QIMR is one of Australia’s only fully integrated biomedical research and development centres
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QIMR: YOUR DEVELOPMENT PARTNER

QIMR is one of Australia’s largest and most successful medical research institutes. Our 600 full time researchers, visiting scientists and students are investigating the genetic and environmental causes of nearly 40 diseases as well as developing new diagnostics, better treatments, and prevention strategies such as vaccines.

The Institute offers a wealth of partnership, collaborative and commercial opportunities for industry and governments. Coupled with a diverse and comprehensive research program is our capacity to translate basic research from the discovery phase through development, scale-up and manufacture, to Phase I and II clinical trials.

We have strategic alliances with research institutes, hospitals, universities, not-for-profits and commercial partners, including Australian and international biotechnology and pharmaceutical companies. In particular, QIMR is interested in commercial partnerships to further early stage technologies which have the potential to rapidly develop into successful technologies.

Opportunities include:

- Collaborative and contract research
- Development and manufacture of novel therapeutics
- Clinical trials
- Consulting
- Technology licences
- Start-up companies
- Business partnerships

QIMR has world class research facilities and laboratories including:

- The Drug Discovery Group
- The Queensland Protein Discovery Centre
- The Australian Centre for Vaccine Development

QIMR has the capability and resources to carry out product development, including:

- Research models and cell banks
- State-of-the-art technologies and equipment
- Scientists with commercial experience

Q-Gen is a cGMP manufacturing facility that offers clean room facilities, state-of-the-art equipment, experienced service and support.

Q-Pharm Pty Ltd conducts Phase I and II clinical trials, pharmacokinetic studies, bioequivalence studies, and drug analysis.
RESEARCH PROGRAMS

QIMR is expanding our understanding, diagnosis and treatment of some of the world’s most devastating diseases

QIMR’s research programs range from identifying the environmental risks and genetic basis of cancers as well as new therapeutics; to developing better diagnostics and vaccines for infectious diseases; to trialling biological controls for mosquitoes to reduce the incidence of debilitating diseases such as malaria and dengue fever.

The Institute takes a multi-faceted approach to medical research. We have a strong international reputation for our investigations into disease genetics and epigenetics, immunology, epidemiology, cellular function and infection. Our use of immunotherapy, vaccines, protein and drug discovery to develop new diagnostics and better treatments is widely respected by the medical community and industry.

Facilities:

- Genomics research
- Microarray and mass array analysis
- Transgenic and gene knockout mice
- Cancer and infectious disease mouse models
- Confocal and laser dissection microscopy
- FACS and cell sorting facilities
- PC2 animal facilities
- Good Laboratory Practice capabilities

Key research areas:

- Oncology
- Vaccines
- Drug development
- Infectious disease
- Genetics
- Mental health
- Indigenous health
Cancer is the second leading cause of Australian deaths. At QIMR, we are committed to understanding how and why cancers develop. Our researchers are extensively investigating the causes of more than 13 cancers, including skin, prostate, colorectal, breast, ovarian, lung cancer and lymphoma.

We are also actively developing better diagnostics, novel targeted drugs, vaccines and immunotherapies. These treatments have the potential to increase survival rates as well as reducing the side-effects of anti-cancer therapies.

**Cancer immunotherapy**
Dr Chris Schmidt, Professor Kay Ellem, Associate Professor Alejandro López

QIMR is a leader in developing, optimising and applying immunologically-based therapies for solid cancers. Our researchers have been working with dendritic cells (DC) and studying the relationship between clinical outcome and immune response to therapy. Clinical trials have been undertaken using these non-invasive therapies against melanoma, advanced prostate cancer and brain tumours. It is expected that they will eventually become an approved treatment for advanced-stage cancer.

Research focus:
- The function of DC in breast cancer patients and a novel DC-based immunotherapy
- Loading DC with tumour antigens
- Evaluating the antigen presentation pathways used by DC
- Identifying target antigens and measuring the immune response
- Manufacture and validation of cancer cell lines

**SKIN CANCER**

Skin cancer is the most common cancer in Australia and the most expensive to treat. One Australian is diagnosed with skin cancer every 90 seconds with more than $200 million spent annually on treatment.

**Melanoma and skin cancer**
Professor Nick Hayward, Professor Peter Parsons, Dr Graeme Walker

Research focus:
- Screening tumour suppressor genes and oncogenes for mutations
- Drug screening and development
- Candidate tumour marker expression
- Defining genetic and environmental skin cancer risk factors
- Improving solar protection
- Investigating the effect of ultraviolet radiation (UVR) on skin cells and its association with primary cancer
- Assessing whether different histological types of melanoma have different patterns of mutation and/or expression of tumour suppressor genes and oncogenes
- Understanding the role of pigmentation genes in melanoma genesis
- Melanocyte stem cells response to DNA damage
- Non cell-autonomous effects in melanocyte response to stress, and melanoma
- What are the critical UVR wavelengths and DNA adducts in melanoma genesis?
- Developing more relevant melanoma mouse models

Unique resource:
- Access to melanoma patients with from the Queensland Cancer Registry.
- Part of the International Melanoma Genetics Consortium (GenoMel)
- Mouse melanoma models
BREAST & OVARIAN CANCER

Breast and ovarian cancer
Professor Georgia Chenevix-Trench

Breast cancer is the most common cancer in women, affecting one in 14 Australian women. Ovarian cancer is less common but has a poor prognosis due to late detection, with 750 Australian women dying each year.

