different asthma phenotypes. Samples are being stored for subsequent measurement of inflammatory markers using enzyme immunoassays and for quantitative analysis of mRNA expression using real-time PCR.



## PATHOPHYSIOLOGY & DIAGNOSIS

The definition, diagnosis, assessment, treatment and monitoring of any medical condition is dependent on a clear understanding of the pathophysiology. The fact that there is still argument about even the definition of asthma is an indication that the pathophysiology is unclear. The projects in this program are designed to provide a better understanding of the fundamental problem in asthma i.e. airway obstruction.

The measurement of airway function in asthma is problematic at several levels. Since variable airway obstruction is universally accepted as a hallmark of asthma it seems appropriate to measure it in patients to diagnose the condition and to monitor the effects of treatment. There are simple tests such as the Forced Expiratory Volume (FEV1) and Peak Expiratory Flow (PEF) which convey information about airway calibre. However, these tests are influenced by the need to take a deep breath. Tests, such as the measurement of airway resistance, reflect airway diameter and do not require a deep breath but need complex equipment only found in specialised respiratory function laboratories. The degree of airway responsiveness can only be assessed by bronchial challenges using a variety of agents with bronchoconstriction measured as described above. In practice, many patients never have lung function tests performed at all.

The monitoring devices project aims to develop new tests of airway function which will reflect not only airway calibre but provide more information about the mechanical properties of the airway wall as well as the dynamics of airway smooth muscle contraction. The Heterogeneity project is exploring whether the airways in asthma are functionally uniformly involved or whether there is

heterogeneity. This is of fundamental importance in understanding airway hyperresponsiveness, symptoms and gas exchange as well as the targeting of inhaled therapeutic agents.

## MONITORING DEVICES

**Project Leader: Dr Greg King**

We have continued to examine airway behaviour in asthma using forced oscillation technique (FOT) to further our understanding of the characteristics of abnormal behaviour of asthmatic airways. The increasing knowledge base of which abnormalities can be measured using FOT and how they relate to asthma symptoms will support the potentially widespread use of this technique in general practice and lung function laboratories. We have also developed a new FOT testing protocol to measure another property of airways called distensibility that to date has been very difficult to measure.

The functional abnormality of airways has been very simply measured by 'forced expiratory flow', which is the maximal flow that can be generated by blowing with maximal force. These spirometric tests only depict part of the story and other useful information can be gained using FOT. Furthermore, although spirometry has been the 'gold standard' test for measuring airway function in asthma, it has not gained universal use because of difficulties in administering and interpreting the test. Thus it seems likely that FOT could play a significant role in lung function measurement in asthma management (and research) in the future, provided there is enough of a knowledge and information base.

# Research

There are many possible ways in which the protective mechanisms that operate in normal subjects are defective in asthmatic subjects. The current research activity and thinking regarding airway narrowing in asthma is focussed on 'velocity' or the speed at which airways narrow; this has been referred to as the 'dynamic model of narrowing'. Deep breaths protect normal airways from narrowing excessively when airway smooth muscle is stimulated to contract and narrow the airways. These deep breaths stretch open the airways which then narrow again ('re-narrowing') slowly, over perhaps 60-100 seconds. In contrast, asthmatic airways re-narrow over several seconds. Our research has therefore been aimed at clarifying why this occurs. We have focussed on the three important abnormalities; airway smooth muscle, lung recoil and distensibility (stiffness of airways).

We found that altering breathing rates altered airway calibre; this evidence supported the importance of the velocity at which airway narrowing determined the overall airway calibre. In our studies nifedipine, (a drug which blocks the movement of calcium into smooth muscle cells and which is necessary for contraction) was shown to have no effect on airway narrowing. Thus we have no evidence to support the role of airway smooth muscle in this particular behaviour of airways. On the other hand, our studies of lung recoil show that nifedipine does have a significant effect, and manoeuvres to reduce recoil profoundly increased the speed and magnitude of airway narrowing.

There has been very little data published on distensibility of airways. Distensibility has been shown to relate to scarring of airways but it has been very difficult to measure. In the long term, reduced distensibility and scarring are thought to lead to irreversible narrowing in patients who have had moderate to severe asthma for many years. We are currently validating a protocol which allows us to measure airway distensibility relatively easily using FOT. We are also conducting studies to see how distensibility relates to asthma severity and how it responds to treatment.

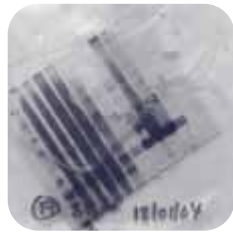
## HETEROGENEITY

**Project Leader: Prof Norbert Berend**

**Deputy Leader: Dr Greg King**

Asthma affects the whole of the airway tree and causes airway thickening, which is patchy and heterogeneous in distribution. This means that the normal, even and predictable nature of lung ventilation is lost in asthmatics. This abnormal ventilation is thought to be determined by small airways disease, which is slow to reverse on treatment. This sensitive measure of abnormality has been very difficult to determine because the number of small airways is so immense and their size so small. We have used a technique called nitrogen washout to measure small airway function in our study of asthmatics. Such tests have become more useful in the last five years due to advances in computer modelling of the way the lungs handle inhaled gases. We are examining how measurements of small and large airway function relate to the severity of asthma and also the response to certain drug aerosols; one might expect smaller aerosol particles to be more suited to treating small airways and future therapeutic aerosols may be designed to target different sized airways.

We have continued our study of the effect of QVAR on small airway function, comparing it to the effects of a larger particle aerosol. In addition to using the nitrogen washout method to measure airway function, we have also used the simpler FOT to assess the potential of FOT to measure small airway function. We have found that bronchial challenge testing using methacholine affects small airway function. This has only previously been studied using histamine which was found to have no effect on asthmatic small airways. Interestingly, we also found that the measurements from FOT using a testing signal of 5 Hz frequency also reflected disease in the small airways (both heterogeneity and airway closure);



again a new and potentially useful finding which supports the use of FOT in measuring airway function in asthma.

We have also looked at how unevenly asthmatic airways narrowed using High-resolution Computed Tomography (HRCT) and found that asthmatic airway narrowing was much more uneven than the equivalent narrowing in non-asthmatic airways. These measurements were in large and medium sized airways and this means that the basis of the uneven ventilation in asthmatics resides at not only the small airways but also at points that affect very large portions of the lung, and that treating the large airways is also important. The measurements of uneven narrowing were also unique in that comparisons were made between 'sister' airways, i.e. they both originated from the same parent airway by branching. Measurements of this sort are valuable in computer modelling studies on how the lungs ventilate. Another novel feature was that these measurements were 3-dimensional in nature. Such measurements have not been previously published and we expect to have the results published shortly.

Although HRCT imaging is not in routine use, it is likely that with ever increasing scanning speeds and spatial resolution, sophisticated 3-dimensional measurement tools will be used routinely by respiratory physicians and radiologists in the future. As part of our continued development of the software and measurement technique, we have collaborated with Dr Allan Jones of the Australian Key Centre for Microscopy and Microanalysis at the University of Sydney. Dr Jones is an expert in 3-dimensional image analysis and his unit operates one of two micro-CT machines in Australia. We have used this technology to image lungs at 100 times greater resolution of HRCT scans. We are now using this technique to validate and improve the accuracy of our HRCT software for measuring human airways.

Along with developing the software for measuring airways from HRCT images, we have also written software for use in bronchial challenge testing. This has been designed in conjunction with the clinical researchers so that the software will be suitable for use in bronchial challenge testing in a variety of settings from lung function laboratories to small consulting rooms. There are few if any software packages that are adequate for such applications.

We have nearly completed a study in which we have compared the responses to two different bronchial challenge agents; methacholine and adenosine monophosphate (AMP). Methacholine has been in widespread use and is a direct airway smooth muscle stimulant whereas AMP is thought to only stimulate airway regions that are affected by inflammation. Given the patchy distribution of airway inflammation and the known differences in sensation induced by AMP, we expect that the responses of the airways to the two agents would differ. This cannot be differentiated using standards tests (spirometry) but we should be able to detect differences by using FOT.

# Research

## ASTHMA MANAGEMENT & PREVENTION

Although there is effective treatment to control asthma there is no known therapy that induces permanent remission for this disease. An individual with established asthma is committed to long-term drug treatment and, in some cases, substantial disability. Both these outcomes have major cost implications, for both the individual and for the community.

This program endeavours to minimise the burden by:

- Studying the effectiveness of interventions in preventing asthma
- Undertaking trials to better target treatment
- Gaining an understanding of the attitudes of consumers and health professionals
- Assessing the economic burden on the individual and community
- Developing enhanced guidelines for health professionals

## CHILDHOOD ASTHMA PREVENTION STUDY

**Project Leader: A/Prof Guy Marks**

**Project Manager: Ms Seema Miharshahi**

Evidence from many studies shows that both a diet rich in omega-3 fatty acids and avoidance of house dust mite allergens play an important role in the development of asthma. The Childhood Asthma Prevention Study (CAPS) is a randomised controlled trial testing whether house dust mite allergen reduction and omega-3 fatty acid supplementation, is effective in reducing the incidence of asthma and allergic sensitisation in children. It is a collaborative project between the Woolcock Institute, the Children's Hospital Westmead and Liverpool Hospital.

The study started in April 1997 when over 600 pregnant women and their families were recruited. The house dust mite reduction intervention, implemented before birth of the child, involved the use of allergen impermeable mattress and pillow covers for parents' and infants' beds and regular use of an acaricide washing detergent. The purpose of the diet intervention was to increase the intake of omega-3 fatty acids by providing a daily fish oil supplement and canola based cooking oil and margarines for use in all family meals.

Children are assessed at 18 months, 3 and 5 years by a research nurse who is blinded to their treatment group allocation. The assessment includes structured parental-interview, limited examination, skin prick tests, blood tests, measurement of exhaled nitric oxide (at ages 3 and 5 years) and measures of lung function (at ages 3 and 5 years). In addition blood is collected to measure total IgE, plasma fatty acids (as an index of the effect of the dietary manipulation) and lymphocyte cytokine production in response to house dust mite allergen stimulation.

Data from the 3 year assessments has been analysed and showed a significant 10.0% reduction in cough among allergic children in the group receiving fish oil supplements and also a 7.2% reduction in sensitisation to house dust mite in the group receiving the house dust mite avoidance intervention. However, no differences in the prevalence of wheeze were found between intervention groups. These results are encouraging because they suggest that our interventions, which are feasible to implement on a large scale, may help to prevent the development of allergic sensitisation and airways disease in early childhood. This offers the prospect of reducing allergic disease in later life. A full report of these findings is currently in press.



To date over 291 children have completed 5 year assessments and the oldest child in the cohort is almost 7 years of age. At the present time, 81 (13%) of the 616 randomised subjects have withdrawn from the study. Further follow up is underway to determine any accretion of the effects of the interventions at age 5 years when asthma can be more reliably defined.

## TARGETING TREATMENTS

**Project Leader: Dr Christine Jenkins**

**Deputy Leader: Dr Helen Reddel**

### STUDY 1

A randomised, controlled trial to assess the impact, clinical meaning and value of improvements in lung function, symptoms and airway hyperresponsiveness on three asthma medications, Formoterol, Montelukast and Fluticasone, each for six weeks.

This study was completed in September 2003 and the final statistical report was received in June 2004. Several posters were presented in 2003 and three papers are currently being written. The study results indicate that the benefit of an intervention may be poorly assessed if only traditional measures are included. Different drugs have different benefits on lung function, symptoms, asthma control and quality of life, and a formulaic approach which uses conventional outcomes such as lung function in clinical trials will underestimate the potential benefits of some drugs. Conversely, improvement in one variable does not necessarily imply benefit for all outcomes. The results of the analysis of relative benefit suggest that patient-centred outcomes rank highly as determinants of benefit. These include the asthma control questionnaire, use of visual scales for patients' perception of asthma control, and quality of life. In relation to the patient centred variables, the long acting beta

agonist and inhaled corticosteroid in the study had similar effects; however the long acting beta agonist was superior to the inhaled corticosteroid for symptom scores, but inferior for lung function variables. The Discrete Choice Experiments (DCE) are adding more information to the patient oriented assessments but have yet to be fully analysed. In order to capture the full benefit of an intervention from both the physician and patient perspective, the study results strongly endorse the inclusion of multiple endpoints as measures of benefit in clinical trials.

### STUDY 2

A randomised controlled trial of the effect of breathing techniques on symptoms, airway responsiveness, quality of life and dose of inhaled corticosteroids (ICS) in subjects with symptomatic asthma.

This study assesses the value of several different breathing techniques which may influence asthma symptoms, medication use and asthma control. The subjects are learning these techniques through watching a video and practising daily. The first part of the study assesses the intervention's effects on clinical and quality of life measures, and the second part of the study will assess whether regular use of these breathing techniques can affect the underlying control of asthma to the extent that preventer medication, particularly inhaled corticosteroids, can be reduced. The subjects in the study are doing well generally and when the study is completed and unblinded, we will know the nature and magnitude of the benefit for each treatment group. The study will be completed in August 2004 and preliminary results available in November 2004.

# Research

## STUDY 3

A randomised, double blind study of 3 different algorithms for maintaining asthma control on combination therapy during down titration on long acting bronchodilators and inhaled corticosteroids.

