Garvan scientists have identified biochemical changes that commonly occur in the DNA of women with ovarian cancer, which may help diagnose the cancer at an earlier stage in the future. Using whole genome DNA profiling methods, Garvan scientists have identified a panel of six genes that are affected by an epigenetic process known as ‘DNA methylation’ in ovarian cancer. The Garvan team collaborated with Professor Neville Hacker, Director, Gynaecological Cancer Unit, Royal Hospital for Women, Randwick, who provided tumour samples from ovarian cancer patients, as well as samples from normal ovaries.

Obesity, especially central obesity, is associated with insulin resistance which precedes diabetes, sometimes by more than a decade. However, it’s not only a question of body weight or fat distribution because some obese people remain insulin-sensitive, with insulin working as well in their bodies as in someone lean. Garvan researchers reviewed 79 publications on this topic and say it also seems that in addition to having a lower risk of Type 2 diabetes than insulin-resistant people of the same weight, individuals who are obese and insulin-sensitive also appear to have greater protection against death from cardiovascular disease.

Anti-psychotic drugs for treating serious mental illness, such as bipolar disorder or schizophrenia are effective and often life-saving, but come with unwelcome side-effects. They dramatically increase weight as well as the incidence of metabolic disorders such as raised blood fats and Type 2 diabetes, say Garvan specialists. The rapid decline in physical health is so clinically significant, and of such concern, that the specialists put together a physical health protection algorithm last year, which they say should run in tandem with mental health treatment. It includes regular and specified measurement of tangibles – weight, waistline and blood chemistry – as well as counselling about lifestyle and diet.
Opinion

There have been three transformational advances in molecular biology: the double helix, gene cloning, and genomics.

The first, in the 1950s and 60s, provided the basis for understanding gene structure, gene expression and gene regulation — the first steps toward deciphering how our genetic inheritance programs our biology. The paradigm that emerged — the so-called ‘central dogma’ — was that each stretch of DNA (a gene) specified a protein through the intermediate of RNA, which was copied when needed and decoded.

The second, beginning in the 1970s, gave medical scientists the first chance to ‘look under the hood’. The ability to isolate and amplify individual DNA sequences led to the discovery of many genes involved in human development, human physiology and brain function, whose protein products were invisible to the relatively crude biochemical approaches of the time. It also enabled the identification of those malfunction in diseases, like cancer, which was the prerequisite to the development of new drugs to block them. These drugs are now, 20 years later (after all the required research and safety testing), being used in the clinic to successfully treat many previously lethal cancers — with many more in development.

The third revolution, genomics, has been made possible by the incredible advances in DNA sequencing technology over the past 20 years. Ten years ago the first human genome sequence cost $3 billion dollars, and took years of work to complete. Now we can do the same thing for $3,000 in a few days, and the cost is dropping by at least half every year.

This is enabling us to determine the full molecular signatures of different cancers, and the best treatment options and approaches. Genome sequencing has already saved lives by identifying rogue mutations that were not obvious from traditional cellular pathology. Garvan is pioneering the introduction of this ‘next gen’ approach to cancer in the soon-to-be-opened Kinghorn Cancer Centre. This is a joint venture with St Vincent’s Hospital, where medical science and the clinic will interact, side-by-side to bring the state of the art to Australia.

Garvan will also bring these next gen approaches to dissecting the other complex diseases that beset our community — diabetes, immune disorders, osteoporosis and neurological disorders. The biological and medical revolution is now moving into top gear. It is clear that this will be the last generation to die from cancer, and there is every reason to expect that the other diseases will succumb to human understanding.
Inside our bodies, there is a powerful mechanism designed to defend against millions of microscopic invaders. However, what happens when that defense is impeded, or worse, stops working altogether?

The immune system is designed to protect our bodies against dangerous attacks. These can come from outside the body in the form of infections, or from inside the body in the form of cancer. At the same time, the immune system must avoid attacking healthy tissue or over-reacting to minor threats like pollen and house dust mites. When the balance is upset and control fails, the result can include diseases ranging from life threatening infections and malignant tumours to autoimmune conditions (eg Type 1 diabetes) and allergies (eg asthma).