Research focus:
1. Understanding breast and ovarian cancer risk factors
2. Understanding cancer development from normal precursor cells
3. Identifying new breast cancer predisposition genes
4. Identifying low penetrance breast cancer susceptibility genes and modifier genes for BRCA1 and BRCA2
5. Evaluating the importance of molecular markers for breast cancer prognosis
6. Identifying low penetrance susceptibility genes in molecular subtypes of ovarian adenocarcinoma
7. Analysing the downstream effects of somatic mutations in ovarian cancer
8. Using molecular pathology to sub-classify breast cancer into more biologically meaningful diagnostic categories
9. Furthering our understanding of the multi-step model of breast carcinogenesis

Unique resource:
A mouse model for the breast cancer-associated mutation in ATM, 7271T>G
Involvement with kConFaB (page 21)
QIMR breast cancer database for assessing predictive and prognostic markers.

Breast cancer/signal transduction
Dr Kum Kum Khanna

Dr Khanna’s group is interested in understanding cellular responses to DNA damage. Deficiencies in the ability of cells to sense and repair damage leads to neurodegeneration, immune deficiency, infertility and aging. This area is also of critical importance to cancer research. The pathway controlling the DNA damage response are involved in tumour suppression and are believed to be mutated at the early stage in the evolution of cancer. Several genes involved in the DNA damage response pathways such as ATM, BRCA1, BRCA2, CHK2 and p53 contribute to breast cancers.

Research focus:
1. Characterising novel proteins directly involved in sensing and repair of DNA damage as well as being involved in tumourgenesis
2. Developing mouse models for novel proteins implicated cancer progression

Unique resource:
Tools and reagents to validate DNA damage repair proteins as possible therapeutic targets in cancer

For further information on breast, ovarian and endometrial cancer research, please refer to pages 16 and 17.
BLOOD CANCERS

Leukaemias, lymphomas and myeloma are haematological or blood cancers. Annually, approximately 9500 Australians are diagnosed with a blood cancer, with lymphomas the fifth most common cancer and leukaemia the second most common cause of child mortality.

Leukaemia
Professor Andrew Boyd

The Leukaemia Foundation laboratory is exploring the biology of leukaemia and other blood cancers through studies of leukaemia-associated proteins.

Research focus:
• Understanding the function of Eph and Ephrin membrane proteins in cancer
• Looking at how antibodies which target Eph proteins and soluble forms of their Ephrin ligands can be used to target tumours and inhibit tumour growth
• Studying the structural basis of the Eph-ephrin interaction to shed light on the outcomes of Eph-ephrin signalling
• Studying the adhesion protein, Fat, to determine how it contributes to leukaemia and related cancers
• Devising therapies which attack cancer cells by targeting the Fat protein

Bone marrow transplantation
Professor Geoff Hill

Allogeneic bone marrow transplantation remains the procedure of choice for curing several haematological malignancies, such as leukaemia and lymphoma as well as severe immunodeficiencies. The procedure results in cure rates up to 80% but is limited by serious complications such as graft-versus-host-disease (GVHD).

Research focus:
• The immunological effects of new growth factors to mobilise stem cells
• Graft-versus-leukaemia and GVHD
• The pathophysiology of acute GVHD
• The effect of B cells on transplantation tolerance
• The effect of donor antigen presenting cells on GVHD and transplant tolerance

Hodgkin’s lymphoma
(and nasopharyngeal carcinoma)
Professor Denis Moss and Associate Professor Rajiv Khanna

Epstein-Barr virus (EBV) causes glandular fever and is associated with several cancers including lymphoma, nasopharyngeal carcinoma (NPC) and Hodgkin’s lymphoma (HL). Our researchers are investigating the biology, immunology and molecular biology of EBV and its disease state interactions. Most recently we have been working with clinicians to conduct immunotherapy trial for NPC.

Research focus:
• Designing recombinant vaccines and immunotherapies to treat EBV associated cancers
• Strategies to enhance the immune response to EBV proteins in NPC and HL
• Understanding EBV infection control
• Investigating EBV cancer instigation
• Determining EBV’s role in several autoimmune diseases

Unique resource:
QIMR holds four patents in the area of EBV and NPC vaccines

COLORECTAL & PROSTATE CANCERS

Colorectal cancer
Professor Barbara Leggett

Colorectal cancer continues to be one of the most common internal malignancies occurring in developed countries. In Australia, one in 23 people will develop the cancer, with half not surviving beyond five years.