It is clear that achieving asthma control on a minimal effective dose of inhaled corticosteroids is a desirable goal of good asthma management. However some of the measures and inflammatory markers proposed for this are not suited to general practice where most patients are managed. The optimal markers for use when predicting whether patients who are taking combination therapy with inhaled corticosteroids and long acting bronchodilators can safely reduce their medication are not known. The proposed study will examine which additional markers of asthma control (compared to clinical assessment alone) are likely to achieve best outcomes when used to assess readiness to down titrate doses in patients taking combination therapy. The study will assess clinical approaches to down titration in terms of their capacity to minimise long-term ICS (and oral steroid) usage while achieving and maintaining optimal asthma control (exacerbation prevention and quality of life). The protocol is in draft at present in preparation for submission to the Institutional Ethics Committees in September 2004. It will be conducted at the Alfred, John Hunter and Liverpool Hospitals, and the Woolcock Institute.

## CONSUMER PRIORITIES

**Project Leader: A/Prof Jo Douglass**

**Project Manager: Ms Dianne Goeman**

### PHASE 1

'A study in Emergency Department Attendees with Asthma'

This study has been completed, with eight papers reporting the consumer perspective on asthma and asthma care now published or accepted for publication.

### PHASE 2

'Health professional priorities in asthma care'

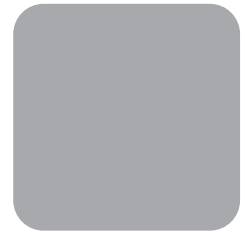
This qualitative study identified the priorities in asthma care of specialists, general practitioners, asthma nurse educators and pharmacists. Two papers, one on the barriers to the delivery of asthma care and one on health professionals' priorities for asthma care are in progress. The findings of Phase 2 reveal that in spite of the availability of asthma guidelines and highly effective asthma treatments many factors hinder good asthma management.

### PHASE 3

'Community care for asthma'

This study will involve a representative sample of people with asthma purchasing beta-2-agonists from pharmacies, ascertaining their lung function, asthma symptoms and other medication use. This study will specifically compare those individuals with asthma who purchase beta-2-agonists over the counter, with individuals simultaneously purchasing beta-2 agonists with a prescription or on advice from their doctor. The second component of this study is a qualitative study of those not taking regular preventative asthma treatments. A representative sample of patients will be recruited from pharmacies to study the barriers to using preventative treatments. Sixty four people and six pharmacies have currently participated in this phase of the project.

The work of this project has provided a unique base to develop an effective intervention in asthma. This is critical whilst asthma morbidity continues to be high yet failure to use appropriate treatment continues in the community and hospitals. Future work of this project will be to develop interventions which can be disseminated to improve asthma care. Such an outcome will be of substantial public benefit.



## ECONOMIC EVALUATION

**Project Leader: Prof Jane Hall**

**Project Manager: Ms Meredyth Chaplin**

Two major economic studies are being undertaken, the first is a longitudinal cohort study designed to investigate the economic burden of asthma. A cohort of 334 asthmatics from throughout NSW was identified, using a market research firm, between November 2001 and November 2002. Six-monthly surveys of participants, covering health service utilisation, out-of-pocket-costs and quality of life, commenced in January 2002. Response rates to the first, second and third surveys were high (88% of the surveys distributed were completed for survey one, 89% for survey two and 93% for survey three). The fourth and fifth surveys are due for completion in January and July 2005. Data collection will be completed by July 2005.

Data on medical attendances and diagnostic tests for the first year of the study have been obtained from the Health Insurance Commission and first year data on hospital admissions have been obtained from NSW Health. This is one of the few Australian studies to combine data from these disparate sources.

Analysis of the first year of follow-up is complete. A methodological discussion paper, reviewing the literature on diary and questionnaire methods for collecting resource utilisation data, has been written and published in the CHERE technical report series. A paper describing health service utilisation and costs in the first year of the study has been submitted to the Medical Journal of Australia. A poster on the same topic was presented at the conference of the Health Services Research Association of Australia & New Zealand in November 2003.

The second major study was carried out as part of the first randomised controlled trial (RCT) undertaken by the Targeting Treatment Project. It includes a stated preference discrete choice modelling (SPDCM) experiment. This study has required the development of the overall study design, the questionnaires to conduct the four discrete choice experiments (DCEs) and comparison of stated and revealed preferences, and the framework for the Cost Effectiveness Analysis and Cost Benefit Analysis. The project team managed the DCE data collection within the RCT. Data collection took longer than expected due to delays in the randomised control trial but is now complete. Some preliminary analyses of the first survey results have been completed and presented at a number of conferences. Related work used the results of the pilot study to investigate the validity of welfare measures derived from willingness to pay; this has recently been published in *Health Economics*.

# Research

## EVIDENCE BASED GUIDELINES

### **Project Leader: Prof Peter Gibson**

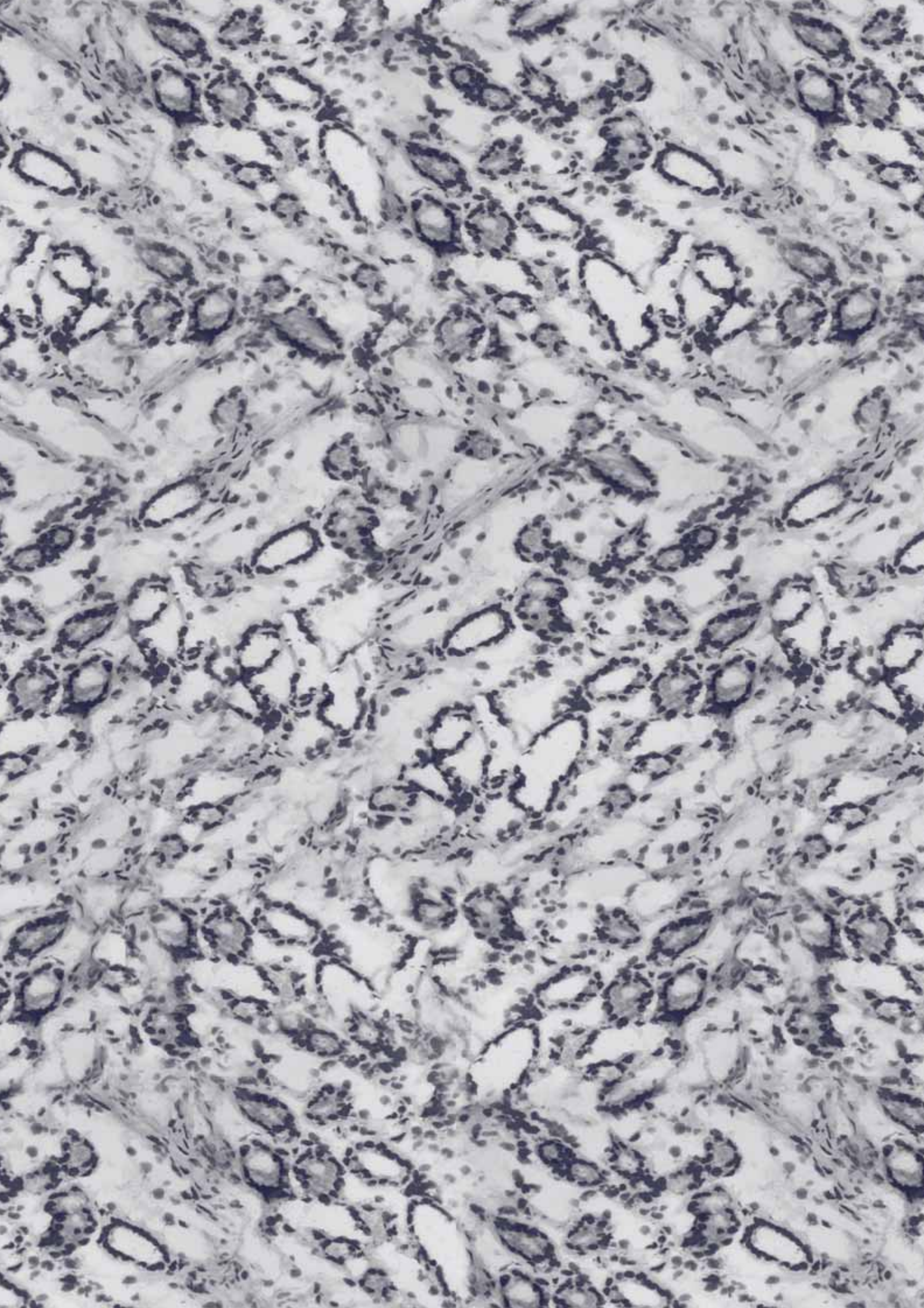
This project team conducts systematic reviews providing best evidence to support and enhance the current Australian Asthma Management Plan (AAMP). The work has been completed for asthma self-management including the publication in Thorax of our review of the individual components of written action plans. This review has provided evidence for establishing the parameters for writing written action plans for asthma. Further reviews are in progress to provide best evidence for achieving and maintaining best lung function with the results translated into clinically meaningful terms.

The optimal starting dose for inhaled corticosteroid (ICS) therapy for asthma is unknown. We have completed a systematic review of high vs low initial starting dose ICS in asthma. This review includes the results of 26 randomised controlled trials that compared high initial ICS to moderate or low initial ICS. This review provides level 1 evidence for optimal starting ICS dose.

A systematic review of predictors of loss of asthma control has been completed. This review includes the results of ten prospective trials conducted to establish the predictive value of non-invasive markers of airway inflammation for monitoring deterioration in asthma control following back titration of inhaled corticosteroid therapy. The results of this review are being used to inform design of the third Targeting Treatment trials.

A new systematic review has commenced on 'The inhaled corticosteroid-sparing effects of addition of long acting beta agonists (LABA) for chronic asthma'. This review will determine the magnitude of maintenance ICS dose reduction possible with the addition of long acting beta agonists while maintaining asthma control.

A review of LABA and ICS combination therapy compared to ICS alone to determine the efficacy and harm at different doses will be conducted. These data will be translated into the evidence-based terms number-needed-to-treat (NNT) and number-needed-to harm (NNH). This will enable our previous graph of efficacy and harm for ICS to be updated to include ICS and LABA.



# Education & Training

## EDUCATION AND TRAINING

### POSTGRADUATE STUDENTS

Postgraduate scholars are involved with the CRCA through direct participation in CRCA research projects, or through a CRCA PhD scholarship. The CRCA offers supplementary scholarships to suitably qualified candidates and adjudicates these through a selection committee nominated by the Education Committee. CRCA scholars receive travel assistance to facilitate attendance at national and international conferences for presentation of their work. They are also encouraged to visit research laboratories where they can further develop their technical skills. In addition to travel scholarships, all PhD scholars attend the CRCA's annual conference.

The scholarship scheme is highly competitive with a very high number of excellent applications received each year. The Education Committee has awarded 22 scholarships since inception of the scheme in 2001 and there are currently 11 postgraduate students being supported by substantial scholarships from the Centre, with an additional 5 students supported via research project funding. In 2004 four new PhD scholars were welcomed to the team. The newly funded PhD students are:

**Ms Joanna Groom**  
Garvan Institute/University of New South Wales

**Mr Adrian Lowe**  
University of Melbourne

**Ms Mary Sisavanh**  
Garvan Institute/University of New South Wales

**Ms Chantelle Dixon**  
Australian National University

PhD student Ms Kate Jeffery is currently spending 3 months on exchange to Geneva, Switzerland. She is working with Dr Montserrat Camps in the Cell Signalling lab at Serono. Ms Sue Liu attended a Mast Cell conference in New Mexico, USA in February where she gave an oral and poster

presentation. Ms Tatyana Chtanova utilised her scholarship to present a poster and give a talk at a T Cell development conference in Banff, Canada. Ms Chtanova also travelled to San Francisco to visit laboratories to explore potential postdoctoral positions. Ms Rachel Collins attended the American Thoracic Society conference in Florida where she gave a presentation and attended a postgraduate course. In addition Ms Collins made laboratory visits to North Carolina and the University of Texas Medical School. Mr Adrian Lowe has utilised his travel scholarship to attend a 5-day intensive biostatistics workshop in Hobart. Mr Andrew Sutherland and Ms Kate Jeffrey, both of the Garvan Institute, have attended the Cytokines, Signalling and Diseases meeting (the Annual meeting of the International Society for Interferon and Cytokine Research) in Cairns. Ms Jeffrey delivered an oral presentation to the international audience.

### IPCRG/AAC

The CRCA conducted a symposium titled *Behavioural Aspects of Asthma - towards a better understanding of integrated asthma management* as part of both the prestigious International Primary Care Respiratory Group Conference (IPCRG) and the Australian Asthma Conference (AAC). The IPCRG is a meeting of international clinicians and general practitioners with a respiratory interest. Members of this group have significant influence in the areas of asthma guidelines and management. Over 85 delegates attended the symposium that bridged the two conferences. Presenters of the symposium explored the influence of psychosocial stress on asthma outcomes and increased participants' skills in dealing with these issues. Dr Christine Jenkins of the CRCA chaired the session. Dr Robert Adams (Queen Elizabeth Hospital, Adelaide) provided a succinct overview of the literature related to 'Clinical aspects of the impact of stress, depression and anxiety on asthma outcomes', while Associate Professor John



Kolbe (Green Lane Hospital, Auckland) discussed 'Stress Management & Asthma Outcomes' with an emphasis on the high risk asthma patient. From the CRCA team, Dr Rosalie Aroni (LaTrobe University) provided a critical review of 'Psychological and Sociological asthma research', while Dr Jo Douglass and Ms Dianne Goeman (CRCA at the Alfred Hospital Melbourne) provided a very interesting session on 'Achieving better adherence with recurrent A&E attendees: scenarios and solutions'. The symposium was extremely well received and the speakers presented clear and stimulating material resulting in a high quality audience discussion and a very successful session. An exhibition booth was also run by the CRCA at the Australian Asthma Conference where CRCA publications and reprints of CRCA research were distributed to delegates.

