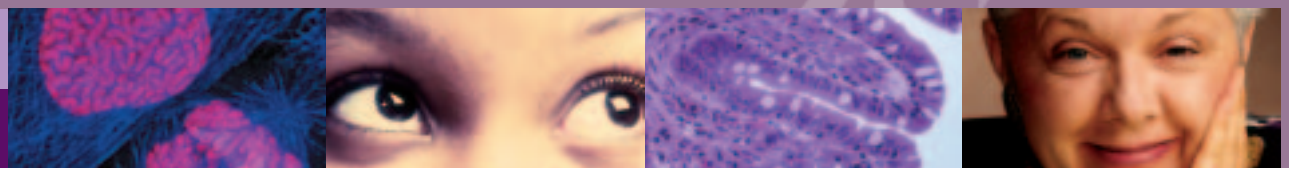

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A Picture of Health

A Selection of Irish Health Research 2003

Health Research Board
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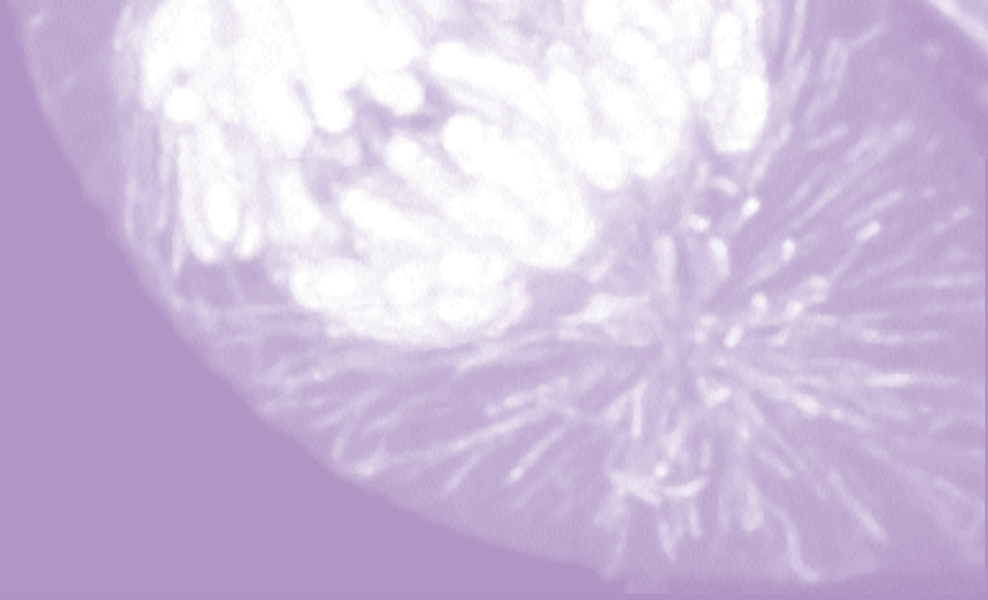
The research described in this report includes research projects, fellowship projects, Ireland-Northern Ireland cooperation projects, co-funded health services research projects and interdisciplinary projects.

FOREWORD

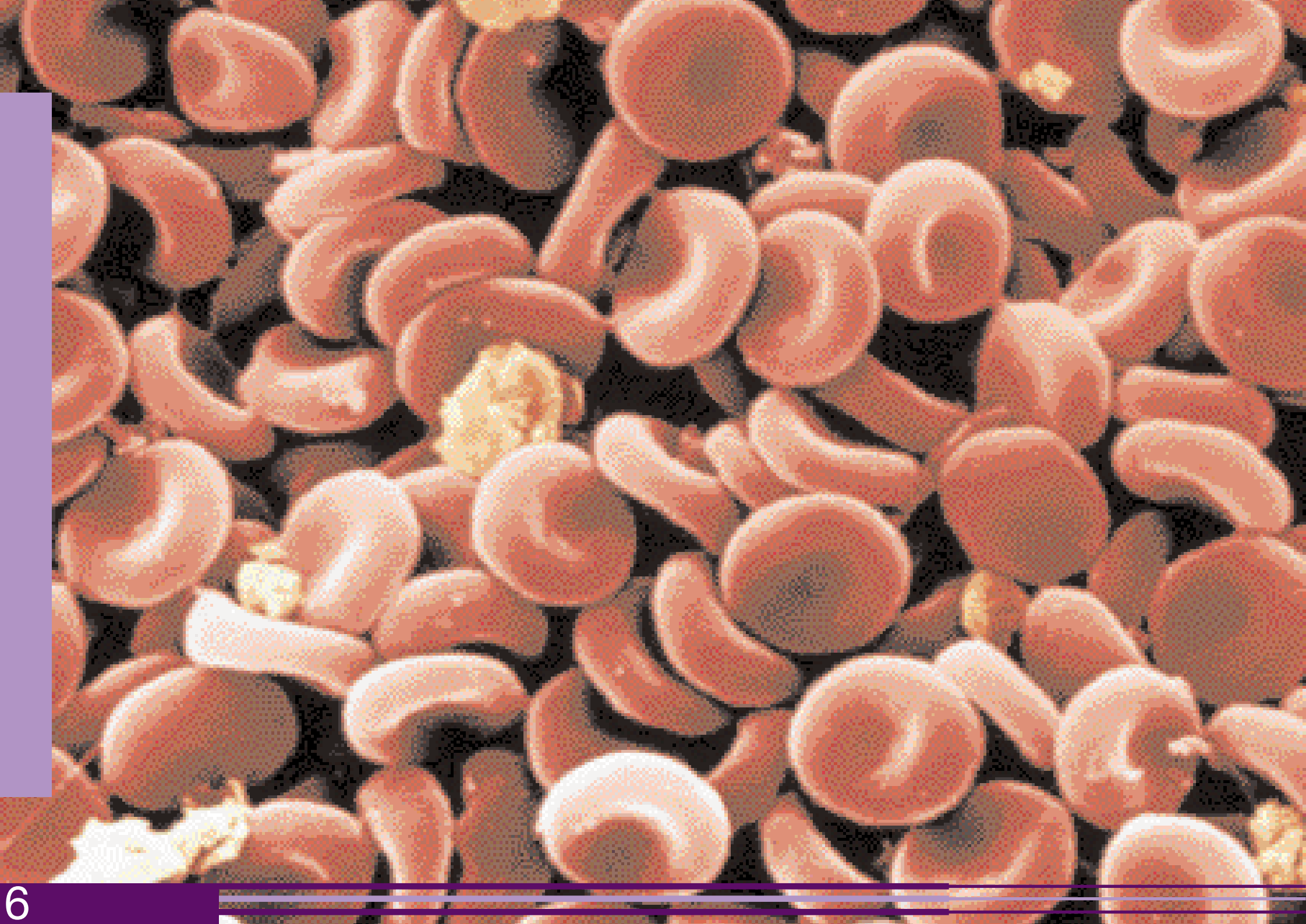
The Irish Government places a high value on research as part of its drive to develop a knowledge-based economy. The Department of Health and Children contributes to this effort through funding of the Health Research Board. Since its inception, the HRB has played a pivotal role in nurturing a culture of research within the health service. There is no higher aspiration in science than solving the mysteries of human disease and there has never been a better time for focusing research on health. As one of the wealthiest nations in the world, we have an obligation to contribute to the global war on disease. Our scientists are capable, committed and renowned for their work. The HRB recognises this talent and herein describes an extraordinary collection of funded projects across a range of disciplines, from basic science to research on how well Ireland delivers an increasingly complex health service. Congratulations to all of you. You have come through a rigorous review that places a high premium on innovation and productivity. Through your efforts, Ireland participates in humanity's greatest challenge.

Professor Desmond Fitzgerald
Chairman of the Health Research Board

CONTENTS



The heart of the matter: cardio-vascular disease



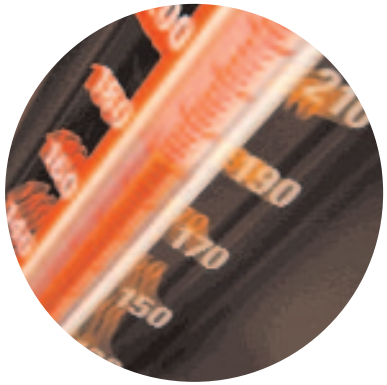
WHAT CAUSES HIGH BLOOD PRESSURE?