Research focus:
• Identifying and understanding the genetic changes underlying different subtypes of colorectal cancer
• Identifying tumour subgroups with similar methylation defects using microarray-based profiling
• Identifying molecular markers for tumour subgroups
• Exploring the functional role of oncogenic mutations using a conditional mouse model

Unique resource:
Large tissue bank (page 21)

Prostate cancer
Professor Martin Lavin

Prostate cancer is the most common cancer in Australian men. Annually 20,000 men are diagnosed and close to 3300 die from the cancer. However, many men who develop the cancer have no symptoms, undergo no therapy, and eventually die of other causes. Many factors, including genetics and diet, have been implicated in the development of prostate cancer.

Research focus:
• Identifying genes as markers
• Developing new approaches to early detection

For further colorectal cancer research, please refer to page 16,18,22. For more on prostate cancer research, see page 6,9,16.
OTHER CANCERS

Ataxia-Telangiectasia
Professor Martin Lavin

Ataxia-Telangiectasia (A-T) can increase infection and cancer susceptibility. A-T patients are sensitive to radiation; exhibit a progressive loss of brain function; and have an elevated risk of developing cancers including leukaemia and lymphoma. A mouse model to mimic this disease has been developed, with cancer susceptibility in the human disease confirmed.

Research focus:
- A-T mouse models
- Relationship between A-T and other genetic instability syndromes
- Role of ATM in DNA damage recognition and radiation signal transduction
- Identification of functional domains on the ATM protein and interacting proteins
- Mutation analysis to study the function of ATM and its role in breast cancer
- Role of ATM in the stress response and effect on neuronal function
- Clinical radio-sensitivity

Endocrine cancers
Professor Nick Hayward

The endocrine system consists of hormone secreting endocrine glands such as the pituitary, thyroid, adrenal, pancreatic and adrenal glands. Cancers of these organs usually result in excessive hormone secretion. Examples include adrenocortical carcinoma, thyroid cancer and Cushing’s syndrome.

Research focus:
- Identifying novel endocrine cancer genes
- Investigating how key oncogene defects are associated with endocrine cancer predisposition or development
- Key approaches include genome-wide linkage analysis, candidate gene mutation screening, gene expression profiling and the use of transgenic or knockout mice

ONCOLOGY MARKERS

New targets are available in the areas of melanoma, prostate and breast cancer diagnostics and prognostics. Some recent examples of QIMR markers are listed below.

BIXP – breast cancer marker: a novel endogenous protein that binds to the breast cancer susceptibility protein, BRCA1 and blocks its function. Over-expression of BIXP leads to marked suppression of tumour cell growth and apoptosis. This novel protein shows potential for the diagnosis and treatment of breast and ovarian cancer.

hVSM1 – tumour marker: a cancer/testis antigen, hVSM1 is a novel human protein involved in DNA repair and protein trafficking in other species. Novel drugs that modulate this target might be useful for the detection and treatment of a variety of tumours.

Cep55 – cancer marker: a centrosome protein also required for the successful completion of cytokinesis in mammalian cells. Abnormal expression of centrosome proteins has been linked to different stages of cancer progression, particularly high cytological grade. Novel drugs that modulate this target might be of use in the detection and treatment of cancer tumours.

Other cancer research at QIMR includes head and neck page 10, oesophageal page 17,22 and pancreatic page 18.
Developing new pharmaceutical therapeutics is integral to many of QIMR’s research programs. Several of our lead compounds with the potential to prevent or treat cancers and infectious diseases are being developed under licence by pharmaceutical companies for clinical trial.

**Drug Discovery Group**
Professor Peter Parsons

Basic and translational research is conducted on novel therapies for human cancer. The group has extensive commercial experience, with research contracts including, preclinical development; compound efficacy in *in vitro* and *in vivo* tumour models; mechanism of action studies; and developing a process for the GMP manufacture of a drug now in Phase II clinical trials.

Commercial services:
- Generating and interpreting pharmacogenomic profiles for anticancer agents
- Functional genomics
- Bioactivity-guided purification of natural products
- Library screening using human tumour and normal cell types including genetically modified cell lines
- Mouse models for *in vivo* validation

Research focus:
- Genetic role in the acute response to solar UVR and progressing melanoma
- Discovering prognostic and progression markers in head and neck and ovarian cancer
- Discovery and pre-clinical development of natural products active against human cancers in collaboration with EcoBiotics

**Australian Centre for Vaccine Development (ACVD)**
Associate Professor Rajiv Khanna

The ACVD is developing novel technology platforms and formulating the next generation of vaccines. Research is focussed on infectious diseases and human cancers, including: malaria, Epstein-Barr virus, Hodgkin’s lymphoma, nasopharyngeal carcinoma, human cytomegalovirus, Group A Streptococcus, hookworm, schistosomiasis, leishmaniasis, and scabies. The Centre has collaborative links with Australian and international institutions as well as the biotech industry.