## PERTH EDUCATION INITIATIVE

A three-part education initiative was developed by the CRCA, the Asthma and Allergy Research Institute and the West Australian Institute for Medical Research. Firstly, a University of Western Australia student of Medicine, Mr John Ding, completed a Summer Studentship in the AARI Genetics Unit studying mutations in the MMP and TIMP genes, implicated in tissue repair and remodelling. In the second part, eight Western Australian high-school students spent two days of their mid-year holidays in the AARI Genetics Unit learning about genetics and genetic testing. The students extracted their own DNA and tested for a common mutation in the asthma candidate gene COX-1. The final part of the education initiative is a pair of asthma-focussed seminars by local, interstate and international speakers, and this is planned for later in the year.

## PROJECT MANAGEMENT COURSE

A very successful project management course for postgraduate students and young scientists was hosted by the CRCA on the day following the CRCA conference. PhD scholars from the Vision CRC also attended. The course covered basic aspects of managing a project, from the set up phase through to implementation and review. Key points covered included planning, time management, resource allocation and implementation. Students also learnt to identify potential risks, the likelihood of these risks occurring and determining the necessary action for mitigation. Time management techniques were also introduced which included the use of Gantt charts. The students reported that they enjoyed the course and would look forward to implementing some new techniques in the management of their research work.

STUDENT	RESEARCH TOPIC	INSTITUTE ENROLLED	SUPERVISORS (& ORGANISATION)	DATE COMMENCED	SOURCE OF FUNDING
Mr Andrew Sutherland	The role of new TNF family members and their receptors in allergic and asthmatic responses	UNSW	Professor C Mackay (Garvan)	March 2002	CRCA APA
Ms Sue Liu	Mast cells and asthma: a functional genomic analysis	UNSW	Professor C Mackay (Garvan) Dr M Rolph (Garvan)	July 2001	CRCA NHMRC
Ms Rachel Collins	Dysregulation of airway tone following viral infection	UWA	Professor P Sly (ICHR) Dr D Turner (ICHR) Dr P Holt (ICHR)	Jan 2002	CRCA APA
Mr Bennett Shum	The role of $\alpha$ 2 in allergic lung inflammation	UNSW	Professor C Mackay (Garvan) Dr M Rolph (Garvan)	Apr 2003	CRCA APA
Ms Kate Jeffrey	The role of PAC-1 in regulating MAP kinase signalling in inflammation and asthmatic responses	UNSW	Professor C Mackay (Garvan) Dr M Rolph (Garvan)	Jun 2002	CRCA APA
Dr Stephen Vincent	Study of mechanisms and treatment of asthma exacerbations due to viral infections and inhaled corticosteroid reduction	USYD	Dr H Reddel (Woolcock)	Feb 2003	CRCA APA
Ms Jodie Simpson	Non-eosinophilic asthma: mechanisms and treatment	Newcastle	Professor P Gibson (HMRI)	Jan 2002	CRCA APA
Ms Cassandra Slader	The use of complementary and alternative therapies by people with asthma	USYD	Dr H Reddel (Woolcock) Dr C Jenkins (Woolcock) Professor C Armour (USYD) Dr S Bosnic-Anticevich (USYD)	Mar 2002	APA
Ms Jessica Dame-Carroll	Heterogeneity of airway narrowing and airway wall thickness are key determinants of asthmatic airway function	USYD	Dr G King (Woolcock) Professor N Berend (Woolcock)	Jul 2001	CRCA
Mr Nathan Brown	The development of simple physiological markers of airway abnormalities in asthma	USYD	Dr G King (Woolcock) Dr C Salome (Woolcock) Dr W Thorpe (Woolcock)	Jan 2004	CRCA
Ms Sue Downie	Small airway function in asthma	USYD	Dr C Salome (Woolcock) Dr G King (Woolcock)	Feb 2003	CRCA
Mr Aneal Chandra	Development and validation of three-dimensional segmentation methods for pulmonary structures from multi-slice high-resolution X-ray computed tomography.	USYD	Dr G King (Woolcock) Dr A Jones (AKCMM)	July 2003	CRCA

STUDENT	RESEARCH TOPIC	INSTITUTE ENROLLED	SUPERVISORS (& ORGANISATION)	DATE COMMENCED	SOURCE OF FUNDING
Ms Joanna Groom	The action and regulation of Sphingosine-1-phosphate and its G coupled-protein receptors in asthmatic and autoimmune disease	UNSW	Dr F Mackay (Garvan) Dr R Newton (Garvan)	Apr 2003	CRCA NHMRC
Mr Adrian Lowe	The role of maternal and childhood exposures in the development of asthma and allergies in genetically predisposed children	Melbourne	Dr S Dharmage (Melbourne) Dr D Hill (Royal Children's Hospital) Professor J Carlin (Melbourne) Professor M Abramson (Monash) Dr C Bennett (Melbourne)	Mar 2004	CRCA Dairy Australia
Ms Mary Sisavanh	The functions of A20 and BAFF in mast cells	UNSW	Professor C Mackay (Garvan) Dr M Rolph (Garvan)	Jan 2002	CRCA APA
Ms Chantelle Dixon	Identification and characterisation of the proteins involved in the STAT 6 dependent pathway of airways hyperresponsiveness in the Murine allergy model.	ANU	Dr D Webb (ANU) Professor P Foster (ANU)	Jul 2002	CRCA ANU

## ABBREVIATIONS:

AARI	Asthma and Allergy Research Institute
AKCMM	Australian Key Centre for Microscopy and Microanalysis
ANU	Australian National University
APA	Australian Postgraduate Award
Garvan	Garvan Institute of Medical Research
HMRI	Hunter Medical Research Institute
ICHR	Telethon Institute for Child Health Research
Melbourne	University of Melbourne
Monash	Monash University
Newcastle	Newcastle University
NHMRC	National Health and Medical Research Council
QUT	Queensland University of Technology
UNSW	University of New South Wales
USYD	University of Sydney
UWA	University of Western Australia
Woolcock	Woolcock Institute of Medical Research

# Collaboration

## COLLABORATION

### STRUCTURE

The structure of the CRCA facilitates collaborative interactions between the partners working at the various research nodes. All stakeholders are represented on the Technical and Research Advisory Committee that oversees the research program and the project working groups include personnel from the various partners. Industry and consumer representatives on the Education Committee play an important part in ensuring the relevance of educational initiatives. Asthma Foundations of Australia and the National Asthma Council are represented on a number of CRCA committees and these organisations provide an important link with major user groups.

### RESEARCH

CRCA researchers at the Sir Charles Gairdner Hospital in Perth, supported by the Monash team at the Alfred Hospital, have collected a large number of samples of DNA from people suffering from various forms of asthma as well as from non-asthmatic controls. In parallel with this activity, gene targets have been generated by the microarray experiments carried out at the Garvan Institute in Sydney. Over the past years these teams have been working together to analyse a large number of single nucleotide polymorphisms (SNPs) in our population of asthmatics and non-asthmatics, in order to determine if there are any associations between these SNPs and asthma.

A second major collaboration is the Targeting Treatment Project. This project incorporates multi-centre clinical trials that are being carried out by the clinical research groups at the Woolcock Institute, Monash University and the John Hunter Hospital with active participation of the major industry partners. The economic aspects of these trials are coordinated by the Centre of Health Economic Research and Evaluation (CHERE) at the University of

Technology Sydney. CHERE is also working on a major longitudinal study into the economic costs of asthma. Researchers at the Woolcock Institute, Monash and UWA have contributed to the design of the protocols utilised in this study.

Over the past year research teams based at Sir Charles Gairdner Hospital in Perth and the John Hunter Hospital in Newcastle have commenced work on a major project to identify markers of airway inflammation in sputum. The outcomes of this work will be the development of advanced diagnostic products.

Researchers based at the Alfred Hospital in Melbourne are working on a study into the individuals who purchase their asthma medication over the counter. This project has been designed in cooperation with the industry partners and the results will assist in the targeting of this under treated group.

Other examples of internal collaborations include the Childhood Asthma Prevention Study. This is a joint undertaking between the Woolcock Institute and University of Sydney scientists based at the Children's Hospital at Westmead. Industry partners are also providing significant support to scientists at the Woolcock Institute, Royal North Shore Hospital and University of Sydney, who are working on the Heterogeneity in Asthma project.

The CRCA team at the Garvan Institute has established a collaboration with Prof Gokhan Hotamisligil of the Department of Nutrition, Harvard School of Public Health. This collaboration has fast tracked the evaluation of the aP2 gene target that has been identified by the Garvan group.



## CRCA ANNUAL CONFERENCE

The fourth CRCA Conference was held in Wollongong in November 2003. This event was attended by over sixty CRCA researchers and support staff from Sydney, Newcastle, Melbourne and Perth. Dr Emery Severin, the Chairman of the CRCA board, other board members and the CRCA Visitor, Professor Sue Serjeantson also participated in the conference. The meeting provided the researchers with an invaluable networking opportunity and strengthened inter-node collaboration. The PhD scholars were also invited to attend and their presentations were one of the highlights of the meeting. Mr Philip Bert opened proceedings with an overview of the future directions for the CRCA. This was a major theme of the conference with two sessions devoted to developing a vision for projects and integrating project proposals within a new CRC. The participants divided into two groups, 'New & Better Treatments' or 'Better Diagnosis & Monitoring' and brainstormed useful ideas and suggestions. Dr Christine Jenkins provided an update on 'Asthma in Australia' and presentations from Project teams following. A poster session facilitated discussions on a range of activities in the CRCA.

## SYMPOSIUM

The CRCA coordinated a symposium titled *Behavioural Aspects of Asthma - towards a better understanding of integrated asthma management* at the important World Conference of the International Primary Care Respiratory Group that was held in Melbourne in early 2004. This symposium was a great success and was organised in collaboration with the National Asthma Council and Asthma Foundations of Australia.

## NEWSLETTER

The CRCA continues to produce a newsletter twice a year to inform all members of the CRCA of the group's latest activities. The newsletter is also distributed to CRCA partners and other stakeholders.

# Management & Operations

## MANAGEMENT & OPERATIONS

The CRCA is administered by the Chief Executive Officer, a Business Manager, an Administrative Assistant and an Education Manager. This unit provides focus for the activities of the CRCA and coordinates the research, education and commercialisation programs. This group also controls the finances of the CRCA and provides administrative support to the operating units.

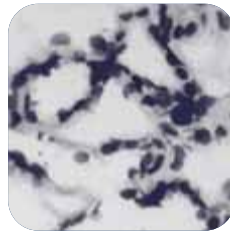
All projects are managed by Project Leaders who are responsible for day-to-day operations, the recruitment of staff and the achievement of milestones. Project plans and milestones are approved by TARAC on an annual basis and Gantt Charts are used to monitor project progress. Quarterly reports are prepared for the Board. Operating budgets are approved by TARAC and

the Board prior to the start of the financial year and management accounts are prepared on a quarterly basis. Expenditure is reviewed in relation to project progress to ensure that resources are being deployed to the best effect.

The CRCA's administrative offices are located in the Medical Foundation Building on the University of Sydney campus. The University is providing this accommodation free of charge.

Over the past year 96 professional and support staff contributed to the CRCA programs. The following table lists the specified personnel of the CRCA for the financial period ended 30 June 2004.

Name	Organisation	% Time on CRCA	Role/Function
Prof Robyn O'Hehir	Monash	48	Program Leader
A/Prof Philip Thompson	University of WA	47	Program Leader
Dr Euan Tovey	Woolcock	>1	Project Leader
Dr Christine Jenkins	Woolcock	15	Program Leader
Prof Charles Mackay	Garvan	45	Program Leader
A/Prof Guy Marks	Woolcock	25	Project Leader
Dr Jo Douglass	Monash	38	Project Leader



# *Publications & Patents*

## PUBLICATIONS & PATENTS

### PUBLICATIONS

In the 2003/2004 financial year, over 27 papers relating to the Centre's activities were published in refereed journals. CRCA researchers were also invited to contribute review articles in a number of relevant journals. In addition, numerous articles were published as proceedings from international and national conferences. Details of these publications are listed in the appendix on page 38.

### PATENTS

#### **PCT/AU00/01182**

Immunointeractive molecules and uses thereof. (Hev b5)

#### **PCT/AU02/01473**

Immunointeractive molecules and uses thereof. (Hev b6)

#### **PCT/AU2004/000374**

Therapeutic and prophylactic compositions and uses thereof. (aP2/mal1).

#### **US PROVISIONAL PATENT 60/543442**

Therapeutic and prophylactic compositions and uses thereof. (Global leukocyte transcriptome and candidate genes).

# Communication

## PUBLIC RELATIONS & COMMUNICATION

A highlight of the year was the symposium titled *Behavioural Aspects of Asthma - towards a better understanding of integrated asthma management* organised by the CRCA that linked two significant conferences, the World Conference of the International Primary Care Respiratory Group and the Australian Asthma Conference. These conferences were very well attended, with CRCA researchers making a significant contribution to both conferences as invited speakers.

Details of all contributions to international and national conferences are provided in the appendix on page 38.

CRCA researchers provided valuable comment on CRCA projects, asthma and related issues through exposure in national media. These included television and radio interviews as well as wide exposure in the print media. Some examples are provided below.

Dr Christine Jenkins achieved extensive publicity on the Breathing Study currently being undertaken within the Targeting Treatment Project. The Sydney Morning Herald and The Age reported on this work and Dr Jenkins spoke on both national and local radio programs. This coverage resulted in significant numbers of subjects volunteering to participate in the study.

A/Professor Jo Douglass and Ms Dianne Goeman discussed the results of the consumer priorities project nationally on ABC TV and Radio and on station 3LO in Melbourne. Reports also appeared in the Herald-Sun.

Professor Peter Gibson discussed Asthma Action Plans and guided self-management on ABC Radio National's Health Report.