Dr Stuart Bund and PhD student Jennifer Hughes (Human Anatomy and Physiology, UCD) believe that thicker artery walls are a consequence and not a cause of high blood pressure

People who have high blood pressure often have a much thicker muscle layer in the walls of their small arteries. Until now, it was widely believed that the thickened muscle caused the high blood pressure, perhaps by producing a more powerful contraction. So the received wisdom was that, to lower the blood pressure, you should ideally use drugs that also thin the walls of the arteries.

In recent years, however, there has been growing debate about whether this picture is right. To investigate **the relationship between blood pressure and the thickness of the artery muscle,** we studied sections of blood vessel in the laboratory using a rig designed to mimic what happens in the body. The blood vessels came from rats that have high blood pressure in one leg, and low blood pressure in the other. Significantly, we found that the two types of blood vessel behaved the same, and there was no difference between the contractions of the thick and the thin muscles.

This leads us to believe that the thicker muscle wall is actually a consequence of the high blood pressure, and not a cause of it. Our results are now being published in international scientific journals, and if we are right, we may need to rethink our approach to how we treat high blood pressure.



THE GENETICS OF HEART DISEASE

Dr Therese Kinsella and PhD student Adrian Coyle (Biochemistry, UCD) are studying the genetics of blood clotting

Thromboxane is a natural compound that is important in regulating blood flow and clotting; add it to some blood platelets and they will quickly clump together or clot. This happens because the surface of each platelet contains receptors that specifically recognise and respond to thromboxane. People who have more of these receptor proteins on their platelets than normal are at greater risk of unwanted blood clotting (thrombosis) and of heart disease. But what determines the number of receptors on blood cells?

Humans actually have two types of thromboxane receptor (all other red-blooded creatures have just one), called TP-alpha and TP-beta. Intriguingly, though they have different compositions, both proteins are encoded by the same gene. One might expect, therefore, that their production would be regulated by the same DNA controlling sequence ('promoter' sequence). Previously, scientists had discovered one promoter sequence that was thought to control the production of both TP-alpha and TP-beta. In this research, we discovered that the previously identified promoter sequence specifically controls TP-alpha expression and have discovered a new promoter that controls TP-beta production, independently of TP-alpha. Our next step is to investigate the factors that interact with these two promoters, and ultimately determine how TP-alpha and TP-beta expression is independently regulated. This work should identify the individual roles of TP-alpha and TP-beta and should greatly improve our understanding of the genetics of heart disease.

BLOOD CLOTS AND MOLECULAR VELCRO

Dr Niamh Moran and Dr Sarah O'Neill (Pharmacology, Royal College of Surgeons in Ireland) are studying how blood clots form

Blood clots can cause strokes and heart attacks. We still don't fully know how the clots form, although we do know that small blood cells called **platelets play an important role,** and people whose platelets are dysfunctional can suffer serious clotting and bleeding disorders. If we knew more about what happens, we might be able to design better clot-busting drugs.

One molecule that seems to be important is called GpIIb/IIIa, which covers about 12% of a platelet's surface. This acts as a kind of molecular Velcro, sticking cells together, but more than that, it also seems to make a clot form. We have now discovered that GpIIb/IIIa is a shape-shifter: when it is activated it changes structure, making and breaking several sulphur-sulphur bonds, so that it re-folds in a different shape. We don't yet know, however, what provokes this change. Significantly, we have also discovered that the molecule controls this process itself. In other words, as well as acting as a structural protein, it can also function as an enzyme.

This sheds considerable light on how GpIIb/IIIa functions, and there is now growing interest in our findings. Our next step is to look for chemicals that block the shape-shifting, as these could be useful as drugs to prevent clots forming.

HOW MOUTH INFECTIONS CAN DAMAGE YOUR HEART

How do bugs from your mouth cause blood clots and heart failure? Dr Dermot Cox and PhD student Ciara McManus (Clinical Pharmacology, Royal College of Surgeons Ireland), think they know why, and are developing a drug to prevent it

Healthy teeth and gums can also mean a healthy heart! That's because, in a healthy mouth, there is less chance of bacteria getting into the bloodstream (as can happen, for instance, if your gums bleed when you brush your teeth). The bacteria to watch for include *Porphyromonas gingivalis,* which new research suggests can cause hardening of the arteries; and *Streptococcus sanguis,* the organism we study, which can trigger blood clots in already damaged heart valves.

To understand how these clots form, we studied the way the bacteria interact with the platelet cells (the blood cells involved in forming clots). We discovered that disease-causing strains of *S. sanguis* are very good at sticking to platelets, a process we call adhesion. We also found that they probably do this by producing a collagen-like protein that binds to a collagen receptor on the platelets. This is surprising, because blood clots usually involve a different protein, called fibrinogen. Our work has allowed us to identify a molecule that blocks the adhesion, and prevents the bacteria and the platelets sticking. We believe this could lead to a new drug for preventing this form of 'infective endocarditis', and we are now patenting our discovery, prior to publishing the results in international journals. A drug that inhibits this interaction would also be useful in coronary artery disease, since the same platelet-collagen interaction is important in the clot that blocks an artery leading to a heart attack.

Cardiovascular disease

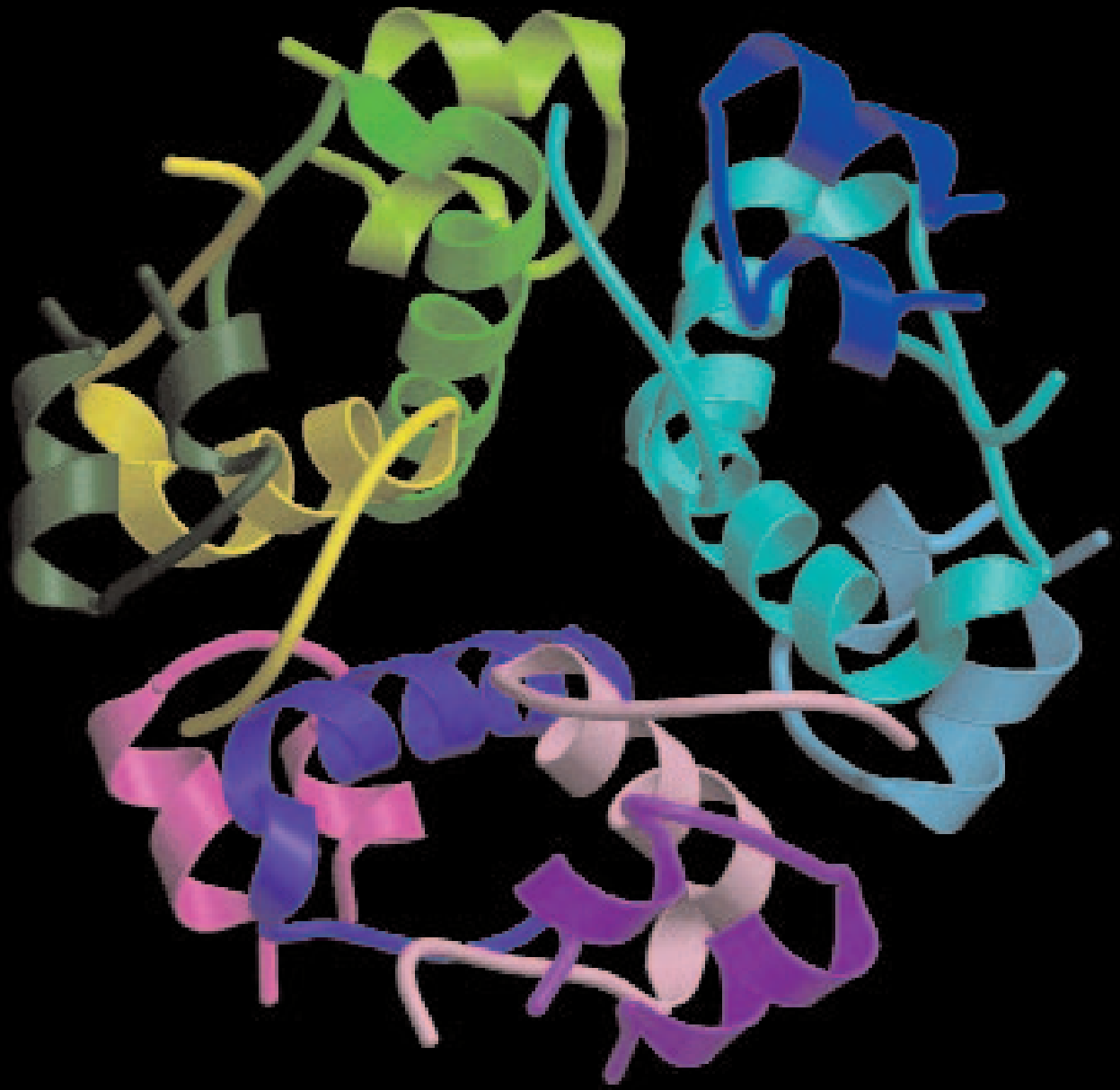
Death rates in Ireland from heart attack have decreased since the 1980's but remain high at 176 per 100,000 population compared to the average for the EU at 108.

