

Research Activities

The Department of Immunology is internationally renowned for its combined expertise in research, teaching and service delivery in immunology and immunopathology. There are extensive research programs in basic and translational immunology, including highly successful collaborations with The Alfred and other AMREP partners.

The department's research activities target diseases including allergy, asthma, autoimmunity, inflammation, diabetes, organ fibrosis, cancer and malaria. The department also focuses on engineering novel treatments such as nanoparticle-based vaccines in cancer and infection, as well as therapeutic proteins and monoclonal antibodies. Researchers are funded by NHMRC, ARC, Cooperative Research Centre and other research grants and have a strong publication output, patent portfolio and biotech activity. In 2010, 13 NHMRC grants were awarded to Department of Immunology researchers.

The department has extended its research activities at the Clayton campus establishing an effective link between basic science and translation/clinical trials at The Alfred. The department also regularly organises scientific retreats to promote scientific integration and spearhead new collaborations within the department.

Current Projects

Allergy, Immunology and Respiratory Medicine Professor Jennifer Rolland and Professor Robyn O'Hehir (AIRmed, The Alfred)

Clinical trials and *in vitro* studies are used to investigate mechanisms of allergen immunotherapy and optimal strategies for down regulation of the adverse T-cell response to allergens in allergic individuals.

Research highlights

- *Peanut allergy peptide immunotherapy development*: Identification of the dominant T cell epitopes of the major peanut allergen Ara h 2. Published in the *Journal of Allergy and Clinical Immunology* (Prickett *et al.* 2010). Continued funding from the Ilhan Food Allergy Foundation and successful NHMRC Project Grant 2011-2013 on 'Human CD4+ T-cell epitope-based therapeutic for peanut allergy'.
- *Grass pollen allergy peptide immunotherapy development*: Incorporation of a panel of grass pollen allergen T cell epitope-based peptides identified by this group into an immunotherapy product entering phase II clinical trial by Circassia Ltd. Mapping of T cell epitopes of the major Bahia grass pollen allergen, Pas n 1, funded by the CRC for Asthma and Airways.
- *Follistatin therapy for cystic fibrosis and other lung inflammatory disorders*: Proof-of-concept studies funded by the CASS Foundation show potential for follistatin to inhibit airway inflammation in cystic fibrosis using a murine model.
- *Nanoparticles inhibit allergic airway inflammation*: Optimal particle size and chemistry determined for nanoparticles that induce lung resistance to airway inflammation. Continued funding by the CRC for Asthma and Airways and an NHMRC Project Grant 2011-2013.

Autoimmune Diseases

Associate Professor Frank Alderuccio

Research centres on processes associated with the autoimmune response and loss of immunological tolerance, with the aim of devising strategies to prevent or reverse autoimmunity. Experimental models of autoimmunity are used to explore the potential of gene therapy strategies aimed at treating these diseases.

- Use of haematopoietic stem cell manipulation to induce immunological tolerance
- Understanding and utilising expression of AIRE for tolerance induction in autoimmunity
- The use of corticosteroids in strategies aimed at promoting disease remission
- Role of regulatory T-cells in experimental models of autoimmunity
- Induction of tissue specific antigen expression using retroviral vectors

Diabetic Retinopathy

Professor Jennifer Wilkinson-Berka

The contribution of vasoactive and growth factor systems to the development of diabetic microvascular complications is studied. Goals are to develop new, safe and effective treatment regimens for patients with diabetic retinopathy, providing a major advance over current invasive therapies such as laser treatment.

- The role of the prorenin receptor in ischemic and diabetic retinopathy
- Aldosterone and angiotensin II: are they conspirators in diabetic retinopathy?
- Pathogenic associations between the microvasculature, glia and neurons in ischemic and diabetic retinopathy
- Do interactions between glyoxalase I and angiotensin contribute to pericyte and endothelial cell death in diabetic retinopathy?

Autoimmune Diabetes

Associate Professor Robyn Slattery

The Autoimmune Diabetes Group is focused on understanding the immunopathogenesis of Type 1 diabetes (T1D). The primary interest of the team is in elucidating the role of β 2M and MHC class I in directing the autoimmune response in diabetes. This is crucial for our understanding of how to regulate the disease in predisposed individuals. Using a sophisticated genetic engineering tool called 'cre/lox', we have been able to track the development of cytotoxic T lymphocytes (CTL) from the time they first become activated to attack the beta cells, until the beta cells are destroyed, insulin production is lost, and diabetes develops. Current projects are focused on:

- The role of β 2M and MHC class I on pancreatic ductal cells in the development of autoreactive CTL
- The role of β 2M and MHC class I on B lymphocytes during the expansion of autoreactive CTL

The Autoimmune Diabetes team identified an important mechanism by which B lymphocytes contribute to the pathogenesis of Type 1 diabetes. Our finding demonstrates a crucial role for the CD19 molecule on B lymphocytes in the expansion of pathogenic CD8 T cells.