In Western Australia, details of high school students attending the hands-on genetic workshops as part of the Perth Education Initiative were reported in local newspapers.

The CRCA continues to publish a newsletter, to enhance communication throughout all projects and nodes of the CRCA. The newsletter is also distributed to pharmaceutical industry partners, the Asthma Foundations and other stakeholders.

# Performance

## PERFORMANCE MEASURES

INDICATOR	OBJECTIVE	ACHIEVEMENT 2000/2001	ACHIEVEMENT 2001/2002	ACHIEVEMENT 2002/2003	ACHIEVEMENT 2003/2004
<b>QUALITY AND RELEVANCE OF THE RESEARCH PROGRAM</b>					
Progress of research	Eighty percent of research projects will reach stated milestones within specified time-frame	10 out of 12 projects (83%) have reached stated milestones on schedule	9 out of 11 projects (81%) have reached stated milestones on schedule	9 out of 11 projects (81%) have reached stated milestones on schedule	9 out of 11 projects (81%) have reached stated milestones on schedule
Relevance to users	All strategic decisions on research are made with input from users	Users are represented on TARAC as well as on project committees	Users are represented on TARAC as well as on project committees	Users are represented on TARAC as well as on project committees	Users are represented on TARAC as well as on project committees
Frequency of refereed journal papers and book chapters	One to two papers per scientist per annum	Seven papers on core research were published in refereed journals	Fourteen papers on core research were published in refereed journals	Twenty papers on core research were published in refereed journals	Twenty seven papers on core research published in refereed journals.
Number of scientific presentations	Three per scientist per annum	Fifty major presentations were given	Twenty five major presentations were given	Forty six major presentations were given	Thirty seven major presentations were given
International visitors and conference papers	Four exchanges per annum	Twenty international conference papers delivered	Twelve international conference papers delivered	Thirteen international conference papers delivered	Thirteen international conference papers delivered
Invited reviews	One invitation per scientist per annum	Fourteen invited papers were presented	Twelve invited papers were presented	Thirteen invited papers were presented	Fourteen invited papers were presented

INDICATOR	OBJECTIVE	ACHIEVEMENT 2000/2001	ACHIEVEMENT 2001/2002	ACHIEVEMENT 2002/2003	ACHIEVEMENT 2003/2004
<b>UTILISATION AND APPLICATION OF RESEARCH OUTPUTS</b>					
Community education programs	Active collaboration with National Asthma Campaign and Asthma Foundations	Both organisations are represented on CRCA committees	Both organisations are represented on CRCA committees	Both organisations are represented on CRCA committees	Both organisations are represented on CRCA committees
Intellectual property	Five provisional patents to be lodged in first four years	First PCT application lodged in September 2000	Three provisional patents lodged in the first three years.	Four provisional patents lodged in the first four years.	Five provisional patents lodged in first five years
Industry connections	One to three approaches by industry per annum	One company approached the CRCA during the year	One company approached the CRCA during the year	Three companies approached the CRCA during the year	Two companies approached the CRCA during the year
Commercialisation agreements	At least three agreements in place by year 7	No agreements in place at this early stage	No agreements in place at this early stage	No agreements in place at this stage	Two agreements are under negotiation
<b>COLLABORATIVE ARRANGEMENTS</b>					
Centre meetings	Annual symposium of all participants	The first CRCA retreat was held in Sydney in October 2000	The second CRCA retreat was held in Melbourne in November 2001	The third CRCA retreat was held in Sydney in December 2002	The fourth CRCA retreat was held in Wollongong in November 2003
Collaborative research	Involvement of more than one partner in more than 50% of the projects	Half the projects have involvement by more than one partner	60% of the projects have involvement by more than one partner	63% of the projects have involvement by more than one partner	63% of the projects have involvement by more than one partner
Management of geographically dispersed operations	Creative use of modern communication technologies	The CRCA website has been commissioned	The CRCA website has been commissioned and electronic newsletter has been distributed	The CRCA website has been enhanced and electronic newsletter has been distributed	CEO carried out regular site visits, inter-node visits are supported and electronic newsletter has been distributed
Increased support of partners	50% increase by existing and new participants by year 5	No increases at this early stage	No increases at this early stage	Three industry partners withdrew from the asthma therapeutic market and retired from the CRCA	No additional partners
Collaborative governance	Board attendance rates of over 80%	An attendance rate of 78% was achieved	An attendance rate of 75% was achieved	An attendance rate of 85% was achieved	An attendance rate of 87% was achieved

INDICATOR	OBJECTIVE	ACHIEVEMENT 2000/2001	ACHIEVEMENT 2001/2002	ACHIEVEMENT 2002/2003	ACHIEVEMENT 2003/2004
<b>EDUCATION AND TRAINING</b>					
Postgraduate students	Four students will initiate programs of study each year	Seven PhD Scholarships were granted in the 2001 academic year	Six PhD Scholarships were granted in the 2002 academic year	Five PhD Scholarships were granted in the 2003 academic year	Four PhD Scholarships were granted in the 2004 academic year
Teaching programs	Development of short courses	One short course was run	One short course was run	One educational seminar presented	One educational seminar presented
Masters program	Establishment of clinical research program by year 3	This program will not be developed due to the number of existing courses available	This program will not be developed due to the number of existing courses available	This program will not be developed due to the number of existing courses available	This program will not be developed due to the number of existing courses available
<b>MANAGEMENT</b>					
Governance	Establishment of core committees in first quarter of operation	All governance committees met regularly	All governance committees met regularly	All governance committees met regularly	All governance committees met regularly
Performance against budget	All programs operating within budgetary constraints	All programs are within budget	All programs are within budget	The CRCA delivered a financial surplus of \$35,000 for the 2002/03 financial year	The CRCA delivered a financial surplus of \$158,756 for the 2003/04 financial year
Project management	Timeliness against milestones	Project progress is monitored on a quarterly basis and 83% of projects have met milestone targets	Project progress is monitored on a quarterly basis and 81% of projects have met milestone targets	Project progress is monitored on a quarterly basis and 80% of projects have met milestone targets	Project progress is monitored on a quarterly basis and 80% of projects have met milestone targets
Planning	Business plan developed by year 2	Strategic and commercialisation plans have been developed	Strategic and commercialisation plans have been developed	Board review was carried out and the Strategic Plan has been revised	Business case for new CRCA developed

# Appendix

## APPENDIX

### PUBLICATIONS

#### Refereed Journal Articles

**Aggarwal S, Phelps S, Thompson PJ, Misso NLA.**

(2004) Leukotriene and prostaglandin production in asthma. *Clin Exp Allergy* 34:624-631.

**Aroni R, Sawyer S, Abramson M, Stewart K, Thien F, Goeman D, Douglass J.** (2003) Asthma self-management: what do we really mean? *Aust J Primary Health* 9:10-17.

**Aroni R, Goeman D, Stewart K, Thien F, Sawyer S, Abramson M, Douglass J.** (2004) Enhancing Validity: what counts as an asthma attack? *J Asthma* (in press).

**Beezhold DH, Hickey VL, Sutherland MF, O'Hehir RE.** (2004) The latex allergen Hev b5 is an antigen with repetitive murine B-cell epitopes. *Int Arch Allergy Immunol* (in press).

**Brown NJ, Thorpe CW, Thompson B, Berend N, Downie S, Verbanck S, Salome CM, King GG.** (2004) A comparison of two methods for measuring airway distensibility: nitrogen washout and the forced oscillation technique. *Physiologic Measurement* (in press).

**Chew YK, Reddel HK, Bosnic-Anticevich SZ, Chan HK.** (2004) Effect of mouthpiece washing on aerosol performance of CFC-free Ventolin™. *J Asthma* (in press).

**Chtanova T, Tangye SG, Newton R, Hodge MR, Rolph MS, Mackay CR.** (2004) T follicular helper cells (TFH) express a distinctive transcriptional profile, reflecting their role as non-Th1/Th2 effector cells that provide help for B cells. *J Immunol* 173(1):68-78.

**Collins RA, Sly PD, Turner DJ, Herbert C, Kumar RK.** (2003) Site of inflammation influences site of hyperresponsiveness in experimental asthma. *Respir Physiol Neurobiol* 139(1): 51-61.

**Colquhoun JR, Marks GB.** (2003) Thunderstorm related asthma in south-eastern Australia - Recent findings and asthma epidemic forecasting possibilities. *J Meteorology* 28: 350-354.

**De Meer G, Marks GB, Postma DS.** (2004) Direct or indirect stimuli for bronchial challenge testing: what is the relevance for asthma epidemiology. *Clin Exp Allergy* 34(1): 9-16.

**De Meer G, Toelle BG, Ng K, Tovey ER, Marks GB.**

(2004) Cat ownership before and after age 18 protects against atopy and asthma at age 28: Results of a long-term follow-up study. *J Allergy Clin Immunol* 113(3).

**De Silva HD, Gardner LM, Drew AC, Beezhold DH, Rolland JM, O'Hehir RE.** (2004) The hevein domain of the major latex glove allergen Hev b6 contains dominant T cell reactive sites. *Clin Exp Allergy* 34:1-8.

**Dobbin CJ, Miller J, van der Hoek R, Baker DF, Cumming RG, Marks GB.** (2004) The effects of age, death period and birth cohort on asthma mortality rates in Australia. *Int J Tuberculosis and Lung Disease* (in press).

**Douglass J, O'Hehir RE.** (2003) Emergency treatment of asthma: how are we doing? *Int Med J* 33: 401-403.

**Douglass J, Goeman D, Aroni R, Thien F, Abramson M, Stewart K, Sawyer SM.** (2004) Choosing to attend an asthma doctor: a qualitative study in adults attending emergency departments. *Family Practice* 21:166-172.

**Fogel-Petrovic M, Long JA, Knight DA, Thompson PJ, Upham JW.** (2004) Activated human dendritic cells express inducible cyclo-oxygenase and synthesize prostaglandin E2 but not prostaglandin D2. *Immunol Cell Biol* 82: 47-54.

**Gardner LM, O'Hehir RE, Rolland JM.** (2003) T cell targeted allergen derivatives for improved efficacy and safety of specific immunotherapy for allergic disease. *Curr Med Chem - Anti-Inflammatory and Anti-Allergy Agents* 2:351-365.

**Gardner LM, O'Hehir RE, Rolland JM.** (2004) High dose allergen stimulation of T cells from house dust mite-allergic subjects induces expansion of IFN- $\gamma$ <sup>+</sup> T cells, apoptosis of CD4+IL-4<sup>+</sup> T cells and T cell anergy. *Int Arch Allergy Immunol* 133:1-13.

**Gardner LM, Spyrogou L, O'Hehir RE, Rolland JM.** (2004) Increased allergen concentration enhances IFN- $\gamma$  production by allergic donor T cells expressing a peripheral tissue trafficking phenotype. *Allergy* (in press).

**Gardner LM, Thien F, Douglass JA, Rolland JM, O'Hehir RE.** (2004) Induction of T regulatory cells by standardised house dust mite immunotherapy: and

increase in CD4+CD25+IL-10+ T cells expressing peripheral tissue trafficking markers. *Clin Exp Allergy* (in press).

**Gibson PG, Powell H,** Coughlan J, Hensley MJ, Abramson M, Bauman A, Walters EH. (2003) Limited (information only) patient education programs for adults with asthma (Cochrane Review). In: *The Cochrane Library*, Issue 1, Oxford: Update Software.

**Gibson PG,** Ram FSF, **Powell H.** (2003) Asthma Education. *Respir Med.* 97:1036-44.

**Gibson PG, Simpson JL,** Hankin R, **Powell H,** Henry RL. (2003) Relationship between induced sputum eosinophils and the clinical pattern of childhood asthma. *Thorax.* 58:116-121.

**Gibson PG.** (2003) Eosinophilic bronchitis in cough, asthma and cough variant asthma. *Zensoku Asthma* 16:63-72.

**Gibson PG,** Henry RL, Shah S, **Powell H,** Wang H. (2003) Migration to a western country increases asthma symptoms but not eosinophilic airway inflammation. *Pediatric Pulmonol* 36:209-15.

**Gibson PG.** (2004) Cough is an Airway Itch. [Letter] *Am J Resp Crit Care Med* 169:1-2.

**Gibson PG.** (2004) Atopic cough: little evidence to support a new clinical entity. [Letter to the Editor] *Thorax* 59:449.

**Gibson PG.** (2004) Asthma Action Plans: Use it or lose it. *Primary Care Res J* 13:17-18.

**Gibson PG.** (2004) Commentary-Smokers and ex-smokers with chronic stable asthma did not respond to high dose oral corticosteroids. *Evidence Based Medicine* (in press).

**Gibson PG, Powell H.** (2004) Written action plans for asthma: an evidence-based review of the key components. *Thorax* 59:94-99.

**Gibson PG, Simpson JL.** (2004) Response to The European Network for Understanding Mechanisms of Severe Asthma Study (ENFUMOSA). [Letter to the Editor] *Eur Respir J* 23:492.

**Glaspole IN,** de Leon MP, **Rolland JM, O'Hehir RE.** (2004) Characterisation of the T cell epitopes of a

major peanut allergen Ara h 2. *Allergy* (in press).

**Goeman DP, Aroni R,** Stewart K, Sawyer SM, **Thien FCK,** Abramson MJ, **Douglass JA.** (2004) Back for more: a qualitative study of emergency department reattendance for asthma. *MJA* 180:113-117.

Hansbro PM, Beagley KW, Horvat JC, **Gibson PG.** (2004) Role of atypical bacterial infection of the lung in predisposition/protection of asthma. *Pharmacol Ther* 101:193-210.