In 2001, 11,914 people died from diseases of the circulation, i.e. 41% of all deaths were due to cardiovascular disease, stroke and other diseases of the circulation.

In people under 65, Ireland has the highest death rate from coronary heart disease in the EU.

Sources: Central Statistics Office, 2001 and WHO HEA Database 2002

Diabetes: understanding the causes



WHY DO MANY DIABETICS DEVELOP KIDNEY DISEASE?

Prof Hugh Brady and colleagues (Mater Hospital, Dublin) are studying the genes involved in diabetes and kidney disease

Up to 40% of people who have diabetes also develop diabetic kidney disease, suggesting that some diabetics are particularly vulnerable to this devastating condition. If doctors could identify susceptible people in advance, they could intervene with more aggressive early treatments. So, to search for the genetic changes that make some people more susceptible to kidney disease, we collected DNA samples donated by diabetes patients, both those with and those without kidney disease. We also studied kidney cells in the laboratory, and have identified over 200 genes which are either switched on or off when the cells are exposed to high concentrations of glucose, as happens in diabetes.

From our genetic analyses we have discovered several genes, including one called caldesmon, that seems to be important. Caldesmon codes for something called an actin-binding protein. Actin binding proteins are vital to maintaining the structure of the cell and are critical in supporting the role of the kidney in filtering blood. One particular form of the caldesmon gene is frequently seen in diabetics with kidney disease. Our next step is to study this gene further, and also some of the other genetic changes we have identified. The work will shed light on how kidney cells function, and may ultimately allow us to develop diagnostic tests to identify diabetics at risk, and perhaps even treatments for kidney disease.

DIET AND DIABETES

People with Type II diabetes should eat less animal fat and more polyunsaturated oils, based on findings from Dr Philip Newsholme and a multidisciplinary team, including postdoctoral scientist Lorraine Brennan, MSc student Áine Shine and PhD student Gordon Dixon (Conway Institute and Biochemistry, UCD)

People who suffer from Type II diabetes not only have high glucose levels in their blood, they also have more saturated fatty acids in their bloodstream. This leaves them open to coronary heart disease, a major complication of Type II, or late-onset diabetes. We have discovered, however, that the saturated fatty acids can make the diabetes worse, by affecting the all-important insulin-producing beta cells in the pancreas. The fatty acids reduce the cells' ability to handle nutrients, and especially the amino acid, alanine, which we have discovered is crucial in stimulating the beta cells to secrete insulin. Net result? The cells fail to secrete enough insulin, setting up a vicious circle: the diabetes gets worse, the fatty acid and glucose levels climb higher, and it's harder for the patient to control their diabetes.

Significantly, we have now also discovered how to break this vicious circle. Studying insulin-producing cells in the laboratory, we found that, increasing the concentration of polyunsaturated oils added to the cells, helps the cells regain much of their ability to respond to glucose and amino acids. In the patient, this would result in more insulin being secreted, thus enabling greater control over blood glucose concentrations. These important results are being published internationally, and meanwhile, we suggest that people with Type II diabetes switch to a diet rich in sunflower or safflower oils, which are primary sources of the 'right type' of polyunsaturated fats.

DYING FOR SOME INSULIN?

Dr Philip Newsholme (Conway Institute, UCD), Dr John Nolan (St James's Hospital) and PhD student Gordon Dixon (Biochemistry, UCD) are probing the causes of autoimmune diabetes

Friend or foe? That's what your immune system has to find out, so it can identify and destroy foreign invaders. Sometimes the system slips up, however, perceiving some of your own proteins as foreign, and triggering an autoimmune disease. One such disease is Type I diabetes, which develops early in life when, for reasons not yet understood, the immune system kills off the insulin-producing beta cells in the pancreas. People with Type I diabetes must inject themselves with insulin. Intriguingly, another form of autoimmune diabetes can develop late in life. In this 'latent autoimmune diabetes of adults' (LADA), the insulin-producing cells are not killed, however, but disabled.

To find what causes these two autoimmune forms of diabetes, we study pancreatic beta cells in the laboratory. We have discovered that one particular component of the immune system, called complement, dramatically reduces the ability of beta cells in Type I and LADA patients to produce insulin. Complement is activated to high levels when cells in the laboratory are exposed to blood from Type-1 and LADA patients. Significantly, we also found that complement reduces the cells' ability to consume an amino acid called alanine (derived from protein metabolism); we believe alanine and glucose are the key nutrients that trigger beta cells to secrete insulin. This important finding has just been published. Our research suggests that Type I and LADA diabetes have much in common, but more research is needed to explain what triggers the complement to attack the cells in the first place.

Diabetes

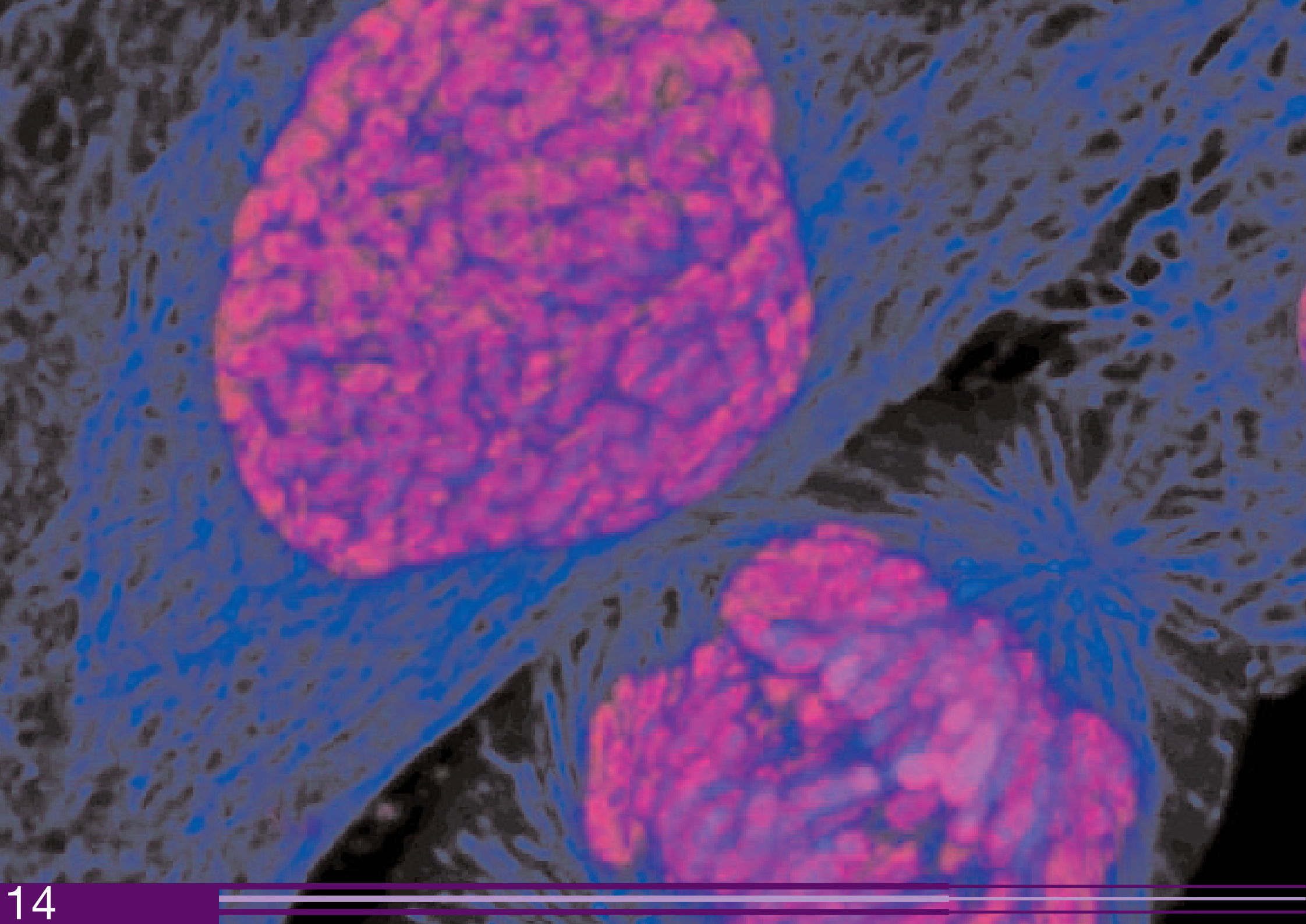
Diabetes affects people of all ages and is now considered a growing epidemic by the World Health Organisation (WHO). It is estimated that the number of people with diabetes will double over the next 10 years to 240 million worldwide. At present in Ireland it is estimated that 200,000 people have diabetes and that 50% of those are unaware they have the condition.