Available expertise:
- *Ex vivo* analysis of human and mouse immune response
- Preclinical models for infectious diseases and cancer
- Bioinformatics and T cell epitope mapping
- Production of preclinical/clinical grade immunotherapies
- Expression and production of recombinant proteins and monoclonal antibodies
- Clinical immune monitoring for vaccine studies
- Phase I, II and III clinical trial design

Collaborators:
- Emory Vaccine Centre
- Sabin Vaccine Institute
- National Institute of Allergy and Infectious Diseases
- Centre for Vaccine Development, University of Maryland
- Johns Hopkins University School of Medicine
- La Jolla Institute for Allergy and Immunology
- Leiden University Medical Centre
- Monash University
- University of Melbourne
- Peter McCallum Cancer Institute
- The Walter & Eliza Hall Institute of Medical Research
The team aims to discover the identity of proteins involved in and/or affected by physiological and disease processes as well as the ways in which these proteins function and interact. Their work has the potential to produce important leads for developing therapeutic agents to treat viral infections – particularly for important childhood diseases – and other important medical conditions.

The Centre is equipped with the latest high-performance mass spectrometers and a range of ancillary equipment required for protein chemistry and proteomics.

Commercial services:
- Access to mass spectrometry infrastructure and expertise
- Mapping protein networks and pathways in cells
- Characterising the proteomes of organisms and organelles
- Edman degradation-based sequencing

Research focus:
- Interactions and structures of proteins in assembled virus particles particularly from the Paramyxoviridae family (mumps, measles, parainfluenza viruses, respiratory syncytial virus and Newcastle disease)
- Interactions of viral proteins with host cell proteins during infection and assembly
- Regulation of signal-activated transcription factors by post-translational modifications and protein-protein interactions
- Characterising proteins secreted by parasitic organisms
QIMR is investigating a range of diseases and parasites which infect and kill millions of people each year.

Our research addresses viral illnesses including HIV and Epstein-Barr; parasite-borne diseases such as malaria, dengue fever and schistosomiasis; as well as bacterial pathogens such as Group A Streptococcus (GAS) – all causes of extensive illness and death globally. The World Health Organisation has recognised QIMR’s work controlling mosquito-transmitted viruses such as Ross River, Japanese encephalitis and dengue.

In addition, we are also studying human parasites such as Giardia, Trichomonas, scabies, hookworms and schistosome blood flukes. Hookworms alone infect more than half a billion people in developing countries.

PARASITES

Echinococcosis (hydatidosis)
Professor Don McManus

Hydatid disease, caused by dog tapeworm parasites of the genus Echinococcus, is a significant cosmopolitan disease. QIMR scientists have recently completed extensive immunogenetic and epidemiological surveys of hydatid disease in several areas of China. They plan to sequence the Echinococcus genome to source of new genetic markers as well as undertake transcriptome studies to determine how the Echinococcus organisms differentiate. Their aim is to find an ‘Achilles heel’ to target for vaccine and drug development.

Research focus:
• Developing new diagnostic methods for human hydatid disease
• Developing a vaccine effective against the adult stage of Echinococcus in the dog definitive host
• Immunogenetic studies of human hydatid disease
• Microarray and transcriptome analysis to study differentiation and developmental processes in Echinococcus organisms

Helminth infections
Dr Alex Loukas

The molecular basis of host-parasite interactions is being investigated with an emphasis on parasitic helminths such as hookworms.

Research focus:
• Hookworm developmental biology and immunology
• Identifying parasite proteins and evaluating their efficacy as vaccine candidates
• Identifying parasite proteins and developing novel anti-inflammatory therapies for autoimmune disorders
• Targets for the prevention and treatment of hookworm
• The molecular basis of cholangiocarcinoma induction by the human liver fluke, Opisthorchis viverrini

Giardia and other anaerobic protozoa
Associate Professor Peter Upcroft

Metronidazole is the drug conventionally used to treat pathogenic protozoa including, Giardia, Trichomonas and Entamoebas. QIMR researchers have found the basic enzymatic mechanisms of drug resistance by these protozoa. This discovery will allow targeted drug design.

Research focus:
• Synthesising and assaying novel anti-parasitic drugs which are active against metronidazole-resistant parasites
• Creating the first model for human giardiasis, by infecting mice with a virulent Giardia strain isolated from sulphur-crested cockatoos
• Giardia targets for immunological and host/parasite studies
PARASITE-BORNE DISEASES

**Leishmania**
Dr Christian Engwerda

Visceral leishmaniasis is a potentially fatal disease caused by the intracellular protozoan parasites *Leishmania donovani* and *L. infantum* (chagasi). They infect mature tissue macrophages throughout the viscera, with the spleen and liver major disease sites.

Research focus:
- Identifying immune mechanisms for controlling leishmania infection and generating long-term immunity
- Distinguishing protective host immune infection responses from those that cause pathology and persistent infection
- Identifying immunological targets to improve vaccine and drug efficiency, as well as reduce tissue pathology

Unique resource:
- Australia’s only established pre-clinical model for visceral leishmaniasis

**Malaria**
Professor Michael Good, Professor James McCarthy, Dr Don Gardiner, Dr Christian Engwerda and Dr Qin Cheng

Each year, 500 million new cases of malaria occur and up to three million people die—mainly children under five years of age.