**Hardy CL, Kenins L, Drew A, Rolland JM, O'Hehir RE.** (2003) Characterisation of a mouse model of allergy to a major occupational latex glove allergen Hev b5. *Am J Resp Crit Care Med* 167:1393-1399.

**Hardy CL, Rolland JM, O'Hehir RE.** (2004) Blocking antibodies in allergen immunotherapy: the Yin and Yang. *Clin Exp Allergy* 34:510-512.

Haque S, Boyce N, **Thien FC, O'Hehir RE, Douglass J.** (2003) Role of intravenous immunoglobulin in severe steroid-dependent asthma. *Intern Med J* 33:341-344.

Henry RL, **Gibson PG,** Vimpani GV, Francis JL, Hazell J. (2004) Randomised controlled trial of a teacher-led asthma education program. *Pediatric Pulmonol* (in press).

Hensley MJ, Chalmers A, Clover K, **Gibson PG,** Toneguzzi R, Lewis PR. (2003) Symptoms of asthma: comparison of a parent-completed retrospective questionnaire with a prospective daily symptom diary. *Pediatric Pulmonol* 36:509-513.

**Jenkins CR.** (2003) Formoterol as relief medication in asthma: the jury is still out. *Eur Respir J* 22:723-724.

**Jenkins CR.** (2003) An update on asthma management. *J Int Med* 33(8):365-371.

**Jenkins CR,** Costello J, Hodge L. (2004) Systematic review of prevalence of aspirin-induced asthma and its implications for clinical practice. *BMJ* 328:434-7.

**Jenkins CR.** (2004) Assessing bronchodilator reversibility: agreed standards are urgently needed. *MJA* 180:605-606.

**Kedda MA, Shi J, Duffy D, Phelps S, Yang I, O'Hara K, Fong K, Thompson PJ.** (2004) Characterisation of two polymorphisms in the LTC<sub>4</sub> synthase gene in an Australian population of mild, moderate and severe asthmatics. *J Allergy Clin Immunol* 113:889-95.

**King GG, Dame Carroll J, Müller NL, Whittall KP, Gao M, Nakano Y, Paré PD.** (2004) Heterogeneity of narrowing in normal and asthmatic airways measured by High-resolution CT. *Eur Resp J* 24(2) (in press).

**Lancsar E, Savage E.** (2004) Deriving welfare measures from discrete choice experiments: a response to Ryan and Santos Silva. *Health Economics* (in press).

Lee YCG, Lane KB, Zoia O, **Thompson PJ, Light RW, Blackwell TS.** (2003) Transforming Growth Factor Beta induces collagen synthesis without inducing IL-8 production in pleural mesothelial cells. *Eur Resp J* 22: 197-202.

Leuppi JD, Anderson SD, Brannan JD, **Reddel HK** et al. (2004) Questionnaire responses that predict airway response to hypertonic saline. *Respiration* (in press).

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**O'Hara KA, Kedda MA, Thompson PJ, Knight DA.** (2003) Oncostatin M: an interleukin -6-like cytokine relevant to airway remodelling and the pathogenesis of asthma. *Clin Exp Allergy* 33(8): 1026-32.

**Peat JK, Mhirshahi S, Kemp AS, Marks GB, Tovey ER, Webb K, Mellis CM, Leeder SR.** (2004) Three year outcomes of dietary fatty acid modification and house dust mite reduction in the Childhood Asthma Prevention Study (CAPS). *J Allergy Clin Immunol* (in press).

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- Weischelbaum ME, Sparrow MP, Hamilton E, **Thompson PJ**, Knight DA. (2003) Characterisation of pulmonary neuroendocrine cells in human airway epithelium by confocal microscopy. *Resp Physiol Neurobiol* (in press).

## PRESENTATIONS

### International Presentations

- Berend N.** Bangkok, Thailand, February 2004 - Invited Lecture - World Asthma Meeting
- Berend N.** Melbourne, February 2004 - Invited Lecture - GSK Landmark Meeting
- Douglass J.** Melbourne, February 2004 CRCA Symposium, IPCRG & Australian Asthma Conference "Achieving better adherence with recurrent A&E attendees: scenarios and solutions."
- Gibson PG.** London UK, November 2003 - Invited presentation - Cochrane Airways Group 2nd International Symposium "Management Plans - What are they for?"
- Gibson PG.** Canberra, August 2003 - Invited speaker - Landmark 2003 Symposium "New directions with combination therapy - initial maintenance therapy."
- Goeman D.** Melbourne, February 2004 CRCA Symposium, IPCRG & Australian Asthma Conference "Achieving better adherence with recurrent A&E attendees: scenarios and solutions."
- Jeffrey K.** New York, 2004 - Poster presentation - Cold Spring Harbour Laboratory meeting 'Gene Expression and Signalling in the immune system.' "Importance of Pac-1 phosphatase for inflammatory responses as demonstrated by gene expression profiling and Pac-1 deficient mice."
- Jeffrey K.** Cairns, October 2003 - Oral Presentation - 'Cytokines, Signalling and Diseases' Annual meeting of the International Society for Interferon and Cytokine Research (ISICR) "Critical Role for Pac-1 phosphatase in inflammatory disease."
- Jenkins CR.** Melbourne, February 2004 IPCRG Biennial Meeting, GlaxoSmithKline Satellite Symposium "Asthma Control in Australia."
- Jenkins CR.** Melbourne, February 2004 GlaxoSmithKline Landmark symposium "Translating the GOAL results into clinical practice : raising the bar on the playing field?"
- Liu S.** New Mexico, USA, March 2004 - Oral presentation - 'Mast cells in physiology, host defence and disease': Beyond IgE' Keystone Symposia "Discovery of novel inflammatory mast cell genes."
- Mackay C.** Cairns, Australia, October 2003 - Invited Speaker - Congress of the International Society for Interferon & Cytokine Research "The role of BAFF in B and T cell immune responses."
- Mackay C.** Helsinki, Finland, June 2004 - Invited Speaker - Sigrid Juselius Symposium on Cell adhesion and migration "The role of chemoattractant receptors in cell migration."
- Marks G.** Wellington, New Zealand, August 2003 - Invited Speaker - Symposium on infant cohort studies, Wellington School of Medicine "Childhood asthma prevention study."
- Marks G.** Kuala Lumpur, Malaysia, December 2003 - Invited Speaker - Ann J Woolcock Memorial Plenary Lecture at the 8th Asia Pacific Society for Respirology Congress "Public health approaches to the problems of asthma and COPD."
- O'Hehir RE.** Melbourne, Australia, February 2004 - Invited Workshop speaker - IPCRG "The usefulness of standard allergy testing."
- O'Hehir RE.** Vancouver, Canada, September 2003 World Allergy Organization Congress XVIII ICACI "Latex Allergy."
- Powell H.** London UK, November 2003 - Invited presentation - Cochrane Airways Symposium "Initial Inhaled Corticosteroids for asthma: a systematic review."
- Powell H.** Dunedin, April 2004 - Invited presentation - Department of Respiratory Medicine, Dunedin School of Medicine "Asthma control and exacerbations."
- Reddel H.** Vienna, September 2003 European Respiratory Society Annual Congress "Exacerbations vs uncontrolled disease: how do we define these?" Assembly Symposium on "Exacerbations - a major outcome in asthma and COPD."

**Reddel H.** Melbourne, February 2004 AstraZeneca symposium, IPCRG "Asthma management 2004 - how did we get to here?"

**Thien F.** Vancouver, Canada, September 2003 International Congress of Allergology and Clinical Immunology "Maternal breast milk long chain n-3 fatty acids are associated with increased risk of atopy in breast-fed infants."

**Thien F.** Vancouver, Canada, September 2003 International Congress of Allergology and Clinical Immunology "Fatty acid levels and risk of asthma in young adults."

## International Abstracts

**Brown NJ, Josefsson A, Salome CM, Thorpe CW, Berend N, King GG.** Measuring Airway Distensibility by the Forced Oscillation Technique. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 169(7): p. A246.

**Brown NJ, Salome CM, Thorpe CW, Unger G, King GG.** Tidal Fluctuations in Airway Caliber are Dependent on Breathing Rate in Healthy Adults. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 169(7): p. A246.

**King GG, Downie S, Verbanck S, Thorpe CW, Berend N, Salome CM.** (2004) Relationship between respiratory resistance and gas trapping in asthma before and after deep inspiration (DI). *Am J Respir Crit Care Med* 169(7):A249.

**King GG, Munoz PA, Thorpe CW, Berend N, Salome CM.** (2004) Mechanism of increased rate of airway re-narrowing following multiple deep inspirations. *Am J Respir Crit Care Med* 169(7):A246.

**King GG, Munoz PA, Thorpe CW, Berend N, Salome CM.** (2003) Multiple deep inspirations cause faster airway renarrowing after methacholine challenge. *Am J Respir Crit Care Med* 67(7):A183.

**Mihrshahi S, Peat JK, Marks GB, Kemp AS, Mellis CM, Tovey ER, Webb K, Leeder SR.** Primary prevention of allergic symptoms at age three in the

childhood asthma prevention study (CAPS). American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 2004;169(7):A722.

**O'Hara K.** Invited Poster. Cloning and Characterisation of the human Oncostatin M (OSM) receptor complex (OSMBR/gp130). The 6th World Congress on Inflammation. Vancouver, Canada, August 2003.

**Salome CM, Munoz PA, Thorpe CW, Berend N, King GG.** (2003) Unloading of airway smooth muscle causes faster airway narrowing and renarrowing. *Am J Respir Crit Care Med* 167(7):A183.

**Simpson JL, Timmins NL, Fakes K, Gibson PG.** Non-eosinophilic asthma - Definition and Reproducibility using Induced Sputum. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 167:A872.

**Sutherland A.** Poster. BAFF stimulates dendritic cell maturation and promotes Th1 type responses. Cytokines, Signalling and Diseases: the conference of the International Society for Interferon and Cytokine Research. Cairns, October 2003.

**Tovey ER, van Overveld AJP, O'Meara TJ, Marks GB.** Trend for asthma severity to be associated with total aeroallergen exposure. American Academy of Allergy and Immunology. *J Allergy Clin Immunol* 2004;113(2, Supplement 1):S231.

**Toelle BG, Ng K, Belousova E, Xuan W, Salome CM, Peat JK, Marks GB.** Among children with wheeze, the presence of AHR determines prognosis for asthma in adults. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 2004;169(7):A711.

**Toelle BG, Dunn SM, Marks GB.** Factors associated with non-adherence to prescribed medication. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 2004;169(7):A364.

**Toelle BG, Dunn SM, Marks GB.** Validated inhaler adherence scale. American Thoracic Society Annual Meeting, Orlando, USA, May 2004. *Am J Resp Crit Care Med* 2004;169(7):A325.

## National Presentations

**Chaplin MA.** Melbourne, November 2003 - Presentation - Health Services and Policy Research Conference Health Services Research Association of Australia and New Zealand "The economic burden of asthma from the perspective of the patient and the health care system: a prospective cohort study."

**Collins R.** August 2003 - Oral presentation - WA Branch Winter Meeting TSANZ "The acute phase of respiratory syncytial virus infection in mice."

**Crisafulli D.** Sydney, March 2004 - Oral presentation - TSANZ Conference "Effectiveness of an intervention to reduce house dust mite allergen in children's beds over three years."

**Douglass J.** Melbourne, February 2004 Australian Asthma Conference "Allergy: the latest."

**Gibson PG.** Melbourne, February 2004 - Invited speaker - Australian Asthma Conference "Looking to the future - evidence based education", "Current controversies."

**Gibson PG.** Sydney, March 2004 - Invited speaker - TSANZ Sydney 2004 ASM "Airway inflammation in chronic cough."

**Gibson PG.** Sydney, March 2004 - Invited speaker - TSANZ Sydney 2004 ASM "Airways disease - a hypothetical."

**Gibson PG.** Sydney, March 2004 - Invited speaker - TSANZ Sydney 2004 ASM "How to make literature findings relevant to clinical practice."

**Goeman D.** Melbourne, February 2004 Australian Asthma Conference "Why do people use emergency departments to manage asthma?"

**Goeman D.** Bendigo, May, 2004 Vic Asthma Health Education Association "Consumer Priorities for asthma care."

**Goeman D.** Melbourne, May 2004 - Invited speaker - Quality Use of asthma medicines workshop, Commonwealth Department of Health, Ageing & Pharm "Consumer Priorities for asthma care."

**Jenkins CR.** Sydney, July 2003 - Update and Education Day for General Practice - Asthma, COPD, respiratory and sleep disorders symposium "Better Diagnosis and Assessment of Asthma : traps and pitfalls."

**Jenkins CR.** Canberra, August 2003 National Asthma and Respiratory Educators Symposium "Australian Asthma Management."

**Jenkins CR.** Orange NSW, September 2003 NSW Health Clinical Frameworks for Chronic Respiratory Disease. Combined Rural Meeting "Setting Statewide Standards for Chronic Respiratory Care."

**Jenkins CR.** Sydney, February 2004 GlaxoSmithKline meeting for general practitioners "National Asthma Survey - implications for practice."

**Jenkins CR.** Sydney, March 2004 GSK Symposium, TSANZ "Bringing the Results of the Asthma in Australia and GOAL study Together."

**Jenkins CR.** Sydney, April 2004 Leadership Forum - Astra Zeneca Specialist and GP meeting "Highs and Lows: Current Aims of Asthma Treatment."

**Jenkins CR.** Melbourne, May 2004 PHARM and National Asthma Reference Group meeting "Quality use of Asthma Medicines."

**Lancsar EJ.** University of NSW Sydney, July 2003 Australasian Meeting of the Econometric Society "Using discrete choice experiments to investigate patient preferences for preventive asthma medication."