Diabetes occurs when the sugar (glucose) level in the blood is too high. This happens when the body is not burning up carbohydrates properly due to a fault in the pancreas, the gland that produces insulin. Diabetes may be present either when no insulin is made or when insulin is made but not working properly.

There are two types of diabetes. Type 1, or insulin dependent diabetes, usually occurs before the age of 35. A person with type 1 diabetes makes no insulin and therefore needs to inject insulin to control blood sugar levels and remain healthy. Type 2, or non-insulin dependent diabetes usually occurs after the age of 40 and is very common in old age. In this case, the person with diabetes makes some insulin, but it does not work properly.

Source: Diabetes Federation of Ireland

Cancer: causes, treatment and possible cures



USING VIRUSES TO KILL CANCER CELLS

Prof Gregory Atkins (Microbiology, TCD), and PhD student Ann Marie Murphy hope to put viruses to good use

Virus infections are normally bad news. That's because when the virus particles get inside your cells they can breed in great numbers there, then burst out of the cells that unwittingly sheltered them, and in the process kill the cells. But we wondered, could we put this cell-killing behaviour to good use, and design a virus to kill cancer cells?

To test our idea, we took cells from human lung cancers and rat prostate cancers, and transplanted these into laboratory mice. The virus we chose for our experiment is a laboratory strain, called the Semliki Forest virus vector. However, we gave it some extra genes that it could use to persuade cells to commit suicide, a process known as apoptosis. Then, we infected the cancer cells with our modified virus, and waited to see what would happen.

As we hoped, the virus particles persuaded many of the cancer cells to commit suicide. But the outcome depended on the type of cancer: most of the lung cancer cells died, for instance, while the rat prostate cancer cells do not seem to have been killed outright, although they were stopped in their tracks. To explore this difference, we have begun a new experiment, looking at further cancer types. Clearly, we are a long way from clinical trials, but one day we may use viruses to treat cancer.

BEATING DRUG-RESISTANT CANCERS

Prof Martin Clynes, Dr Robert O'Connor (National Institute for Cellular Biotechnology, DCU) and Dr Anita Maguire (Chemistry, UCC) are looking for new drugs that would make chemotherapy more effective

Chemotherapy is now widely used to treat cancer, but unfortunately some cancer cells are resistant to the drugs used. This could happen if the cancer cells possess a 'drug pump': in essence, an enzyme that pumps the chemotherapy drug out of the cell, and allows the cancer to survive. Needless to say, the hunt is on to find chemicals that can inhibit drug pumps.

Intriguingly, some non-steroidal anti-inflammatory drugs (NSAIDs), including those widely used to treat diseases such as arthritis, seem promising. Our group has already shown that one of these, indomethacin, can inhibit a particular drug pump known as 'multi-drug resistant protein 1' (MRP-1). Also we have shown in the laboratory that, when you combine this drug with the standard chemotherapy drugs, you can successfully kill more cancer cells. A small clinical trial is now underway, to see if this effect can improve specific cancer therapies for patients.

Meanwhile, we want to see if we can design a new drug that is even better at inhibiting the drug pump, and hopefully is also less toxic. For this, we manufactured over 30 different derivatives of indomethacin (UCC), and then screened their performance in the laboratory (DCU). From these we have identified two new compounds that are very effective at inhibiting the MRP-1 drug pump. We are hopeful that, one day, this approach will help to improve the success rate of chemotherapy.

NEW SCREENING TEST FOR CERVICAL CANCER

Prof John O'Leary and his team, including PhD student Niamh Murphy (Pathology, Coombe Women's Hospital, Dublin) have invented a radical new test for cervical cancer that is fast and effective and already attracting considerable international interest

Cervical cancer is a major health problem for women, but one which can be difficult to test for. That's because, in the conventional test, thousands of cervical cells are smeared on a glass microscope slide, then someone must laboriously examine the cells down a microscope, looking for abnormalities. It is time-consuming and tedious work, and depends on an individual's subjective judgment. Although some laboratories ask two or sometimes three people to examine every slide, an abnormality can occasionally be missed.

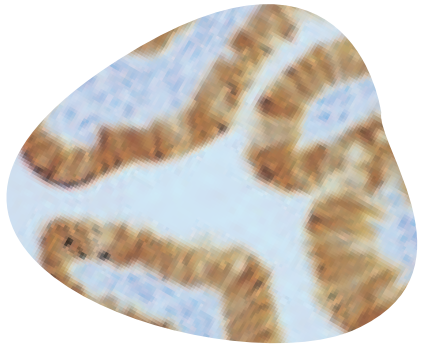
So the search was on for a new test, fast and effective, easy-to-use, and not dependent on an examiner's personal judgment. We believe we have invented just such a test.

Instead of looking down a microscope for abnormalities, **our test is essentially a chemical reaction that detects the genetic changes which occur in an abnormal cell.**

We considered five genetic changes, or markers, one of which, called p16, we found in all abnormal cervical cells. This forms the basis for our screening test: simply add p16 antibody to the cervical cells, and if any are abnormal, the mixture changes colour. The test takes just a couple of hours, and is so simple it can be done by a machine.

The other four genetic markers (called HPV, MCM5, CDC 6, and telomerase) yield additional information on the seriousness of the abnormality, and provide a valuable second test when the first one shows a problem: by combining information from all five markers, we can categorise women who are at risk of developing cervical cancer into low, medium and high risk groups, depending on which markers they have. This gives us a kind of 'molecular traffic light' screening approach, with green (low risk), orange, and red (high risk) channels.

Already there is considerable international interest in our test and, to make it as widely available as possible, we have decided not to patent our invention. Trials are under way in several countries to refine the procedure, and we are now talking to companies about designing a machine to automate the test. It is a fine success story for Irish research, and one which should make a major contribution to improving women's health and the detection rate of cervical cancer.



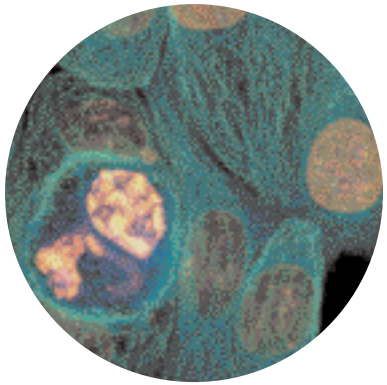
UNDERSTANDING HOW BREAST CANCER CELLS SURVIVE

Prof Finian Martin and PhD student Janice Murtagh (Pharmacology, UCD) are studying the chemical signals that are essential for cell survival

If we are ever to fully understand how tissues become diseased, we must first know how normal, healthy tissues grow and behave and organise their cells. We can then use this fundamental information to understand diseases and to learn how to treat them. So in our research into breast cancer, we study the behaviour of breast cells that are normal but have the ability to change (transform) and grow into tumours.