Research focus:
- Developing and trialling new vaccines
- T cell memory to blood stage malaria
- Deleting parasite-specific memory B cells during infection
- Changes in dendritic cell function during malaria infection
- Gametocytogenesis in *Plasmodium falciparum*
- The role of antiretroviral protease inhibitors in the prophylaxis and treatment of malaria, particularly in individuals co-infected with HIV-1
- Potential targets for new drugs

**Scabies**
Professor David Kemp

Scabies is a skin disease caused by a mite. This distressing disease leads to skin sores which can become infected with streptococci and lead to kidney damage, rheumatic fever and rheumatic heart disease. Scabies mites are often found in places where overcrowding occurs.

Research focus:
- Molecular biology of scabies mites
- Developing a vaccine or other control measures for scabies

**Schistosomiasis**
Professor Don McManus, Dr Alex Loukas

Schistosomiasis is caused by blood flukes. It affects more than 200 million people, mainly in rural agricultural and peri-urban areas of the developing world.

Research focus:
- Developing effective schistosome vaccines
- The protein-protein interactions in the outer surface of the parasite, and how these might be exploited to develop better vaccines
- The field ecology of schistosomiasis in China
- Mining the newly published sequence of the *Schistosoma japonicum* genomes to identify new vaccine, drug and diagnostic targets for Asian schistosomiasis
- Pathogenesis of schistosomiasis
- Epidemiological and immunopathological studies in China and the Philippines
VIRUSES

Arboviruses
Associate Professor Andreas Suhrbier

This team is exploiting the new knowledge of viruses and immune system interactions to develop novel strategies against pathogens, cancer and inflammatory disease. Specific research areas include alphaviruses (Ross River, chikungunya), HIV, vaccination, SerpinB2, macrophages, T cells, cytokine analysis, cancer models and anti-inflammatory drugs.

Unique resource:
Extensive contract R&D and consultancies have been undertaken for local and international biotech and pharmaceutical companies. The group has produced 16 patents and co-published numerous papers with companies. They have also helped companies including Aventis, CSL, Peplin and CBio undertake preclinical, mechanism of action and bioassay studies.

Arbovirus/mosquito control
Dr Peter Ryan

Designated by the World Health Organisation as an official global Collaborating Centre for Environmental Management for Vector Control, this group is designing new mosquito surveillance and control strategies. Their research also covers mosquito-transmitted arboviruses such as Ross River, Barmah Forest, Japanese encephalitis and dengue.

The group recently achieved the first eradication of dengue vectors from northern Vietnam using biological control and community participation.

Research focus:
• The biology and control of mosquito-borne viruses
• Evaluating public health insecticides and biorationals and their suitability for contemporary mosquito control and disease prevention programs
• Mathematical modelling of arboviral diseases

Unique resource:
Australia’s largest mosquito breeding facility, with temperature, humidity and photoperiod controlled rooms

Epstein-Barr virus and cytotoxic T cells
Associate Professor Scott Burrows

Cytotoxic T cells are critical for controlling viral infection and sometimes tumours. They recognise and kill cells by scanning their surfaces for foreign peptides. At QIMR, there is a focus on understanding how T cells recognise these peptides to exploit this process to better control viral infection and cancer in humans. Much of this work has involved a comprehensive investigation into how cytotoxic T cells control Epstein-Barr virus (EBV).

Research focus:
• Identifying EBV peptides recognised by cytotoxic T cells for developing vaccines against EBV
• Characterising the T cell receptors involved in peptide recognition
• Determining if T cells raised in response to EBV infection play a role in several autoimmune diseases

Previous commercial activity:
• Licensing EBV peptides for developing vaccines/diagnostics
• Expanding cytotoxic T cell clones specific for viral peptides
• Providing frozen virus-specific cytotoxic T cell populations for product development

For further information on EBV research, see page 8.
**Human cytomegalovirus (HCMV)**
Associate Professor Rajiv Khanna

HCMV is the most significant microbial cause of birth defects in developed nations and a reduction in the virus load would improve health and reduce health care costs.

QIMR is developing a prophylactic vaccine for HCMV which is undergoing preclinical testing. We have also established collaborative links with several biotechnology companies to develop HCMV diagnostic applications.

**Unique resource:**
- Two patents around CMV CTL epitopes and their use in HCMV diagnostics and vaccines.

**Human immunodeficiency virus (HIV)**
Associate Professor David Harrich

With a focus on the discovery of key viral or cellular molecules required for HIV to grow, this group aims to target their action and block HIV growth.

**Research focus:**
- Investigating the drug target, Tat—reverse transcription; mechanisms of trafficking; and methods to block function
- Cellular factors required for reverse transcription
- The role of protein methylation in HIV replication
- Regulation of HIV by viral RNA sequences

**Unique resources:**
- Sophisticated assays to monitor HIV-1 fusion, reverse transcription, transcription, and translation
- Transmission electron microscopy to monitor HIV-1 morphology

**OTHER INFECTION DISEASES**

**Streptococcus**
Professor Michael Good, Professor Kadaba Sriprakash, Dr Michael Batzloff

Streptococcus pyogenes, commonly known as Group A Streptococcus (GAS), infects the throat and skin. It can cause a wide range of diseases including, pharyngitis (or ‘strep throat’) and rheumatic heart disease. GAS diseases are a major health concern in developing countries and indigenous populations. Australia’s Northern Territory Aboriginal population has the highest incidence worldwide.