**Mackay C.** Centenary Institute, Sydney, May 2004 Australian Autoimmunity Meeting "PAC-1 facilitates mediator production and inflammatory responses."

**Marks G.** Melbourne, February 2004 - Invited Speaker - Keynote address. Australian Asthma Conference "The impact and burden of asthma."

**Munoz P.** Sydney, March 2004 - Oral presentation - ANZSRS Conference "The feasibility and utility for the measurement of respiratory system resistance in the Childhood Asthma Prevention Study."

**O'Hehir RE.** Sydney, April 2004 - Invited symposial Chair TSANZ "Asthma Control - Can We Expect More?"

**O'Hehir RE.** Melbourne, October 2003 - Invited Chair - Australasian Society for Clinical Immunology and Allergy "Mechanisms of SIT."

**O'Hehir RE.** Perth, December 2003 - Invited symposial Chair - ASI "Mucosal Immunology."

**Powell H. Sydney,** March 2004 - Invited presentation - TSANZ "Initial Inhaled Corticosteroids for asthma: a systematic review."

**Reddel H. Sydney,** July 2003 - Invited presentation - Asthma, COPD, Respiratory and Sleep Disorders 2003, Update & Education Day, University of New South Wales "Asthma exacerbations: management, self-management, and appropriate use of prednisolone."

**Reddel H.** Sydney, May 2004 - Invited presentation - Annual Scientific Conference of Royal Australasian College of Physicians "Asthma therapy: anti-inflammatory and  $\beta_2$ -agonist strategies."

**Brown NJ,** Josefsson A, **Salome CM,** **Thorpe CW,** **Berend N,** **King GG.** Measuring airway distensibility by the forced oscillation technique. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*; 9(Suppl 2): p. A32.

**Chandra A,** Jones A, Magnussen J, Yee B, Grunstein R, **King G.** Development of segmentation methods for pulmonary structure measurement in MR and HRCT data. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A65.

Correll PK, Williamson M, **Marks GB.** Asthma severity and the impact on quality of life. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A24.

**Crisafulli D,** **Mihrshahi S,** **Peat J,** **Tovey E,** **Marks G.** Effectiveness of an intervention to reduce house dust mite allergen in children's beds over three years. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A5.

## National Abstracts

**Aggarwal S,** **Misso N,** **Beard R,** **Blackwood M,** **Thompson P.** Measurement of eicosanoids, 8-isoprostane and nitrate in induced sputum of asthmatic patients and control subjects. TSANZ Annual Scientific Meeting, Sydney, March 2004.

**Ampon RD,** **Mihrshahi S,** **Peat JK,** **Marks GB.** Time to first diagnosis of asthma among the CAPS cohort. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A24.

**Ampon RD,** Williamson M, Poulos LM, **Marks GB.** The impact of asthma on quality of life. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*; 9(Suppl 2):A24.

**Belousova E,** **Toelle B,** **Ng K,** **Marks G.** Alternative definitions of current asthma: Belmont cohort. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A5.

**Dame-Carroll JR, Chandra A, Jones A, Berend N, Magnussen J, King G.** Airway lumen dimensions measured by micro-computed tomography (CT) and whole body-Ct. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl):A3.

**Davies J, Rolland J, O'Hehir R.** Bahia grass pollen is an important allergen in Australian patients with seasonal rhinitis and fails to show cross-reactivity with other clinically important grasses. Australasian Society of Clinical Immunology and Allergy, Melbourne, October 2003.

**Davies JM, Bright ML, Rolland JM, O'Hehir RE.** IgE reactivity with Bahia grass pollen in patients with seasonal rhinitis; no cross-reactivity with other grasses. Australian Society of Immunology, Perth, December 2003.

**Davies JM, O'Hehir RE.** VH gene usage in IgE responses of seasonal rhinitis patients allergic to grass pollen is oligoclonal and antigen-driven. Australia Society of Immunology, Perth, December 2003.

**de Meer G, Ng K, Toelle B, Marks GB.** Relation between change in asthma prevalence and use of preventer medications. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* ;9(Suppl 2):A30.

**Diba C, King GG, Downie S, Brown NJ, Berend N, Salome CM.** Respiratory conductance (Grs) better predicts improved exercise after bronchodilator in COPD than spirometry. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl 2): p. A6.

**Dixon C.** Identification of the proteins involved in the onset and development of airways hyperresponsiveness (AHR) in allergic mice. Inaugural National Institute of Biosciences Postgraduate Symposium. Canberra, December 2003.

**Downie S, Verbanck S, Unger G, King G, Salome C, Berend N.** Detection of small and large airway heterogeneity in asthma by the multiple breath

nitrogen washout test. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl 2):A31.

**Drew A, Kenins L, de Silva H, Suphiolgu C, Rolland J, O'Hehir R.** Hypoallergenic mutant of the major latex glove allergen Hev b6. Australasian Society of Clinical Immunology and Allergy, Melbourne, October 2003.

**Gardner L, O'Hehir R, Rolland J.** Stimulation of atopic donor PBMC with high allergen concentrations promotes the expansion of CD4+IFN $\gamma$  + T cells expressing surface markers for peripheral tissue trafficking. Australasian Society of Clinical Immunology and Allergy, Melbourne, October 2003.

**Gardner LM, Thien FC, Douglass JA, Rolland JM, O'Hehir RE.** House dust mite immunotherapy increases IL-10+ T cells with a peripheral tissue trafficking phenotype. Australasian Society of Immunology, Perth, December 2003.

**Glaspole I, de Leon M, Rolland J, O'Hehir R.** Cross-reactivity within the cellular immune response to peanut and hazelnut among nut allergic subjects. Australasian Society of Clinical Immunology and Allergy, Melbourne, October 2003.

**Marks G, Crisafulli D, Davis S, Criss S, Mahrshahi S, Peat J, Britton W.** T cell cytokine responses to house dust mite (HDM) stimulation in vitro: Relation to HDM avoidance and to HDM sensitisation at age 3 years. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A21.

**Mahrshahi S, Marks GB, Kemp AS, Ampon MR, Peat JK.** Risk factors for wheeze at 3 years of age. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* ;9(Suppl 2):A20.

**Munoz P, King GG, Mahrshahi S, Ng K, Marks GB.** (2004) Effect of preventive interventions on respiratory system resistance in the childhood asthma prevention study. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl 2): p. A30.

**O'Hara K.** Invited Poster. Cloning and Characterisation of the human Oncostatin M receptor [OSMBR/gp130]. TSANZ Annual Scientific Meeting, Sydney, March 2004.

Poulos L, **Xuan W, Ampon RD,** Williamson M, **Marks GB.** Access to spirometry in less accessible and remote areas of Australia. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* ;9(Suppl 2):A64.

**Reddel H, Salome CM, Desai M, Thien FK, Jenkins CR.** Change in perception of airway obstruction is associated with change in FEV1 and airway hyper-responsiveness. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl 2):A28.

**Salome C, Munoz P, Thorpe CW, Berend N, King GG.** Increased rate of airway re-narrowing following multiple deep inspirations. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* 9(Suppl 2): p. A33.

**Salome C, Ng K, Toelle B, Belousova E, Marks G.** Exhaled nitric oxide as a predictor of asthma - a 5 years follow up. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A30.

**Shum B,** Frost MJ, Wong A, **Mackay CR, Rolph MS.** A novel role for fatty acid binding proteins in asthma. Australasian Society for Immunology, Perth, December 2003.

**Simpson JL,** Timmins NL, Smart J, **Gibson PG.** Proteolytic enzyme activation in Neutrophilic asthma. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*.

**Toelle BG, Ng K, Belousova E, Xuan W, Salom CM, Peat JK, Marks GB.** Prognosis of childhood asthma in later life. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A5.

**Toelle BG,** Dunn SM, **Marks GB.** Factors associated with asthma practical knowledge. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology* ;9(Suppl 2):A19.

Vally H, **Misso N, Aggarwal S, Thompson P.** Changes in bronchial hyperresponsiveness and urinary eicosanoids following wine challenge in wine-sensitive asthmatic patients. TSANZ Annual Scientific Meeting, Sydney, March 2004.

Ware S, Yates D, **Marks G, Toelle B, Belousova E, Ng K,** Johnson A. Prevalence of self-reported asthma and respiratory symptoms among middle aged and older adults in New South Wales. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A54.

**Xuan W, Toelle BG, Ng K, Belousova E, Marks GB.** Asthma in childhood and lung function decline in adulthood. TSANZ Annual Scientific Meeting, Sydney, March 2004. *Respirology*;9(Suppl 2):A28.

**Yu E, Goeman D,** Abramson M, **Douglass J.** The asthma 3+ visit plan. Australian Asthma Conference, Melbourne, February 2004.

# STAFF GRANTS

Researchers	Organisation	Project title	Source	Period	\$
J Hall D Fiebig J Louviere P Apps R Viney	CHERE	Individual decision making, welfare measurements and policy evaluation in the health sector: A microeconomic approach	NHMRC	2003-2007	\$6,825,000
C Mackay F Mackay In Collaboration with Centenary Institute	Garvan Institute	Cellular and molecular studies of the adaptive immune response in health and disease	NHMRC Program Grant	2002-2007	\$630,000
P Gibson E Walters R Wood-Baker B Smith	John Hunter Hospital	Australian Based Cochrane Collaboration Review Activities	Commonwealth Department of Health and Aged Care	2001-2003	\$71,000
P Gibson M Boyle M Hensley P Jones D Shafren	John Hunter Hospital	Virus induced asthma: mechanisms and management	NHMRC	2003	\$130,000
PG Gibson ML Grag LG Wood	John Hunter Hospital	Oxidative stress, isoprostanes, and antioxidant defences in asthma	Asthma Foundation of NSW	2003	\$50,000
PG Gibson ML Grag LG Wood	John Hunter Hospital	8-iso-PGF $\alpha$ and asthma exacerbations	John Hunter Charitable Trust	2003	\$20,000
PG Gibson	John Hunter Hospital	Equipment Grant	University of Newcastle	2003	\$37,000
PG Gibson M Boyle R Scott	John Hunter Hospital	Non-eosinophilic asthma: mechanisms and treatments	NHMRC Project Grant	2003-2005	\$145,000
PG Gibson EH Walters R Wood-Baker B Smith	John Hunter Hospital	Australian Based Cochrane Collaboration Review Activities	Commonwealth Department of Health and Aged Care	2003-2005	\$78,800pa
PG Gibson DR Shafren MJ Hensley	John Hunter Hospital	Characteristics and mechanisms of persistent asthma after common cold virus infection	NHMRC	2004-2006	\$400,250
J Douglass D Goeman	Monash University	A qualitative study of individuals who recurrently attend emergency departments with asthma and an evaluation of the 3+ asthma visit plan when used by recurrent accident and emergency department attendees	The Asthma Innovation Grant from the Commonwealth Department of Health and Ageing	2003	\$49,000

Researchers	Organisation	Project title	Source	Period	\$
DJ Philips CL Hardy RE O'Hehir	Monash University	Loss of activin expression in allergen-induced airway inflammation	Monash Small Grants	2003	\$20,000
RE O'Hehir J Davies	Monash University	Immunoglobulin epsilon VH gene usage and cross reactivity in allergic disease	Monash University Research Fellowship	2002-2003	\$56,000
RE O'Hehir C Suphioglu JM Rolland	Monash University	Couch grass allergy: cellular and molecular studies directed at improved specific immunotherapy	NHMRC	2002-2004	\$405,000
M Hibbs G Anderson RE O'Hehir	Monash University	Couch grass allergy: cellular and molecular studies directed at improved specific immunotherapy.	NHMRC	2003-2005	\$360,000
RE O'Hehir C Stockley	Monash University	The identification and measurement of potential allergens in wine	Grape and wine research and Development Corporation Grant	2002-2004	\$270,000
RE O'Hehir JM Rolland JA Douglass F Thien	Monash University	Allergy to medications: understanding the mechanisms and better diagnostic tests.	The Harold Michell Foundation	2003-2005	\$270,000
RE O'Hehir	Monash University	Allergy to medications	Grant-In-Aid The Benjamin Slome Charitable Foundation	2003-2007	\$100,000
RE O'Hehir G Anderson J Hamilton JM Rolland	Monash University	The interface between innate and adaptive immunity in allergy and asthma	NHMRC Program	2005-2009	\$4,408,220
JK Peat GB Marks CM Mellis SR Leeder	University of Sydney	The Childhood Asthma Prevention Study	NHMRC Project Grant	2004	\$150,000
PJ Thompson DA Knight	UWA		Medical Health Research Infrastructure Council Round 6	2003	\$150,000
DA Knight PJ Thompson	UWA	Integrin – growth factor interactions in the development of airway wall remodelling	NHMRC Project Grant	2003-2005	\$354,000
PJ Thompson NL Misso KD Bhoola	UWA	The regulatory role of the kallikrein-kinin cascade in neutrophils and eosinophils in asthma	Sir Charles Gairdner Hospital Research Fund	2004	\$10,000

Researchers	Organisation	Project title	Source	Period	\$
PJ Thompson P Foster S Hogan K Matthaei I Young	UWA	Molecular mechanisms in the regulation of allergy and inflammation	NHMRC Program Grant	2003-2007	\$4,870,000
G King C Salome	Woolcock Institute of Medical Research	Abnormal smooth muscle behaviour in asthma: toward an <i>in vivo</i> test	NHMRC	2001-2003	\$65,000
GG King J Magnussen	Woolcock University of Sydney	Airway wall thickness and heterogeneity are key determinants of asthmatic airway function	NHMRC	2001-2003	\$69,000
GG King CM Salome	Woolcock University of Sydney	Abnormal airway smooth muscle behaviour in asthma toward an <i>in vivo</i> test	NHMRC	2001-2003	\$180,000
N Berend G King C Salome	Woolcock	Nitrogen analyser for multiple Breath Nitrogen Washouts	Clive and Vera Ramaciotti Foundation Equipment Grant	2002-2003	\$180,000
H Reddel	Woolcock Institute of Medical Research	The role of $\beta_2$ -receptor dysfunction in viral asthma exacerbations	Ann J Woolcock Research Fellowship (competitive), founded by Asthma NSW	2002-2004	\$100,000

# *Financial Statement*

## FINANCIAL STATEMENT

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# Directors

## DIRECTORS

### **Dr Arthur Emmett, MB, BS**

Dr Emmett, the Chairman of the Board, has over thirty years of experience in the pharmaceutical industry. For seven years from 1971 he was Medical Director of the Australian Affiliates of G.D. Searle, Parke Davis and W.S. Merrell. Dr Emmett spent the next 20 years with Ciba Geigy Pharmaceuticals where he held a variety of senior roles responsible for business strategy and development. In 1989 he was appointed Senior Vice-President, Medical and Public Affairs based in the US and in 1994 he was appointed President and Vice-Chairman of the Board of Beijing Ciba Geigy Pharma Ltd. Dr Emmett is currently Chairman of Metabolic Pharmaceuticals Ltd.