We study these breast cells in the laboratory, by maintaining them in suitable bathing fluids and supporting them on a specialised natural protein scaffold called an extra-cellular matrix. This allows us to study the cells' 2-dimensional and 3-dimensional organisation. From this, we were able to identify the key molecules that are used to carry the signals, inside the cells, that are essential for cell survival. While the various signals had previously been known, we were the first to show that cells need these signals if they are to organise properly.

Our work also explains why many tumour cells resist efforts to switch off the survival signals (indeed, many tumour cells actively produce molecules that keep these survival signals going). Providing an in-depth description of this 'survival' signalling pathway, as we have, suggests ways we could make it more difficult for cancer cells to survive, and may help the design of new drugs for combating breast cancer.



CASTRATION AND CANCER

Mr Kevin McEleny, Dr William Watson and Prof John Fitzpatrick (Mater Misericordiae University Hospital, and Conway Institute, UCD) are studying the life and death of prostate cancer cells

The male hormone androgen is vital to the survival of prostate cancer cells: deprive them of androgen, and most of them die. Consequently, the main prostate cancer treatment is 'androgen-deprivation therapy' - in a word, castration. Whether by drugs or surgery, this removes the androgen, and forces the tumour cells to kill themselves through a process called apoptosis. Some tumour cells eventually become resistant, as they devise a way of surviving without the androgen, and the tumour recurs. To find out how, we are studying apoptosis in prostate cancer cells in the laboratory, and in tumour cells taken from prostate cancer patients.

The enzymes that trigger apoptosis are called caspases; and they can be prevented from acting by certain 'inhibitor of apoptosis proteins' (IAPs). When you deprive prostate cancer cells of androgen, it seems they switch off their IAP genes, the caspases can then act, and the cells essentially commit suicide. To understand what happens in tumour cells that are resistant, we looked at which proteins are present and which are absent. We found that the resistant cancer cells have more of the IAPs that are seen in aggressive tumours. We believe these IAPs keep the cells alive by inhibiting the caspases, and preventing apoptosis. As proof of this, when we switched off the IAP genes in prostate cancer cells in the laboratory, we found that more of them died. This might one day lead to a new treatment for prostate cancer.

THE GENETICS OF INFLAMMATORY BOWEL DISEASE

Dr John Morgan (Microbiology, UCC), Prof Fergus Shanahan (Cork University Hospital) and colleagues, and PhD student Avril O'Riordan are investigating the genetic changes associated with bowel disease and colon cancer

People who have had a longstanding inflammatory bowel disease (IBD) are more at risk of developing **colon cancer** than healthy people. To understand why this should be, we are investigating the genetic changes that occur in the colon of people who have had IBD for at least 20 years.

For this study we were able to call on a potent new technique, known as gene chip, or gene array, technology, that essentially provides a snapshot of the genes that are active in cells at any time. Turning this technique on biopsy material taken from IBD patients revealed that genes associated with inflammation are switched on in their colon cells. This confirms what one would expect for an inflammatory disease. We also applied this technique to biopsies taken from mice, who are genetically predisposed to developing IBD-like disease, and found that, as their disease progressed, their colon became increasingly inflamed, and significantly, the activity of the inflammation genes also increased. While more work is needed to identify the genes that make some people susceptible to colon cancer, ultimately, this genetic approach might help us develop a diagnostic test for IBD and colon cancer.

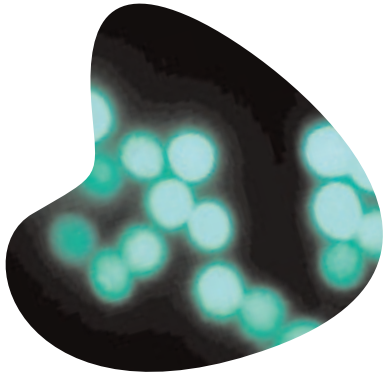
WHAT MAKES SOME CANCER CELLS MALIGNANT?

Dr Aideen Long, Prof David Croke and PhD student Eilis Foran (Biochemistry, Royal College of Surgeons in Ireland) are studying the genetic changes that make some tumour cells malignant

Why do some cancer cells become malignant, leaving the primary tumour site, and forming secondary tumours elsewhere in the body? To answer this, we are studying the genetic differences between primary tumour cells, and malignant or metastatic secondary tumour cells. Our first cell line (SW480), was taken from a primary colon tumour, the other (SW620) comes from a secondary tumour in the lymph node. Both have been widely studied around the world, and significantly, both came from the same person, and so have the same genetic make-up.

We previously compiled 'gene expression profiles' for these two cell lines, showing which genes are switched on at any time. This revealed nearly 100 differences between the primary and the malignant cells (ie, genes switched on in one cell, and switched off in the other). Now, we want to identify the changes that make the SW620 cells malignant, and for this project focused on one gene, L-Plastin, which is associated with malignant cancers: in general, the more active the L-Plastin gene, the more aggressive the tumour.

So we modified the primary tumour cells (SW480), switching on their L-Plastin gene, and found that these cells now grew faster. Significantly, we also discovered that this modification switched off a gene called E-cadherin, which is responsible for sticking cells together in tissues. The loss of expression of this gene may play a role in the metastatic spread of tumours.



THE SEARCH FOR BETTER CANCER TREATMENTS

Dr Paul Ryan (Cork Cancer Research Centre, UCC) has found a way to detect the tiny tumours that sometimes escape a patient's initial cancer treatment

Many cancer patients will undergo not just one, but often two and sometimes even three different therapies. They might have chemotherapy, for instance, combined with radiotherapy, and then surgery, the aim being to kill as many cancer cells as possible. But despite our best efforts, some tumour cells may escape even this multi-pronged attack. If they spread to form secondary tumours elsewhere, then the outlook is poor. We have used a new technique to help in the study of how cancer spreads.

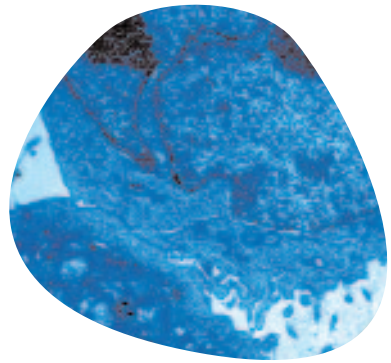
We study **oesophageal cancer,** a disease where, sadly, the outlook is often poor: in up to 80% of patients undergoing surgery, tiny clumps of tumour cells have already broken away and spread elsewhere. Called micro-metastases, these tumour cells are too small to be detected by conventional means such as CT scans. However we have detected them in rib bone marrow in a majority of oesophageal cancer patients, and our results have been replicated by scientists in Italy. Our study sheds light on the nature of tumour cell spread: if micrometastases are present in rib bone marrow, they are probably present elsewhere. Our technique is therefore a useful new tool for evaluating how successful cancer therapies are at clearing tumours.

THE CAUSES OF MALIGNANT LYMPHOMA

As part of a European study, Dr Anthony Staines and colleagues (Public Health, UCD) are investigating the causes of lymphomas and leukaemias in Ireland

It is now generally accepted that some cancers, notably leukaemias and lymphomas, can be caused by exposure to certain viruses and cancer-causing chemicals. A major EU study (called Epilymph) is now underway across Europe to investigate this, and we are conducting the Irish analysis. For this, we recruited 200 people here who have either a leukaemia or a lymphoma, and 200 healthy people for a comparison. All the data were in by March 2003, and we are now analysing the information, and expect to have the final results by the end of 2004.

So far, none of the countries taking part in the study has reported any findings regarding occupational exposure to chemicals at work. The Spanish team have reported, however, that the hepatitis-C virus is an important cause of lymphomas in Spain. However as hepatitis-C is relatively uncommon in Ireland, we do not expect that it will be a major cause of lymphoma here.