Molecular Signalling

Head: Associate Professor Jun-Ping Liu

Studies of the mechanisms regulating the maintenance of telomeres (chromosome ends) in health and disease:

- Cancer inhibition by targeting telomerase using peptide inhibitors
- Cancer inhibition by GAPDH signalling to telomeres
- Cancer inhibition by cytokine signalling to telomeres
- Immune senescence and the roles of telomere maintenance
- Studies of trace metal homeostasis in health and disease
- The roles of ATP13A2 P-type ATPase transporter in lysosomal homeostasis and neurodegenerative diseases

Leucocyte Membrane Protein

Associate Professor Mark Wright

The Leucocyte Membrane Protein Laboratory is fascinated by the role of tetraspanin cell surface proteins in the immune system. Tetraspanins play a vital role in the molecular organisation of the cell surface. Our analyses of tetraspanin deficient mice show a key role for these molecules in all aspects of immunity including pathogen recognition, antibody production, inflammation and cellular immunity. Key tetraspanins studied include CD37, TSSC6, CD82 and CD53.

Research highlights

- *CD37 is important for plasma cell survival:* Collaborative studies have shown that CD37-deficient mice make poor IgG responses to model antigens. This poor humoral immunity is caused by a failure to establish an adequate population of long lived plasma cells. Found evidence that a functional regulation of a4b1 integrin underlies this phenotype.
- *Functional co-operation between tetraspanins CD37 and TSSC6 in adaptive cellular immunity:* Analyses of mice lacking both CD37 and TSSC6 shows that these tetraspanins functionally co-operate to regulate both T cell proliferation and antigen presentation. Published in the *Journal of Immunology* (Garltan *et al.* 2010).
- *A key role for CD37 in cellular immunity and dendritic cell migration:* CD37-deficient mice make poor T cell responses to tumour antigens. This poor cellular immunity is caused by deficient migration of CD37-deficient dendritic cells from the periphery to draining lymph nodes.
- *CD37 is necessary for neutrophil inflammation:* Collaborative studies have shown an important role for CD37 in mediating adhesion between neutrophils and inflamed vascular endothelium.



Leukocyte Signalling

Associate Professor Margaret Hibbs

The Leukocyte Signalling Laboratory studies signalling pathways that play a role in immune system development and function. This group is primarily interested in regulation of the development of immunity and understanding the processes that are perturbed when autoimmunity and inflammatory diseases develop.

Allergy research nurse, Karen Symons, performs a skin prick test.

The group is also interested in understanding the regulation of blood cell development, and believe that it will lead to a greater understanding of the signals that go awry in the development of blood cell cancers. Another major interest is understanding the mechanisms underlying chronic inflammatory lung disease and they aim to identify key pathways or targets for therapeutic intervention.

Vaccines and Infectious Diseases

Professor Magdalena Plebanski

This group is investigating the development of novel vaccines against cancer and infectious diseases as well as immunoregulation (immune evasion and immune suppression).

- Development of malaria and cancer vaccines using a novel nanovaccine technology
- Investigation into the effect of nanoparticles on dendritic cells and other immune cells
- Nanoparticle induction of lung resistance to allergy and inflammation
- Understanding immunosuppression in malaria and cancer by studying changes in dendritic cells and regulatory T-cells (Tregs)
- Study of altered peptide ligand-mediated regulation of T-cell activity and the use of peptide superagonists to enhance malaria vaccine efficacy
- Discovery and validation of new surface markers to distinguish Th1, Th2 and Treg subsets and their use to monitor diverse infectious diseases and cancer

B-cells, BAFF and Autoimmunity

Professor Fabienne Mackay

BAFF is a cytokine from the tumour necrosis factor family that is essential for B-cell development and survival. BAFF production drives autoimmunity and is linked to many autoimmune conditions in humans. The BAFF gene was cloned by Professor Mackay in 1999 and her laboratory was the first to publish a role for BAFF in systemic lupus erythematosus (SLE). In 2009, the BAFF inhibitor belimumab showed efficacy in SLE clinical trials and on 9 March 2011, belimumab was approved by the FDA as a new treatment for lupus, the first new treatment in over 50 years.

- Investigation of the cooperation between BAFF and the innate immune system
- Studies on the role of BAFF in immunoregulation and immune tolerance
- Studies on the role of BAFF in human diseases
- Investigating new forms of autoimmune processes independent of T-cells
- Development of a chemokine receptor inhibitor for the treatment of fibrosis
- Studies of novel microRNAs involved in regulation of BAFF and its receptors in cancer and autoimmunity
- Investigations into the complex interaction between the gut microbiota and immune cell function
- Studies on the role of BAFF in regulating telomeric function and its role in immunosenescence

Postgraduate Students

30 PhD Students
1 Masters Student

Publications

53 Journal Articles