The work of Garvan’s Immunology program is divided between studying how a normal immune system functions in a balanced way, and how it goes wrong when disease occurs. Understanding the way the cells and molecules of the immune system function is key to both dampening the immune system or harnessing its power in order to fight disease.

Here we explore some of the diseases that are currently being researched by the Immunology team, as well as some of the progress being made in this important field of medical research.

Type 1 diabetes affects more than 140,000 children and adults in Australia, making it one of the most common serious diseases among children.

People with Type 1 diabetes produce very little, if no insulin. Insulin is the hormone that regulates the body’s use of glucose (sugar), which is a major fuel source for our bodies. Insulin is only produced by specific cells in the pancreas called beta cells. Insulin travels through the blood and helps to get sugar from the blood into cells, where it can be used for energy. Without insulin, blood sugar levels rise to dangerously high levels that can cause organ damage.

Type 1 diabetes comes when the beta cells that make insulin have been destroyed by the body’s own immune system. Like many complex human diseases, we are not sure why this occurs, but we do know that it is caused by an interaction between genes and the environment.

In people with Type 1 diabetes, the immune system treats the beta cells like it would a bacteria or virus, and for this reason, diabetes is called an autoimmune disease.

Garvan’s Immunology program has several teams of scientists looking into different aspects of Type 1 diabetes. They focus on understanding how and why the immune system turns on itself and destroys the insulin-producing cells. They are also trying to create new beta cells from other cell types.

Recently, Garvan scientists developed a reagent that could prevent rejection of transplanted insulin-producing cells into people with Type 1 diabetes. It is one of the most promising immunology developments in the last 5 years.

The best hope for restoring insulin production is for people to receive transplanted clusters of insulin-producing cells from the pancreas known as islets of Langerhans. Each pancreas has around a million islets, which maintain the body’s blood sugar levels in exquisite balance.

However, transplanting islets is a process fraught with challenges. Islets are delicate, the body rejects donor cells strenuously, and anti-rejection drugs are highly toxic. Even when heavy duty immunosuppressive drugs are given to a patient, that person will still have Type 1 diabetes – the autoimmune disease that destroyed their insulin-producing cells in the first place.

The new reagent, generated in-house by Garvan scientists has the potential to turn this situation around. Given to diabetic mice for two weeks, starting the day before islet transplantation, the reagent allows mice to accept the donor cells as their own, with no need for immunosuppressive drugs, and no Type 1 diabetes. Permanently.

Sjogren’s syndrome is a disorder of the immune system, where glands that normally produce tears, saliva and sweat are attacked and destroyed by immune cells. This results in abnormally dry eyes, mouth and/or other mucous membranes such as the intestines, lungs or vagina.

Sjogren’s syndrome may occur by itself, known as Primary Sjogren’s syndrome, or together with other autoimmune diseases such as lupus and rheumatoid arthritis. This is known as Secondary Sjogren’s syndrome.

The cause of Sjogren’s syndrome is still a mystery, though there appears to be a genetic influence, as it tends to occur in families where there are other autoimmune diseases.

Garvan scientists have identified a new group of immune cells that, for the first time, directly link two autoimmune diseases, Type 1 diabetes and Sjogren’s syndrome. The newly identified population of cells is a sub-class of “T helper cells”, white blood cells that help other immune cells perform their tasks.

Garvan scientists hope to determine whether these cells could become a biomarker of disease as well as a therapeutic target for patients with both Type 1 diabetes and Sjogren’s syndrome.

Lupus (also known as Systemic Lupus Erythematosus – SLE) is an autoimmune disease that causes various tissues in the body to become chronically inflamed. It is a complex disease that can affect many parts of the body, typically the skin, joints, kidneys, lungs, heart and brain. Lupus can be mild or life-threatening, depending on the area of the body that is affected.

Lupus affects one in 700 Australians. Nine out of every ten people with lupus are women, mostly aged between 15 and 45 years.

In the case of lupus, the immune system inadvertently produces antibodies that attack various structures in the body. It is the accumulation of these “autoantibodies” in the tissues that can cause inflammation, damage and pain. In other autoimmune diseases, particular tissues such as the peripheral nerves (Guillain-Barré syndrome) or the heart muscle (rheumatic carditis) are attacked by “organ-specific auto-antibodies.”