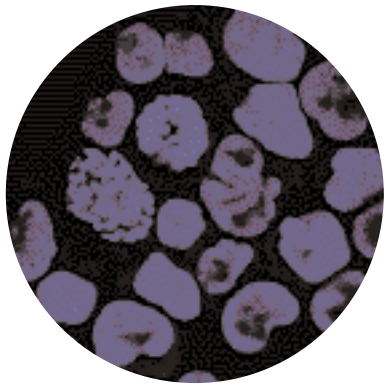
KILLER CELLS IN THE LIVER

Dr Derek Doherty and PhD student Tony Kenna in collaboration with Drs Cliona O'Farrelly and John Hegarty (St Vincent's University Hospital, and Institute of Immunology, NUI Maynooth) are studying some natural immune system lymphocytes that can kill cancer cells

The immune system produces many types of cells in its fight against infection and disease. Many are involved in recognising and killing 'foreign bodies', but **natural killer T-lymphocytes** can recognise 'friendly' cells that have become cancerous. Activate these NKT cells in mice, and they can seek and destroy liver cancer cells, for instance. But, does the same thing happen in people?

We compared NKT cells in mice and people, and significantly, found major differences. For instance, up to 40% of T cells in a mouse liver will be NKT cells, and the figure for blood is 5%. But in humans, we find fewer NKT cells: 0.5% of liver T cells, and 0.01% in blood. Furthermore, mouse and human NKT cells function differently: in mice, just one type of molecule helps NKT cells to tell friend from foe (called the 'antigen-presenting molecule', or CD1); but humans have at least five, and possibly more.

So do NKT cells play a role in killing cancer cells in humans? If this was so, you would expect cancer patients to have higher NKT levels. However, when we analysed samples from a number of colon cancer patients we discovered they had *fewer* NKT cells, although they had more of another type of immune system lymphocyte, called gamma delta T cells. Clearly, there is much we have yet to learn. NKT cells are powerful and important, and we may one day treat cancer by controlling them, but we have shown that what works in mice will not necessarily apply in humans.



Cancer

More than 21,000 Irish people will develop cancer this year, and 7,800 will die of the disease. Cancer numbers are increasing by about 1.5% every year, mainly due to population growth and aging

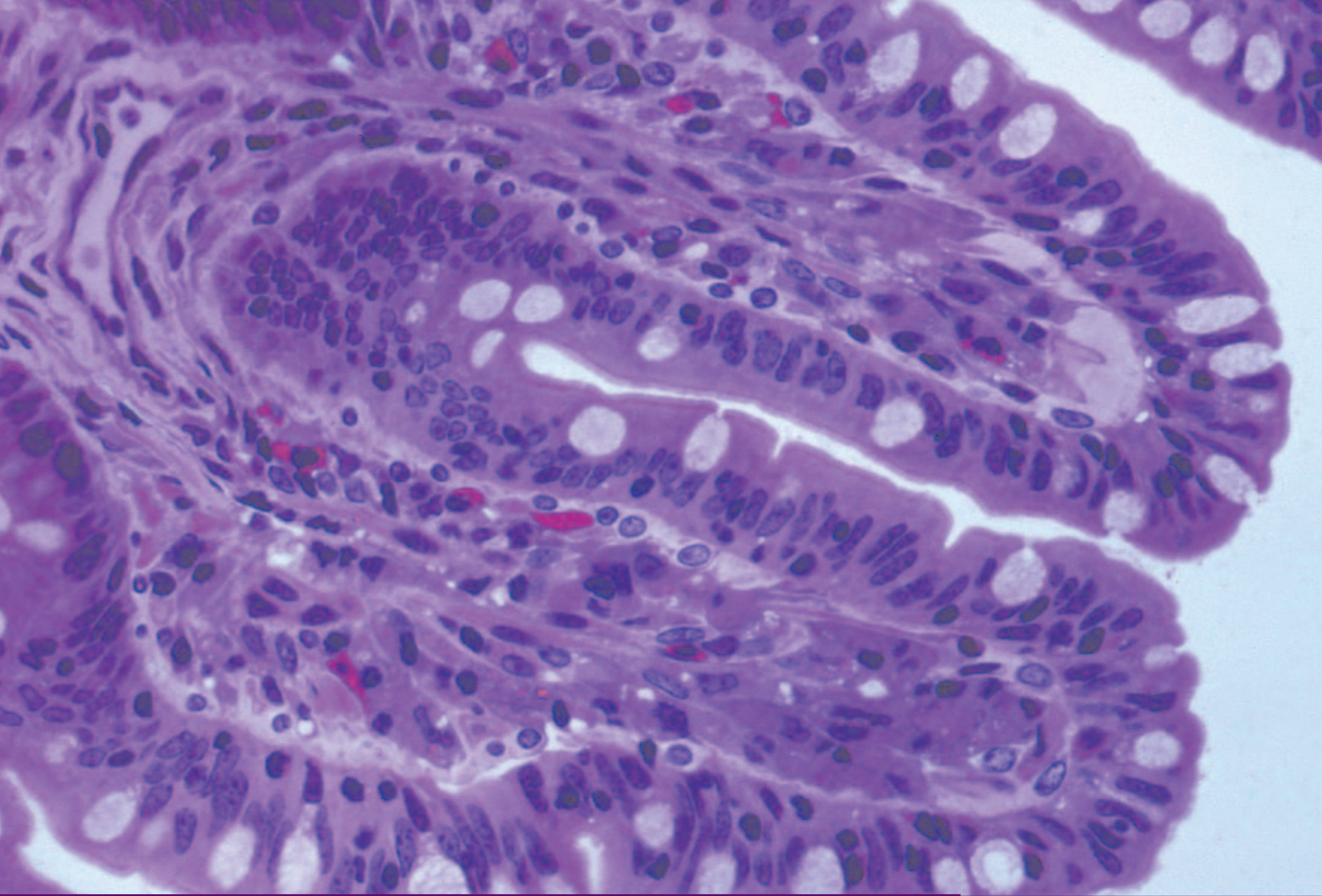
Cancer causes one-quarter of all deaths in the State and is the largest single cause of death

Cancer is responsible for more than half of the deaths of women aged between 40 and 60

The commonest type of cancer is skin (non-melanoma) followed by breast, colorectal, lung, and prostate.

Source: The National Cancer Registry

Tummy trouble: food poisoning, gastritis and heartburn



MEET THE GERM THAT CAN CAUSE STOMACH CANCER

Two TCD research teams are studying *Helicobacter pylori,* the bacterium that can cause stomach cancer and gastritis

First, Prof Cyril Smyth and PhD student Ian Carroll (Microbiology, TCD) are curious as to why some strains of the bacterium are more dangerous than others

Helicobacter pylori is a major health hazard. It can cause stomach and duodenal ulcers, gastritis, and even some forms of stomach cancer. Stomach cancer is a major killer, second only to lung cancer in the league of cancer deaths, so it is no surprise that the WHO rates *H. pylori* as a Class I carcinogen. Amazingly, over half the world's population is infected with this bacterium (most people catch it when they are young, usually from a family member who is infected). Even more intriguing, is that many people will never develop any symptoms, and may never know that they are infected. We wondered if this is because some strains of the bacterium are more likely to cause disease than others.

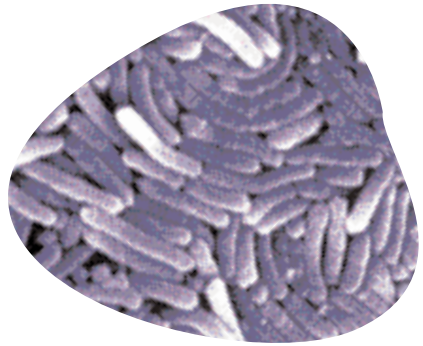
To investigate this, we studied bacteria from individuals and from members of Irish families infected with *H. pylori.* Comparing the genetic fingerprints revealed that family strains of bacteria were very similar. The Irish isolates were closely related to other northern European and eastern Asian strains. Next, we focused on a particular gene called *cagA*, which is thought to be involved in triggering the gastric problems. Our initial results suggest that the length of the bacterium's *cagA* gene, may be associated with the ability of the bacterium to cause disease or to lie silent and dormant. We intend to investigate this tantalising finding further.