### **Dr Emery Severin, BSc (Hons), D.Phil**

Dr Severin is President of Boral Industries Inc in the USA. Prior to this he was the Executive General Manager at Boral, Australian Construction Materials. Dr Severin received the UNSW Medal for Chemistry and went on to become a Rhodes Scholar for South Australia in 1978.

### **Mr Philip Bert, BSc (Hons), MBA**

Mr Bert, the Chief Executive Officer, has over twenty years experience in the medical devices and pharmaceutical industry. Before taking up his present position he was the Managing Director of Australian Hearing for six years. Prior to this he held a number of senior management positions at Kendall Australasia and Baxter Healthcare both in Australia and overseas. Mr Bert is a board member of the Cooperative Research Centres Association Inc.

### **Professor Michael Berndt, PhD, BSc (Hons)**

Professor Berndt is currently a NHMRC Senior Principal Research Fellow, a Professorial Fellow in the Department of Biochemistry & Molecular Biology at Monash University and Associate Dean (Research) for the Faculty of Medicine at Monash University. He has received numerous national and international research awards including the Glaxo-Wellcome Medal in 1996, and serves on several editorial boards.

### **Professor David Burke, AO, MD, DSc, FAA, FTSE, FRACP**

Professor Burke is currently Dean of Research & Development, College of Health Sciences at the University of Sydney. Before taking up his present position, he was Professor of Neurology at University of New South Wales, Director of the Institute of Neurological Sciences at the Prince Henry and Prince of Wales Hospitals, and Director of Clinical Research at the Prince of Wales Medical Research Institute. In 1995 he was elected Fellow of both the Australian Academy of Science (FAA) and the Australian Academy of Technological Sciences and Engineering (FTSE), and in 1999 he was appointed Officer in the Order of Australia (AO). He is currently President of the Australian Association of Neurologists (2004-2007).

### **Mr Martin Hoffman, BEc, MBA, MFinance**

Mr Hoffman is the Chief Executive Officer at Ninemsn Ltd. He previously held senior roles with John Fairfax Holdings and the Garvan Institute of Medical Research. He is a director of Aza Research Pty Ltd and director and honorary treasurer of the Garvan Institute of Medical Research.

### **Professor Lou Landau, AO, MD, FRACP**

Professor Landau is a Paediatric Respiratory Physician and has worked at the Royal Children's Hospital in Melbourne and the UWA Department of Paediatrics at Princess Margaret Hospital for Children in Perth where he was Professor of Paediatrics. He has been Executive Dean of the Faculty of Medicine and Dentistry since 1996. He has been Chairman of the Telethon Institute for Child Health Research and the WA Institute for Medical Research. He has served on committees of the NHMRC and The Australian Medical Council. He was awarded the Order of Australia for his contribution to paediatrics and respiratory medicine in 1996.

### **Mr Mervyn Michell**

Mr Michell is the former General Manager and Director Pharmaceutical Division of Bayer Australia. He was responsible for the strategic management and direction of the pharmaceutical business within Australasia.

### **Ms Julie Nutting, BPharm, MSc, MBA**

Ms Nutting is currently CEO and a director of Psiron Ltd and a non-executive director of Analytica Ltd. She has both private and public sector experience in the pharmaceutical and health care industry taking projects through clinical study to registration, reimbursement and commercialisation. Her technical background includes primarily regulatory affairs and health economics.

### **Professor Nick Saunders, MD, FRACP, FRCP(C)**

Professor Saunders is currently the Vice-Chancellor and President of the University of Newcastle. He served as Dean of Medicine, Nursing and Health Sciences at Monash University from 1998 to 2003. Professor Saunders has been involved in many national and state advisory committees and councils, including the NHMRC (Chair 2000-2003), Australian Research Council and the Prime Minister's Science Engineering and Innovation Council.

# Directors' Report

## DIRECTORS' REPORT

The Directors of CRC for Asthma Ltd submit herewith the annual financial report for the financial year ended 30 June 2004. In order to comply with the provisions of the Corporations Act 2001, the Directors report as follows:

The names and particulars of the Directors of the Company during or since the end of the financial year are:

### Name

Dr Emery Severin, Chairman	Resigned 08-07-04
Dr Arthur Emmett	Existing Director, appointed Chairman 05-08-04
Mr Philip Bert, Chief Executive Officer	
Mr Martin Hoffman	Resigned 16-02-04
Professor Lou Landau	
Ms Julie Nutting	
Professor Nicholas Saunders	Resigned 19-08-03
Mr Mervyn Michell	
Professor David Burke	
Professor Michael Berndt	Appointed 03-08-04

### Principal Activities

The Company is a limited by guarantee company which commenced operations on 1 October, 1999 with the principal objective of operating as a non-profit scientific institution to create a centre of excellence in the areas of asthma research, education and training.

### Review of Operations

The activities of the Company for the period ended 30 June 2004 were in establishing and promoting cooperative research and educational programmes focusing on asthma prevention, treatment and diagnosis, in order to reduce the burden of asthma on the Australian community.

### Operating Results

The operating surplus for the year ended 30 June 2004 was \$158,756 and the total equity at year end was \$320,506.

### Dividends

Under the terms of the Company's constitution it is not entitled to pay dividends.

### **Changes in State of Affairs**

During the financial year there was no significant change in the state of affairs of the Company other than that referred to in the financial statements or notes thereto.

### **Subsequent Events**

There has not been any matter or circumstance, other than that referred to in the financial statements or notes thereto, that has arisen since the end of the financial year, that has significantly affected, or may significantly affect, the operations of the Company, the results of those operations, or the state of affairs of the Company in future financial years.

### **Future Developments**

Disclosure of information regarding likely developments in the operations of the Company in future financial years and the expected results of those operations is likely to result in unreasonable prejudice to the Company. Accordingly, this information has not been disclosed in this report.

### **Indemnification of Officers and Auditors**

During the financial year, the Company paid a premium in respect of a contract insuring the Directors of the Company (as named above), the Company Secretary, Paul Breeze, and all executive officers of the Company and of any related body corporate against a liability incurred as such a Director, Secretary or executive officer to the extent permitted by the Corporations Act 2001. The contract of insurance prohibits disclosure of the nature of the liability and the amount of the premium.

The Company has not otherwise, during or since the financial year, indemnified or agreed to indemnify an officer or auditor of the Company or of any related body corporate against a liability incurred as such an officer or auditor.

# Directors' Meetings

## DIRECTORS' MEETINGS

The following table sets out the number of Directors' meetings (including meetings of committees of Directors) held during the financial year and the number of meetings attended by each Director (while they were a Director or committee member). During the financial year, 4 Board meetings and 1 Remuneration Committee meeting were held.

Directors	Board of Directors		Remuneration Committee	
	Eligible to attend	Attended	Eligible to attend	Attended
Dr Emery Severin	4	4	1	1
Mr Philip Bert	4	4		
Professor David Burke	4	3		
Dr Arthur Emmett	4	3	1	1
Mr Martin Hoffman	2	2		
Professor Lou Landau	4	4		
Mr Mervyn Michell	4	3	1	0
Ms Julie Nutting	4	4		
Professor Nicholas Saunders	1	0		

### Director's Interest in Contracts

No contracts involving Director's interest were entered into during the year or existed at the end of the year.

Signed in accordance with a resolution of the Directors made pursuant to s.298(2) of the Corporations Act 2001.

On behalf of the Directors



P. Bert  
Director



A. Emmett  
Director

SYDNEY, 22 September 2004

# Audit Report

## INDEPENDENT AUDIT REPORT

**To the members of CRC for Asthma Ltd**

### **Scope**

#### *The financial report and directors' responsibility*

The financial report comprises the statement of financial position, statement of financial performance, statement of cash flows, accompanying notes to the financial statements, and the directors' declaration for CRC for Asthma Ltd, for the financial year ended 30 June 2004 as set out on pages 59 to 71.

The directors of the company are responsible for the preparation and true and fair presentation of the financial report in accordance with the Corporations Act 2001. This includes responsibility for the maintenance of adequate accounting records and internal controls that are designed to prevent and detect fraud and error, and for the accounting policies and accounting estimates inherent in the financial report.

#### *Audit approach*

We have conducted an independent audit of the financial report in order to express an opinion on it to the members of the company. Our audit has been conducted in accordance with Australian Auditing Standards to provide reasonable assurance whether the financial report is free of material misstatement. The nature of an audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal controls, and the availability of persuasive rather than conclusive evidence. Therefore, an audit cannot guarantee that all material misstatements have been detected.

We performed procedures to form an opinion whether, in all material respects, the financial report is presented fairly in accordance with the Corporations Act 2001 and Accounting Standards and other mandatory professional reporting requirements in Australia so as to present a view which is consistent with our understanding of the company's financial position, and performance as represented by the results of its operations and its cash flows.

Our procedures included examination, on a test basis, of evidence supporting the amounts and other disclosures in the financial report, and the evaluation of accounting policies and significant accounting estimates made by the directors.

While we considered the effectiveness of management's internal controls over financial reporting when determining the nature and extent of our procedures, our audit was not designed to provide assurance on internal controls.

The audit opinion expressed in this report has been formed on the above basis.

#### *Independence*

In conducting our audit, we followed applicable independence requirements of Australian professional ethical pronouncements and the Corporations Act 2001.

*Audit Opinion*

In our opinion, the financial report of CRC for Asthma Ltd is in accordance with:

(a) the Corporations Act 2001, including:

(i) giving a true and fair view of the company's financial position as at 30 June 2004 and of its performance for the year ended on that date; and

(ii) complying with Accounting Standards in Australia and the Corporations Regulations 2001; and

(b) other mandatory professional reporting requirements in Australia.

**DELOITTE TOUCHE TOHMATSU**



.....  
Julia Bickerstaff

Partner

Chartered Accountants

SYDNEY, 28 September 2004

The liability of Deloitte Touche Tohmatsu, is limited by, and to the extent of, the Accountants' Scheme under the Professional Standards Act 1994 (NSW).

# Declaration

## DIRECTORS' DECLARATION

The Directors declare that:

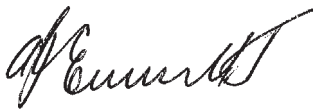
- a) the attached financial statements and notes thereto comply with Accounting Standards;
- b) the attached financial statements and notes thereto give a true and fair view of the financial position and performance of the Company;
- c) in the Directors' opinion, the attached financial statements and notes thereto are in accordance with the Corporations Act 2001; and
- d) in the Directors' opinion, there are reasonable grounds to believe that the Company will be able to pay its debts as and when they become due and payable.

Signed in accordance with a resolution of the directors made pursuant to s.295(5) of the Corporations Act 2001.

On behalf of the Directors



.....  
P. Bert  
Director



.....  
A. Emmett  
Director

SYDNEY, 22 September 2004

# Statement

## STATEMENT OF FINANCIAL PERFORMANCE

FOR THE FINANCIAL YEAR ENDED 30 JUNE 2004

	Note	2004	2003
		\$	\$
Contributions from ordinary activities	2a,b	6,166,506	6,335,743
Depreciation and amortisation expense	2c	(38,113)	(36,007)
Other expenses from ordinary activities	2c	(5,969,637)	(6,263,343)
<b>Profit From Ordinary Activities</b>		<u>158,756</u>	<u>36,393</u>
<b>Net Profit</b>		<u>158,756</u>	<u>36,393</u>
<b>Total Changes in Equity Other than those Resulting from Transactions with Owners as Owners</b>		<u>158,756</u>	<u>36,393</u>

Notes to the financial statements are included on pages 63 to 71.

# Statement

## STATEMENT OF FINANCIAL POSITION

AS AT 30 JUNE 2004

	Note	2004	2003
		\$	\$
<b>Current Assets</b>			
Cash		1,167,532	1,079,663
Receivables		32,975	27,500
Goods and services tax receivable		8,778	11,267
Prepayments		-	1,737
<b>Total Current Assets</b>		<b>1,209,285</b>	<b>1,120,167</b>
<b>Non-Current Assets</b>			
Property, plant and and equipment	6	21,436	54,906
<b>Total Non-Current Assets</b>		<b>21,436</b>	<b>54,906</b>
<b>Total Assets</b>		<b>1,230,721</b>	<b>1,175,073</b>
<b>Current Liabilities</b>			
Payables	7	767,901	838,606
Provisions	8	40,117	29,814
Other	9	102,197	144,903
<b>Total Current Liabilities</b>		<b>910,215</b>	<b>1,013,323</b>
<b>Total Liabilities</b>		<b>910,215</b>	<b>1,013,323</b>
<b>Net Assets</b>		<b>320,506</b>	<b>161,750</b>
<b>Equity</b>			
Retained profits	12	320,506	161,750
<b>Total Equity</b>		<b>320,506</b>	<b>161,750</b>

Notes to the financial statements are included on pages 63 to 71.