**Research focus:**
- GAS vaccines
- Rapid streptococcal infection diagnostics
- The molecular epidemiology of GAS
- The role of streptococcal virulence factors in pathogenesis

**Unique resource:**
- GAS vaccine in Phase I Clinical Trial

**Clinical tropical medicine**
Professor James McCarthy

Using modern microbiology, molecular biology and immunology techniques, this group is studying clinical problems associated with infectious diseases in tropical environments. Areas of interest include drug resistance in parasites and the development of novel diagnostic techniques.

**Research focus:**
- Drug resistance and techniques for detecting drug resistance in human helminth infections
- Novel diagnostics for helminth infections
- Rapid diagnostic kits for malaria diagnosis
- The epidemiology of Q Fever in Queensland
- The epidemiology of tuberculosis drug resistance in Papua New Guinea
- Drug resistance in human scabies
- Evaluating novel anti-malarial agents
- Pathogenic and public health issues related to malaria during pregnancy
QIMR is involved in some of the world’s largest population studies. Collections of samples and data are compiled from thousands of people to help us understand the role of environmental factors and genetics in health and illness.

Diseases currently studied include cancer, mental health and depression, alcoholism, endometriosis, migraine, inflammatory bowel diseases and drug dependence. QIMR’s Indigenous Health Program is also using population studies to look at a range of issues affecting Australia’s Indigenous communities including asthma, diabetes and the quality of health care.

**BASIS OF DISEASE**

**Genetic and environmental factors**
Professor Nick Martin, Professor Peter Visscher, Professor Grant Montgomery

QIMR research groups are investigating the pattern of disease in families, particularly identical and non-identical twins, to assess the relative importance of genes and environment in a variety of important health problems. Diseases being studied include alcoholism and smoking addictions, allergy, asthma, anxiety and depression, cognition, eczema, endometriosis, iron metabolism, melanoma, personality, and fertility.

Unique resource:
- Data base of more than 30,000 twins and family members
- Sequenom MassARRAY genomics platform and an Illumina BeadStation

**Neurogenetics**
Dr Dale Nyholt

The Neurogenetics Laboratory is studying the role of genetics in the development and mechanism of the nervous system. It aims to identify genes that cause neurological disorders, in particular genetic variants causing migraine and investigate the molecular mechanisms through which these genes act. The co-morbidity between migraine and endometriosis has recently been confirmed, finding that common genetic influences explained their co-occurrence within individuals.

**CANCER**

**Familial inheritance**
Dr Amanda Spurdle, Associate Professor Joanne Young

It is known that familial inheritance of genes can predispose family members to develop cancer. Several cancers are being studied within families with a pattern of inheritance to specific oncogenes.

Breast and ovarian cancer
- BRCA1 and BRCA2 variants of unclassified pathogenic potential
- Breast and ovarian cancer predisposition genes
- Genetic modifiers of risk in BRCA1 and BRCA2 mutation carriers
- Ovarian cancer survival genes

Colorectal cancer
- The genetics of serrated neoplasia
- Breast and colon families
- Lynch syndrome families

Endometrial neoplasia
- Molecular epidemiology of endometrial cancer
- Genes associated with breast and endometrial cancer predisposition in families
- Markers of prognosis

Prostate cancer (joint study with QUT Institute of Health and Biomedical Innovation)
- Prostate cancer predisposition genes
- Genetic markers of prognosis

Unique resource:
- Australian National Endometrial Cancer Study
- Genetics of Serrated Neoplasia Study
- Collaborative Family Registry for Colorectal Cancer Studies Colon
Environmental and genetic causes
Professor Adèle Green,
Associate Professor David Whiteman

The environmental and genetic factors that cause cancer are being investigated as well as research into early diagnosis, treatment and survival. The research involves understanding how genes modify the effect of environmental factors to cause or prevent cancer. Research is also undertaken with laboratory colleagues to use molecular markers to investigate mechanisms of carcinogenesis. Research centres on five areas.

Barrett's oesophagus and oesophageal cancer
- Molecular epidemiology of Barrett's oesophagus (a pre-cancerous condition) and oesophageal cancer
- Prognostic markers for oesophageal cancer
- Clinical measures of obesity and risk of Barrett's oesophagus
- Tissue markers for progression of Barrett's to cancer
- Health economics of oesophageal cancer prevention and treatment

Melanoma, skin cancer and photo-ageing
- Exploring the causal pathways to cutaneous melanoma especially interactions of genes and environment
- Risk prediction for cutaneous melanoma
- 20-year study of skin cancer in a Queensland community
- Dietary factors and actinic skin damage
- The association between Human Papilloma Virus and squamous cell carcinoma of the skin

Pancreatic cancer
- Case-control study of genetic and environmental risk factors for pancreatic carcinoma

Indigenous health research
- Asthma in children in the Torres Strait
- Evaluation of education intervention program for childhood asthma by Aboriginal and Torres Strait Islander health workers
- Bronchiectasis in Indigenous children, causation and intervention
- Cancer in Aboriginal and Torres Strait Islander people in Queensland

Gynaecological cancers
Associate Professor Penny Webb

Gynaecologic cancer affects almost 4000 women in Australia each year and causes more than 1400 deaths. QIMR is investigating all aspects of gynaecological cancer from aetiology to diagnosis, patterns of care, to quality of life and survival.