Prof Colm Ó Moráin, Dr Barbara Ryan, and PhD student Gwen Murphy (Clinical Medicine, TCD, Adelaide & Meath Hospital), are studying why some people are more susceptible to infection

Why do some people, when infected with *H. pylori,* develop stomach cancer while others remain asymptomatic? It could be that their immune system is highly sensitive, and over-reacts to the infection, triggering excessive inflammation which may do more harm than good.

Inflammation is important: gastritis, and a related disorder called intestinal metaplasia (thought to be an early stage in the development of stomach cancer) are both forms of inflammation, provoked by a patient's immune system in response to the *H. pylori* infection. One gene involved in provoking inflammation, IL-1B, is associated with an increased risk of developing some forms of stomach cancer.

We investigated whether this and another inflammation gene, TNF, were associated with gastritis and intestinal metaplasia in patients infected with *H. pylori.* We studied these genes in 100 patients with *H. pylori* -related gastritis, and 60 patients with *H. pylori* -related intestinal metaplasia, and compared these with the results for 100 asymptomatic *H. pylori* -negative controls. In contrast to previous studies, we found no association between a person's TNF and IL-1B genes and their susceptibility to a *H. pylori* gastric disease. This may mean there are several routes to stomach cancer, and that some do not involve the protein from the IL-1B gene. Clearly, more research is needed. Projects such as ours are beneficial not only in studying *H. pylori* -related disease but also in understanding inflammation and its implications for the development of cancer.



HOW YOUR DIAPHRAGM KEEPS A GRIP ON YOUR OESOPHAGUS

Dr James Jones (Human Physiology, UCD) and Dr Deirdre Campion (Veterinary Physiology, UCD) with PhD student Mark Pickering, are investigating the relationship between breathing and eating

Heartburn, difficulty swallowing, and an ulcerated oesophagus . . . Just some of the symptoms associated with **gastro-oesophageal reflux disease.** That's the technical term for what happens when the ring of muscle at the base of your oesophagus relaxes, allowing your stomach contents to reflux with every breath. Some people are particularly susceptible to reflux, and we'd like to know why.

The muscle in question is your breathing muscle, the diaphragm, which forms a cross-shape, called the crural diaphragm, at the base of the oesophagus. To understand what happens in gastro-oesophageal reflux disease when the crural diaphragm temporarily fails, we studied the nerves controlling various parts of the diaphragm. We discovered that, first, nerves supplying the crural diaphragm are subtly different from the nerves supplying the rest of the diaphragm; and second, that there are not one but two nerve pathways carrying pain information from the oesophagus to the brain. This new anatomical information could be important for doctors treating oesophageal pain.

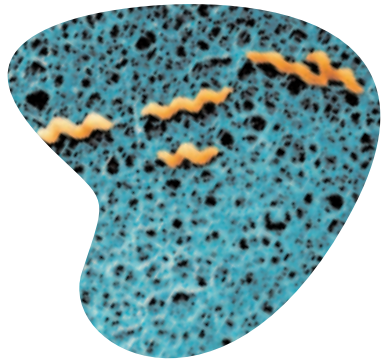
But why should a breathing muscle be so important in digestion? Perhaps the diaphragm originally evolved to control the oesophagus? To answer this evolutionary question we looked at the pipid frog *Xenopus laevis.* It has a muscle which, like our diaphragm, encircles the oesophagus, and was thought to move air in and out of the frog's lungs. We found that this muscle attaches to the oesophagus near the stomach, and when it contracts, oesophageal pressure increases. So we now believe the diaphragm probably evolved as an aid to digestion, rather than breathing.

A NEW FOOD POISONING BACTERIUM

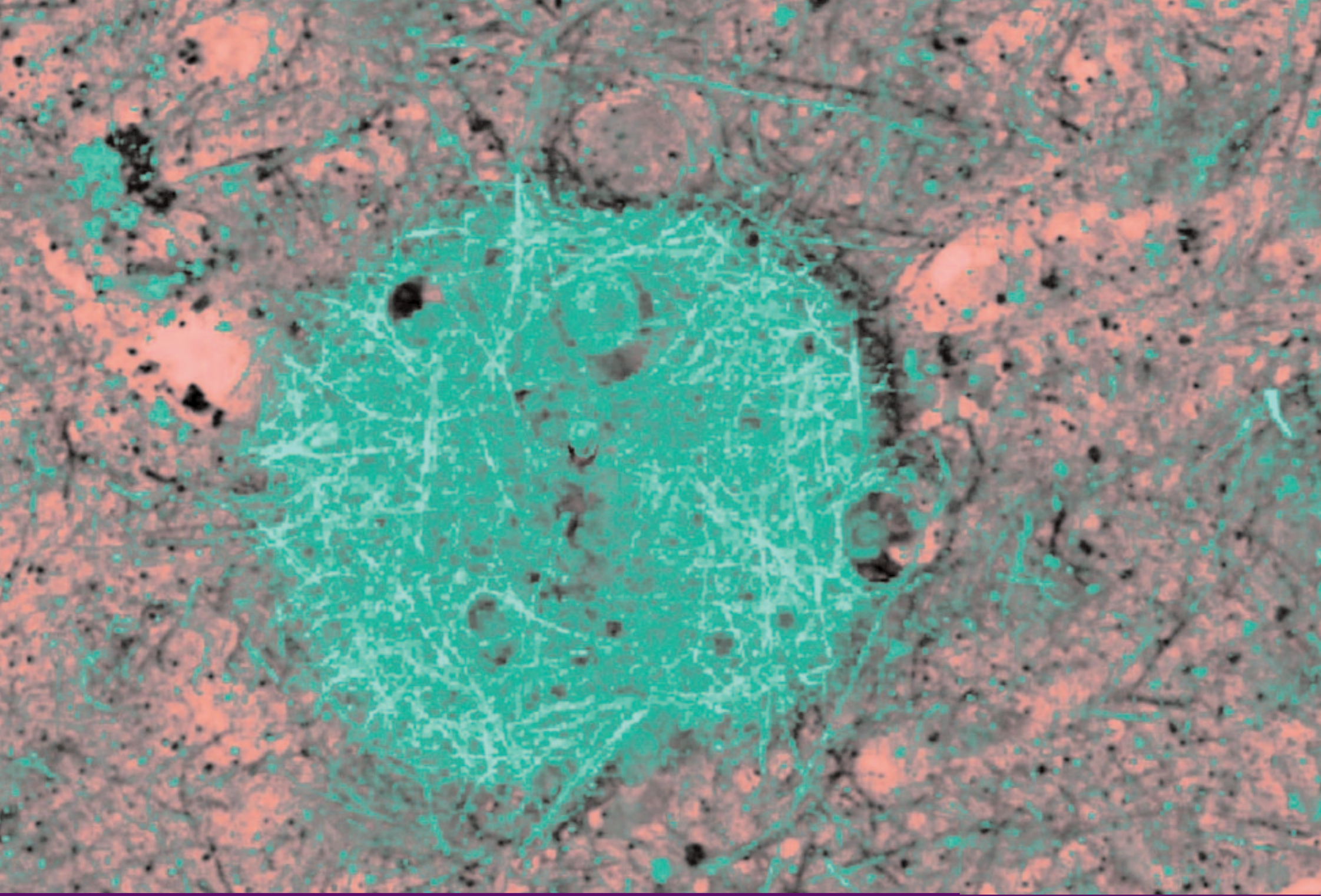
Dr Adele Mooney and Dr Billy Bourke (Children's Research Centre, Our Lady's Hospital for Sick Children) have greatly added to our knowledge about *Campylobacter upsaliensis*

One of the major causes of food poisoning are the Campylobacter family of bacteria. The most common and best-known member is *C. jejuni,* but a relatively new species called *C. upsaliensis,* which was discovered only in 1982, is now recognised as an important cause of diarrhoea, especially in children. Not much is known about it, not least because it is difficult to work with and to grow in the laboratory. However, we have managed to conduct a number of experiments which help explain how *C. upsaliensis* causes disease.