# Statement

## STATEMENT OF CASH FLOWS

FOR THE FINANCIAL YEAR ENDED 30 JUNE 2004

		Inflows (Outflows)
Note	2004	2003
	\$	\$
<b>Cash Flows From Operating Activities</b>		
Receipts from partners	3,233,176	3,286,800
Payments to suppliers and employees	(3,207,431)	(3,135,455)
Interest and other revenue received	66,767	43,641
Net cash provided by operating activities	15 (b) 92,512	194,986
<b>Cash Flows From Investing Activities</b>		
Payment for property, plant and equipment	(4,643)	(24,271)
Net cash (used in) investing activities	(4,643)	(24,271)
<b>Cash Flows From Financing Activities</b>		
Net cash provided by/(used in) financing activities	-	-
<b>Net Increase In Cash Held</b>	87,869	170,715
<b>Cash At The Beginning Of The Financial Year</b>	1,079,663	908,948
<b>Cash At The End Of The Financial Year</b>	15 (a) 1,167,532	1,079,663

Notes to the financial statements are included on pages 63 to 71.

# Notes

## NOTES TO FINANCIAL STATEMENTS

FOR THE FINANCIAL YEAR ENDED 30 JUNE 2004

### 1. SUMMARY OF ACCOUNTING POLICIES

#### Financial Reporting Framework

The financial report is a general purpose financial report, which has been prepared in accordance with the Corporations Act 2001, applicable Accounting Standards and Urgent Issues Group Consensus Views, and complies with other requirements of the Act.

The financial report has been prepared on the basis of historical cost and except where stated, does not take into account changing money values or current valuations of non-current assets. Cost is based on the fair values of the consideration given in exchange for assets.

#### Significant Accounting Policies

Accounting policies are selected and applied in a manner which ensures that the resulting financial information satisfies the concepts of relevance and reliability, thereby ensuring that the substance of the underlying transactions or other events is reported.

The following significant accounting policies have been adopted in the preparation and presentation of the financial report:

##### a) Accounts Payable

Trade payables and other accounts payable are recognised when the company becomes obliged to make future payments resulting from the purchase of goods and services.

##### b) Acquisition of Assets

Assets acquired are recorded at the cost of acquisition, being the purchase consideration determined as at the date of acquisition plus costs incidental to the acquisition.

In the event that settlement of all or part of the cash consideration given in the acquisition of an asset is deferred, the fair value of the purchase consideration is determined by discounting the amounts payable in the future to their present value as at the date of acquisition.

##### c) Depreciation

Depreciation is provided on property, plant and equipment, including freehold buildings but excluding land and investment properties. Depreciation is calculated on a straight-line basis so as to write off the net cost or other revalued amount of each asset over its expected useful life. Individual items less than \$2,500 are not capitalised. The following estimated useful lives are used in the calculation of depreciation:

Computer equipment	2 years
Laboratory equipment	5 years
Furniture and fittings	7 years

#### **d) Employee Entitlements**

Provision is made for benefits accruing to employees in respect of wages and salaries and annual leave when it is probable that settlement will be required and they are capable of being measured reliably.

Provisions made in respect of wages and salaries, and annual leave expected to be settled within 12 months are measured at their nominal values using the remuneration rate expected to apply at the time of settlement.

Superannuation contributions to employee funds are charged as expenses as the contributions become payable.

#### **e) Goods and Services Tax**

Revenues, expenses and assets are recognised net of the amount of goods and services tax (GST), except:

- where the amount of GST incurred is not recoverable from the taxation authority, it is recognised as part of the cost of acquisition of an asset or as part of an item of expense; or
- for receivables and payables which are recognised inclusive of GST.

Cash flows are included in the statement of cash flows on a gross basis. The GST component of cash flows arising from investing and financing activities which is recoverable from, or payable to, the taxation authority is classified as operating cash flows.

The net amount of GST recoverable from, or payable to, the taxation authority is included as part of receivables or payables.

#### **f) Income Tax**

The Company is exempt from income tax under Item 50-B of the Income Tax Act 1997, as a non-profit charitable institution.

#### **g) Intellectual Property**

The Company expenses all costs associated with intellectual property in the year incurred. No intellectual property is capitalised in the balance sheet. In the 2003/4 year \$64,374 was incurred in IP costs and this amount is included under "Commercialisation".

## **h) Receivables**

Trade receivables and other receivables are recorded at amounts due less any allowance for doubtful debts.

## **i) Recoverable Amount of Non-Current Assets**

Non-current assets are written down to recoverable amount where the carrying value of any non-current asset exceeds recoverable amount. In determining the recoverable amount of non-current assets, the expected net cash flows have not been discounted to their present value.

## **j) Revenue Recognition**

### **Cash Contributions**

Cash contributions from the Commonwealth Government and Partners of the Company during the financial year represent the cash component of annual contributions in accordance with the Joint Venture Agreement.

### **In-Kind Contributions**

In-kind contributions from Partners are brought to account as revenue received and expenditure incurred. In-kind contributions have been valued on the basis of pre-agreed formulae as defined in the Commonwealth Agreement.

## **k) Impacts of adopting the Australian equivalents to International Financial Reporting Standards**

The first financial report to be prepared by the Company in accordance with the Australian equivalents to International Financial Reporting Standards ("A-IFRS") will be the financial report for the year ending 30 June 2006. As a result, the opening statement of financial position of the Company as at 1 July 2004 will be restated so that all transactions and balances are recognised and measured in accordance with A-IFRS. Transitional adjustments will be reflected either as a reclassification of items in the statement of financial position, or an adjustment of opening retained earnings.

The directors have reviewed the effects of the adoption of A-IFRS and due to the size of the Company and the nature of its operations believe that they will be able to transition smoothly to A-IFRS when required and have begun to plan this process. The Company has not identified any significant areas of differences affecting the consolidated entity on adoption of A-IFRS. Some differences may not yet have been identified, and further analysis may change the Company's assessment of the importance or otherwise of the various differences.

	2004	2003
	\$	\$
<b>2. Profit from Ordinary Activities</b>		
<b>a) Operating Revenue</b>		
Contribution revenue:		
Contributions from government and partners, cash	2,972,030	2,883,000
Contributions from partners, in-kind	3,127,709	3,409,102
	<u>6,099,739</u>	<u>6,292,102</u>
Other	8,495	-
	<u>6,108,234</u>	<u>6,292,102</u>
<b>b) Non-Operating Revenue</b>		
Interest Revenue	58,272	43,641
	<u>6,166,506</u>	<u>6,335,743</u>
<b>c) Expenses</b>		
Cash Expenditure		
Research	1,996,333	2,103,784
Administration	433,408	429,334
Commercialisation	159,413	145,471
Education	222,799	175,652
In-Kind Expenditure		
Research	2,556,972	2,971,587
Administration	423,985	257,406
Commercialisation	42,861	14,516
Education	133,866	165,592
	<u>5,969,637</u>	<u>6,263,343</u>
Depreciation of non-current assets:		
Property, plant and equipment	38,113	36,007

### 3. Directors' Remuneration

The directors of CRC for Asthma Ltd during the year were:

Dr Emery Severin	(Non-Executive)
Mr Philip Bert	(Chief Executive Officer)
Professor David Burke	(Non-Executive)
Dr Arthur Emmett	(Non-Executive)
Mr Martin Hoffman	(Non-Executive)
Professor Lou Landau	(Non-Executive)
Mr Mervyn Michell	(Non-Executive)
Ms Julie Nutting	(Non-Executive)
Professor Nicholas Saunders	(Non-Executive)

	2004 \$	2003 \$
The aggregate of income paid or payable, or otherwise made available, in respect of the financial year, to all directors of the Company, directly or indirectly, by the Company or by any related party	226,260	208,518

Non-executive directors have received no remuneration.

	2004 No.	2003 No.
The number of directors of the Company whose total income falls within each successive \$10,000 band of income (commencing at \$0)		
\$0 - \$9,999	8	8
\$200,000 - \$209,999	-	1
\$210,000 - \$219,999	-	-
\$220,000 - \$229,999	1	-

	2004 \$	2003 \$
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### 4. Directors' Retirement Benefits

Aggregate retirement benefits paid to all directors of the Company, by the Company or by any related party

20,070	16,732
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	2004 \$	2003 \$
<b>5. Remuneration of Auditors</b>		
<b>a) Auditor of the Company</b>		
Auditing the financial report	13,000	12,000
Other services	-	-
	<u>13,000</u>	<u>12,000</u>

## 6. Property, Plant and Equipment

	Plant and Equipment \$	Total \$
<b>Gross Carrying Amount at Cost</b>		
Balance at 30 June 2003	159,810	159,810
Additions	4,643	4,643
Balance at 30 June 2004	<u>164,453</u>	<u>164,453</u>
<b>Accumulated Depreciation</b>		
Balance at 30 June 2003	104,904	104,904
Depreciation expense	38,113	38,113
Balance at 30 June 2004	<u>143,017</u>	<u>143,017</u>
<b>Net Book Value</b>		
As at 30 June 2003	54,906	54,906
As at 30 June 2004	<u>21,436</u>	<u>21,436</u>
	<b>2004</b>	<b>2003</b>
	<b>\$</b>	<b>\$</b>

Aggregate depreciation allocated, whether recognised as an expense or capitalised as part of the carrying amount of other assets during the year:

Plant and equipment	38,113	36,007
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	2004 \$	2003 \$
<b>7. Current Payables</b>		
Trade payables	128,289	256,590
Accrued expenses (mainly relating to outstanding research expenses)	639,612	582,016
	<u>767,901</u>	<u>838,606</u>
<b>8. Current Provisions</b>		
Employee entitlements (note 10)	40,117	29,814
<b>9. Other Current Liabilities</b>		
Income Received in Advance	102,197	144,903

#### 10. Employee Entitlements

The aggregate employee entitlement liability recognised and included in the financial statements is as follows:

Employee entitlements: Current (note 8)	40,117	29,814
---	--------	--------

	2004 No.	2003 No.
Number of employees at end of financial year	<u>5</u>	<u>5</u>

#### 11. Members' Guarantee

##### Contributed Equity

The Company is a Company limited by guarantee. If the Company is wound up, the Corporations Act 2001 and the Constitution state that each member severally guarantees the liability of the Company up to \$100 per member.

	2004 \$	2003 \$
<b>12. Retained Profits</b>		
Balance at beginning of financial year	161,750	125,357
Net Profit	158,756	36,393
Balance at end of financial year	<u>320,506</u>	<u>161,750</u>

### 13. Segment Information

The activities of the Company for the year ended 30 June 2004 were in establishing and promoting cooperative research and educational programs focusing on asthma prevention, treatment and diagnosis, in order to reduce the burden of asthma on the Australian community. The directors consider this to be one business segment and all activity takes place within Australia.

### 14. Related Party Disclosures

#### a) Directors' Remuneration and Retirement Benefits

Details of directors' remuneration and retirement benefits are disclosed in notes 3 and 4 to the financial statements.

### 15. Notes to the Statement of Cash Flows

	2004	2003
	\$	\$
<b>(a) Reconciliation of Cash</b>		
For the purposes of the statement of cash flows, cash includes cash on hand and in banks and in term deposits. Cash at the end of the financial year as shown in the statement of cash flows is reconciled to the related items in the statement of financial position as follows:		
Cash assets	1,167,532	1,079,663
	<u>1,167,532</u>	<u>1,079,663</u>
<b>(b) Reconciliation of Profit From Ordinary Activities to Net Cash Flows From Operating Activities</b>		
Profit from ordinary activities	158,756	36,393
Depreciation and amortisation of non-current assets	38,114	36,007
Changes in net assets and liabilities		
(Increase)/decrease in assets/liabilities:		
Current assets	(3,738)	4,369
Current liabilities	(100,620)	118,217
Net cash from operating activities	<u>92,512</u>	<u>194,986</u>

## **16. Financial Instruments**

### **a) Significant Accounting Policies**

Details of the significant accounting policies and methods adopted, including the criteria for recognition, the basis of measurement and the basis on which revenues and expenses are recognised, in respect of each class of financial asset, financial liability and equity instrument are disclosed in note 1 to the financial statements.

### **b) Interest Rate Risk**

The only interest bearing financial assets are cash and term deposits at an average interest rate of 4.8% (2003: 4.3%). All other financial assets and liabilities are non-interest bearing.

### **c) Credit Risk**

Credit risk refers to the risk that a counterparty will default on its contractual obligations resulting in financial loss to the company. The company has adopted the policy of only dealing with creditworthy counterparties and obtaining sufficient collateral or other security where appropriate, as a means of mitigating the risk of financial loss from defaults. The company measures credit risk on a fair value basis.

The Company does not have any significant credit risk exposure to any single counterparty or any group of counterparties having similar characteristics.

## **17. Additional Company Information**

CRC for Asthma Ltd is a public Company limited by guarantee, incorporated and operating in Australia.

### **PRINCIPAL REGISTERED OFFICE**

CRC FOR ASTHMA LTD  
Level 6, Medical Foundation Building  
92 Parramatta Road,  
Camperdown, New South Wales 2050  
Australia

### **PRINCIPAL PLACE OF BUSINESS**

CRC FOR ASTHMA LTD  
Level 6, Medical Foundation Building  
92 Parramatta Road,  
Camperdown, New South Wales 2050  
Australia









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CRC for Asthma Limited

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