At Garvan, scientists are using sophisticated strategies and technologies to examine the reasons why in the case of lupus and other autoimmune diseases, the immune system produces antibodies that attack the body, and not invading micro-organisms.

An important clue that we are following up is the fact that autoimmune diseases often occur after bacterial or viral infections. It appears that, in these cases, the immune system’s response against the infection has inadvertently resulted in the production of antibodies that attack the body’s own tissues as well as the invading organism.

So far we have found that our immune system has a way of preventing the production of these “cross-reactive” autoantibodies under most conditions. However, we have identified that autoimmune attacks on particular organs are particularly likely to occur in the weeks following infections. By devising a way to look directly at the immune cells responsible for making autoantibodies, we have now positioned to look at how this process is controlled and how, in the future, to devise ways of preventing the movement of infection to autoimmune disease.

Asthma is an inflammatory condition that affects the bronchial tubes in the lungs. People with asthma have sensitive or hyperreactive airways which narrow in response to certain stimuli. The narrowing is due to inflammation and swelling of the lining, tightening of the airway muscles (spasm) and production of excess mucus. This reduces the airflow in and out of the lungs.

More than two million Australians have asthma, yet the causes are still not clearly understood, but genetic and environmental factors do come into play. There is often a family history of asthma, eczema and/or hay fever or other allergies. Children with one asthma-like parent are three to six times more likely to develop asthma.

Garvan researchers are focused on understanding the key pathways in asthma and identifying unique sets of genes, inflammatory molecules and proteins that can be used to intervene in the process of asthma. Garvan is also looking to develop new therapeutic approaches for asthma, such as monoclonal antibodies as a treatment to reduce inflammation in the airways of asthma patients.

Research into diagnostics is also important: more effective tools to identify which patients will respond best to which treatments. Garvan research will lead to more effective use of existing treatments and the development of new and improved therapies.
Staff Profile: **Professor Peter Croucher**

Highly-respected bone researcher Professor Peter Croucher recently joined Garvan from the University of Sheffield to take up the Chair so generously funded by Mrs Janice Gibson and Ernest Heine Family Foundation. We are pleased to welcome Professor Croucher as the leader of Garvan’s Osteoporosis and Bone Biology program, a role previously held by Professor John Elsom who stepped down as program leader in late 2011.

We recently sat down with Professor Croucher to discuss his new role.

What does your role as Director of Garvan’s Bone Program involve?

As the Program Director, my overall role is to develop a world-class research program with the aim of having a significant impact on the most common diseases of the skeleton. To do that, I will be looking to recruit more of the best possible people, and create a high quality infrastructure to support the best possible research.

So far, what are you enjoying most about working at Garvan?

I like the positive attitude that everyone has here, whether they are related directly to the research, or from those that support research. I also like having the time to be much more directly involved in research. In my previous role there was increasing levels of administration which meant I had less and less time to do the research that I really enjoyed. I even hope to get back into the lab myself here at Garvan.

So far, what are you enjoying most about living in Australia?

I really like Sydney, but surprisingly, the thing I like most so far is the climate. All the Sydney-siders I’ve met are complaining that this summer was the worst they can remember, but I have to say, I’ve loved it. However, I suspect this probably says more about UK weather than it does about Australia! I have also really enjoyed travelling around Australia, particularly western NSW and Kakadu National Park.

What is the biggest challenge facing your area of research?

Raising awareness about the importance of musculoskeletal diseases is a real challenge. Most people see the skeleton as a dead tissue – a structure that just holds you up. They don’t realise it’s a tissue that is constantly changing – the skeleton you wake up with is not the one you go to bed with. Most are unaware that we are all likely to develop some form of musculoskeletal disease in our lifetime, whether this be one of the more common diseases such as osteoporosis, osteoarthritis or rheumatoid arthritis, or a less common disease such as the cancers that grow in bone.

Raising funds to be able to work on these diseases is a real challenge. Unfortunately we don’t have the same high profile as other diseases, such as cancer or heart disease, so we are not at the top of people’s lists when it comes to supporting research. However, the impact on people’s health is just as significant as some of the more high profile disease areas.