A particular focus is the role of environmental factors and the interaction between genetic and environmental factors in the cause and prognosis of gynaecological cancer. Much of this work is conducted within two national population-based case control studies: the Australian Ovarian Cancer Study (AOCS) and the Australian National Endometrial Cancer Study (ANECS).
OTHER RESEARCH AREAS

QIMR is investigating more than 40 diseases

QCF Transgenics Laboratory
Dr Graham Kay

The Queensland Cancer Fund Transgenic Laboratory generates knockout and transgenic mice, as well as undertaking mouse embryo freezing on a contract research basis.

Research focus:
• X chromosome inactivation
• Pocket protein gene function in cell differentiation, development and cancer
• Men1 gene function in cell differentiation, development and cancer

Epigenetics
Professor Emma Whitelaw

Epigenetics is the study of mechanisms which modify DNA structure and change gene expression without influencing the DNA base sequence. This is an emerging field and its importance has been highlighted by the discovery that epigenetic changes can cause cancer. Molecules which can change epigenetic marks are being tested on colorectal cancer patients.

Research focus:
• Identifying epigenetically regulated genes in mice and humans
• Finding the genes involved in establishing and maintaining the epigenetic marks

Spinal injury regeneration
Professor Andrew Boyd

Professor Boyd’s team is investigating the potential to treat damage to the nervous system.

Research focus:
• An EphA4 gene knockout mouse, displaying spinal cord development defects have been shown to recover completely after spinal injury
• Role of EphA4 inhibitors in promoting healing in normal mice after spinal cord injury

Molecular psychiatry
Dr Corinne Lendon

This group is investigating factors that modify dementia susceptibility (in particular Alzheimer’s disease) as well as related neurological and psychiatric disorders, including psychosis and depression.

Research focus:
• Discovering factors that predispose to or protect individuals from dementia and Alzheimer’s disease
• Searching for novel genes and investigating the mechanisms that incur risk for dementia and Alzheimer’s disease
• Investigating the molecular mechanisms of interaction between genes and environment factors known or suspected to be involved in dementia as well as developing screens for discovering novel factors.
• Use of in-house developed drug screen involving human brain cell for discovering novel drugs that alter detrimental gene expression

Unique resource:
• UK patient control cohorts

Hepatic fibrosis
Associate Professor Grant Ramm

This group is investigating the cell biology of hepatic stellate cells (HSC). These cells are transformed into myofibroblasts when exposed to liver toxins and are responsible for excess collagen deposition, fibrosis and cirrhosis in liver injury.

Research focus:
• HSC role in fibrogenesis associated with iron overload disease Haemochromatosis in adults and biliary obstruction diseases in children and infants such as cystic fibrosis and biliary atresia
• Switches for initiating HSC transformation into scar-forming liver fibroblasts
• Diagnostic markers of early and end-stage liver fibrosis
Iron metabolism
Professor Greg Anderson

Iron is an essential trace element and disturbances of iron metabolism are implicated in several significant human diseases.

Research focus:
• Investigating the biology of iron export to define the role played by hephaestin and associated proteins
• Analysing the relationship between basolateral iron export and the expression of the brush border iron transport molecules, the ferrous iron transporter DMT1 and the ferric reductase Dcytb
• Studying the systemic regulation of intestinal iron transport with an emphasis on the role played by hepcidin
• Investigating the mechanism of intestinal iron absorption
• Investigating Haemochromatosis penetration and relevance to population screening for mutations in the HFE gene
• Other iron related studies including iron overload in end-stage liver disease; the molecular basis of the elevated iron absorption associated with pregnancy; and the diagnosis and prevalence of iron deficiency in the Australian population

Unique resource:
• Haemochromatosis patient database

Membrane transport
Associate Professor Nathan Subramaniam

Many human diseases are associated with defects in the localisation and trafficking of membrane receptor proteins. This QIMR group is studying how mammalian cells regulate the trafficking, localisation and protein-protein interactions of membrane transporters associated with disorders to potentially aid in developing better treatments.