Recruiting good people is also a challenge. People see that working in the bone field is challenging, particularly in getting long-term funding. Certainly in my experience in the UK, we lost a lot of great researchers in the field because of a lack of funding. I hope we can address this challenge at Garvan.

What do you enjoy doing away from the lab?

I spend much of my spare time with my children because they are still young. Outside of that, I do as much running as I can, particularly trail running and, when possible, I also enjoy cycling.

Professor Croucher will host Garvan’s free Osteoporosis and Bone Public Seminar on Thursday 9 August 2012.

To register for this event, visit www.giving.garvan.org.au/seminars or phone (02) 9295 8110.

**City2Surf**

It’s time to start training! Elite athletes will once again be rubbing shoulders with locals to run, walk or watch the iconic City2Surf race. Starting at Hyde Park in Sydney’s CBD and finishing at Bondi Beach, the City2Surf also offers participants the opportunity to raise funds for a charity.

Entries will open in late May. For more information about registering for the City2Surf, and selecting the Garvan Institute of Medical Research as your charity of choice, visit www.city2surf.com.au

**Ask Garvan**

**Q:** Why will the new Kinghorn Cancer Centre include a Wellness Centre?

**A:** The Wellness Centre forms part of the Kinghorn Cancer Centre’s integrative approach to medicine. The first of its type in NSW to be integrated with conventional cancer care, the purpose-built Wellness Centre will be a place where patients can retreat and get help coping with their cancer diagnosis and treatment.

With a ‘Day Spa’ feel, the Wellness Centre’s design will provide a calm, caring and soothing environment for cancer patients to access the latest information and advice and the very best in evidence-based complementary health care. Services offered at the Wellness Centre will help alleviate stress, relieve symptoms and reduce pain and anxiety as well as promoting feelings of well-being.

Relieving the physical and emotional side-effects of cancer treatment is important in encouraging the completion of a treatment regimen. For example, it is estimated that more than 30 percent of chemotherapy patients prematurely cease treatment because of emotional difficulties.

At the Wellness Centre, evidence-based and non-invasive complementary therapies will be offered as an adjunct to conventional medicine in a patient-centred and holistic care program. This will allow open communication between all care providers and the patient, while promoting patient choice and quality of life. Importantly, researchers will be able to evaluate various therapies for efficacy, so that we build our knowledge of what really works for individuals.

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Clinical Studies

Metabolism – Genetics of Obesity Study
Do you think you could be overweight? Volunteers are needed to screen for a gene that links to obesity at the Garvan Institute. It involves only one visit during which measurements and a blood test will be taken. If you are suitable, you may enter the second part of the study to receive a full metabolic assessment.

For further enquiries, please contact: Dr Daniel Chen (02) 9295 8557, or email d.chen@garvan.org.au or Vanessa Travers (02) 9295 8232, or email v.travers@garvan.org.au (St Vincent’s Human Research Ethics Ref HREC/10/SVH/133).

Pre-diabetes study
We need healthy volunteers for a study looking at the effects of immune function and autonomic nervous activity in Type 2 diabetes. We especially need people with a family history of Type 2 diabetes. If you are willing and are aged 50 to 60 years and healthy, please contact: Lynne (02) 9295 8231, or Dorit (02) 9295 8309, or email crf@garvan.org.au (St Vincent’s Human Research Ethics Ref 06/147).

Coming Up

24 May – Ovarian Cancer Public Seminar. 10am to 12 noon.
6 June – Young Garvan Forum. Topic TBC. 6pm to 8pm.
9 August – Osteoporosis and Bone Public Seminar. 10am to 12 noon.
20 September – Alzheimer’s disease and other neurodegenerative disorders. 10am to 12 noon.
14 November – Type 2 diabetes and obesity. 10am to 12 noon.

For more information about any of these events, visit www.giving.garvan.org.au or phone (02) 9295 8110.

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Please use this coupon if you would like to make a donation to Garvan’s breakthrough medical research, or if you would like further information. We would love to hear from you.

In Memoriam November 2011 – February 2012. Donations have been made in memory of:

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