Research focus:
• Molecular analysis of the Haemochromatosis gene product, HFE
• Molecular, cellular and functional characterisation of a transferrin receptor homologue, Tfr2
• Role of SNAREs in exocytosis and endocytosis
Our disease models, technologies and tissue banks are used globally

RESEARCH AND TECHNOLOGY PLATFORMS

<table>
<thead>
<tr>
<th>Platform</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Oncology</strong></td>
<td>- Compound screening for anti-tumour activity against a panel of human cancer cell lines (cell growth and reporter gene assays)</td>
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<td>- Mechanism of action of candidate anti-cancer drugs</td>
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<td>- Mechanisms of gene regulation by agents, including use of microarray technology</td>
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<td>- Monoclonal antibodies for research and diagnosis</td>
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<td>- Xenograft models</td>
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<td>- Models investigating human cancer susceptibility</td>
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<td>- EBV models</td>
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<td><strong>Cell and tissue biology</strong></td>
<td>- Confocal, electron, and laser dissection microscopy</td>
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<td>- Signal transduction assays</td>
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<td>- Histology and histopathology</td>
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<td>- Cell sorting</td>
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<td>- Fluorescence microscopy</td>
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<tr>
<td><strong>Epidemiology</strong></td>
<td>- QIMR has access to extensive resources to facilitate nationwide studies on important diseases. We combine classical epidemiological methodology with genetic analysis of blood and tissue samples.</td>
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<tr>
<td><strong>Genomics</strong></td>
<td>- Mass array SNP typing facility</td>
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<td>- Genome scans</td>
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<td>- Zebra fish facility with many cutting edge methods for gene detection and analysis</td>
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<td>- Gene expression profiling of cancer cell lines and tumours</td>
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<td>- cDNA library construction</td>
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<td>- Information database on 30,000 twins and relatives</td>
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<td>- DNA database of 5000 twins</td>
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<tr>
<td><strong>Infectious disease</strong></td>
<td>- Models for investigating the efficacy of vaccines or candidate drugs against infectious disease, including malaria, leishmaniasis, Group A streptococcus, schistosomiasis and hook worms</td>
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<td>- Viral protection assays</td>
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<td>- Models for the effects of compounds on viruses including alphaviruses, poxvirus (vaccinia) and herpes virus (cytomegalovirus)</td>
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<td>- Models for evaluating drug resistance</td>
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<td><strong>Immunology</strong></td>
<td>- Graft versus Host Disease transplantation models</td>
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<td>- Models for evaluating anti-viral activity</td>
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<td>- Effect of novel compounds, drugs, vaccines, immune-suppressants and immune-stimulators on cytotoxic T lymphocytes</td>
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<td></td>
<td>- In vitro and in vivo assays of activation of macrophages, NK cells, T cells, B cells, Dendritic cells</td>
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<td>- FACS analysis</td>
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<td>- Multi-analyte system – multiplex for antibody and cytokine assays</td>
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<tr>
<td><strong>Transgenic/knockout mice</strong></td>
<td>- Generation of knockout and transgenic mice</td>
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<td>- Mouse embryo freezing</td>
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<td>- Production of gene knockouts in specific tissues in mice</td>
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<td>- Live animal imaging – detection of reporter gene expression</td>
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</tbody>
</table>

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# TISSUE BANKS

<table>
<thead>
<tr>
<th>Tissue type</th>
<th>Background</th>
<th>Samples available</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian cancer (1)</td>
<td>Blood, tissue and urine samples and matching clinical data have been collected from more than 1500 women with ovarian cancer. Blood samples were also collected from 1000 cancer-free control women across Australia. Epidemiological data is available.</td>
<td>Blood, urine and tumour tissue Held at the Peter MacCallum Cancer Centre</td>
<td>Australian Ovarian Cancer Study</td>
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<tr>
<td>Ovarian cancer (2)</td>
<td>Blood samples have been collected from 200 women with ovarian cancer, 250 with benign ovarian tumours,</td>
<td>Blood and tumour tissue</td>
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<td>Breast cancer</td>
<td>A cohort study of multiple case breast cancer families from whom extensive genetic, clinical and epidemiological data is available as well as biological specimens. Collection is complete on more than 900 families.</td>
<td>Blood and tissue samples Held at the Peter MacCallum Cancer Centre</td>
<td>Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer</td>
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<td>Colon cancer</td>
<td>This bank contains over 800 fresh frozen primary colorectal cancers. Collection started in 1992 and is ongoing. There are matched normal mucosa and blood samples. Most samples have had DNA extracted and paraffin fixed blocks and RNA is available from selected samples.</td>
<td>Tissue from primary tumours Held at QIMR</td>
<td>Walter Paulsen Tumour Bank</td>
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<td>Melanoma and skin cancer</td>
<td>Newly-diagnosed patients with melanoma have been identified from the Queensland Cancer Registry. Information is collected on age, ethnicity, medical history and family history of melanoma and skin cancer. A brief sun exposure history has been recorded, including details of residential ambient solar exposure, as well as occupational and recreational sun exposure for each decade of life.</td>
<td>Paraffin sections of tumour tissue Held at QIMR</td>
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<tr>
<td>Oesophageal cancer</td>
<td>These samples are part of a national population-based study of oesophageal cancer. Blood and questionnaire data is available for 1000 patients and 1500 cancer-free controls. Paraffin tissue blocks are available for 800 patients.</td>
<td>Blood, tumour tissue and paraffin blocks of tumour tissue Held at QIMR</td>
<td>Australian Cancer Study</td>
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<tr>
<td>Barrett's oesophagus and reflux conditions</td>
<td>Blood samples are available from 380 patients with Barrett's oesophagus, 250 with gastro-oesophageal reflux disease and 700 controls.</td>
<td>Blood samples</td>
<td>Study of Digestive Health</td>
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