First, we have shown that *C. upsaliensis* possesses the gene for a toxin called cyto-lethal distending toxin. Several other food poisoning organisms, such as *E. coli*, also produce this toxin, which prevents cells completing their normal cell cycle. This toxin probably explains our second finding, which is that if you add some *C. upsaliensis* to cultures of human intestine and immune cells growing in the laboratory, the cells are prevented from reproducing and ultimately die through a form of cell suicide called apoptosis. Finally, we have also shown that *C. upsaliensis* bacteria are good at invading both tissue culture cells grown in the laboratory and cells taken directly from the lining of the small bowel. Taken together, these findings are a valuable insight into how *C. upsaliensis* causes disease, and should help in the search for a treatment.



In the mind: memory and brain disorders

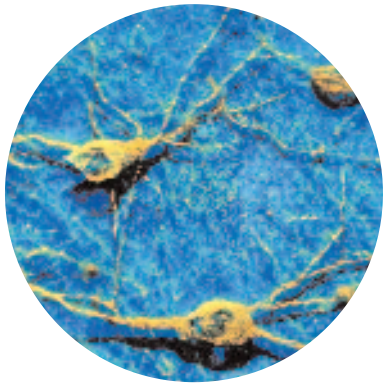


THE SCIENCE OF ABSENTMINDEDNESS

Why are older people more absent-minded? Prof Ian Robertson and PhD student Nicola Porter (Psychology, TCD) are investigating with their ‘oops test’

Oops! It is easy to make a simple mistake when we are doing something routine, because we are not paying attention to what we are doing. Why are some people more prone to this absent-mindedness than others? To study this in the laboratory, we ask people to take our **Oops Test.** It is a relatively simple task: just press a button every time a number shows on the screen, but not if the number is 3. The trick is that the 3 doesn't appear very often and people can be easily 'lulled' into pressing it by mistake.

We find that older people make more mistakes on this test than their younger counterparts. By recording people’s brain activity while they are doing our test, we can see that the pattern of activity is different in a young person compared to an older person. This is also true of young people who are very good at maintaining their attention (and consequently make fewer absent-minded slips) compared to those with poor concentration. Ultimately, we want to improve people’s attention and memory skills, and we are now designing exercises that will hopefully help older people to become less absent-minded.



MEMORIES ARE MADE OF THIS

Dr Áine Kelly and Prof Marina Lynch (Physiology, TCD) are studying what happens in the brain when we learn and remember something

Thinking involves nerve cells in the brain signalling to, or communicating with, each other. Learning and remembering are thought to occur when connections between nerve cells are strengthened, but this process declines with age and is impaired in patients with **neurodegenerative diseases such as Alzheimer's disease.** Neurobiologists are attempting to identify the causes of the decline by studying an animal model of learning and memory called call long-term potentiation (LTP).

For our investigation into LTP (and, by extension, learning and memory), we focused on a natural brain chemical called nerve growth factor (NGF), which improves the growth and survival of nerve cells. By studying the brains of rats, we were able to examine the cellular changes that happen during LTP and to follow the signalling pathways that are stimulated by NGF. Significantly, we identified one pathway that is more active when LTP occurs. We also identified one protein in this pathway, ERK, that is required for consolidating memories. This sheds light on how memories are made, and ultimately it may help scientists to design new treatments to prevent, or possibly even cure, neuro-degenerative diseases.

FISH OIL IS GOOD FOR YOUR BRAIN

Prof Marina Lynch, PhD student Emily Vereker and MSc student Peter Lonergan (Physiology, TCD) believe that eating fish oil could help protect your brain from neurodegenerative diseases

Older people, and people with neurodegenerative disorders such as Alzheimer's disease, have trouble remembering and learning. These problems seem to arise because the hippocampus region of the brain, which plays an important role in memory and learning, is particularly susceptible to damage. That damage might be simply accumulated 'wear and tear', or perhaps caused by some disease. Either way, the immune system often responds to such damage by triggering inflammation. Our laboratory has previously shown that this inflammation causes brain cells to become stressed and eventually die, just as in an older brain. We have also discovered that exposing rats to radiation triggers the same inflammation, and the same kind of brain cell damage. The net result is a reduction in the nerve cell signalling that is associated with learning.

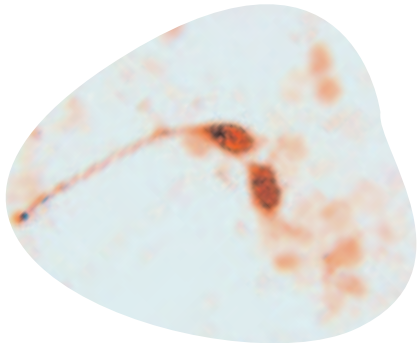
We have now discovered, by studying the brains of rats, that one protein involved in provoking the inflammation reduces the polyunsaturated fatty acids in the membrane of the nerve cells, making the cell membranes more rigid. Significantly, when we fed rats a diet that included a polyunsaturated fatty acid found in fish oil (eicosapentaenoic acid, or EPA), it helped protect their brain from this kind of damage, and even reversed the damage caused by radiation. Our evidence suggests that the EPA works by increasing the amount of an anti-inflammatory protein in the brain. These discoveries could have significant implications for the treatment of people with neurodegenerative diseases.

UNDERSTANDING PARKINSON'S DISEASE

Dr Kieran McDermott, Dr Aideen Sullivan and PhD student Terri Wood (Biosciences, UCC) are studying the neurobiology of nerve cells in the brain

If you could peer inside the brain of somebody who has Parkinson's disease, then you would see that certain nerve cells in the substantia nigra were progressively degenerating and dying. These are the dopamine-producing neurons, and their loss causes profound effects. Normally, our brain produces chemicals called neurotrophins, which encourage nerve cells to grow and survive, and several researchers are experimenting with these to treat Parkinson's. But while some positive effects are seen, overall the results are ambiguous.

As neurobiologists, we are keen to understand how neurotrophins affect nerve cells, how the various nerve cells interact, and **why dopamine-producing neurons sometimes die.** So we took cells from the substantia nigra (both dopamine-producing neurons and the glial cells which provide them with essential support), grew them in the laboratory, and looked at the effect of adding two neurotrophins, GDF-5 and GDNF. Adding both together doubled the survival rate of the neurons, but it also increased the number of glial cells. Our next step is to understand why: do more neurons survive simply because there are now more glial cells? Or do the neurotrophins have a direct effect on the neurons? This information could help in treating Parkinson's disease: one experimental operation involves transplanting stem cells into a patient's brain, but the transplanted cells don't survive well. Our results suggest that adding the GDF-5 and GDNF neurotrophins might improve the success rate of these transplants.



THE BRAIN, THE IMMUNE SYSTEM AND ALZHEIMER'S DISEASE

Dr John O'Connor and PhD student Hilary Murray (Physiology, UCD) are studying how the immune system can hit our ability to learn and remember

Ever noticed how, when you are ill with an infection, it can be harder to learn and remember things? That's because some of the compounds your immune system produces to fight the infection have a downside: they can also affect the brain processes involved in learning and remembering. This also explains some of the symptoms seen in neurodegenerative diseases such as Alzheimer's and Parkinson's: in these cases, the immune system triggers inflammation in the brain, perhaps because it wrongly perceives the brain damage as some kind of infection that needs to be fought.

The immune chemicals involved include a group of proteins called cytokines, which are important in triggering inflammation. To understand how these affect learning processes, we studied rat brain, which we keep bathed in artificial cerebral-spinal fluid in the laboratory. When we add a cytokine to the fluid, it reduces the nerve cell communications (called 'long-term potentiation') that are fundamental to learning. We have now discovered two proteins (called JNK and p38) which inhibit the cytokine, and restore the long-term potentiation. As well as shedding light on how brain inflammation can cause neurological problems, our discovery suggests new avenues to explore in the search for drug treatments for Alzheimer's and Parkinson's disease.

Alzheimer's disease

It is estimated that 33,000 people in the Republic of Ireland have dementia. Most of these have Alzheimer's disease, which is the most common cause of dementia and represents about 60% of all cases. Alzheimer's disease is a progressive degenerative disease, which destroys brain cells. Currently there is no effective treatment to stop this process and ultimately the disease is fatal. However, there are some drugs available that appear to alleviate some of the symptoms of Alzheimer's disease in some people.

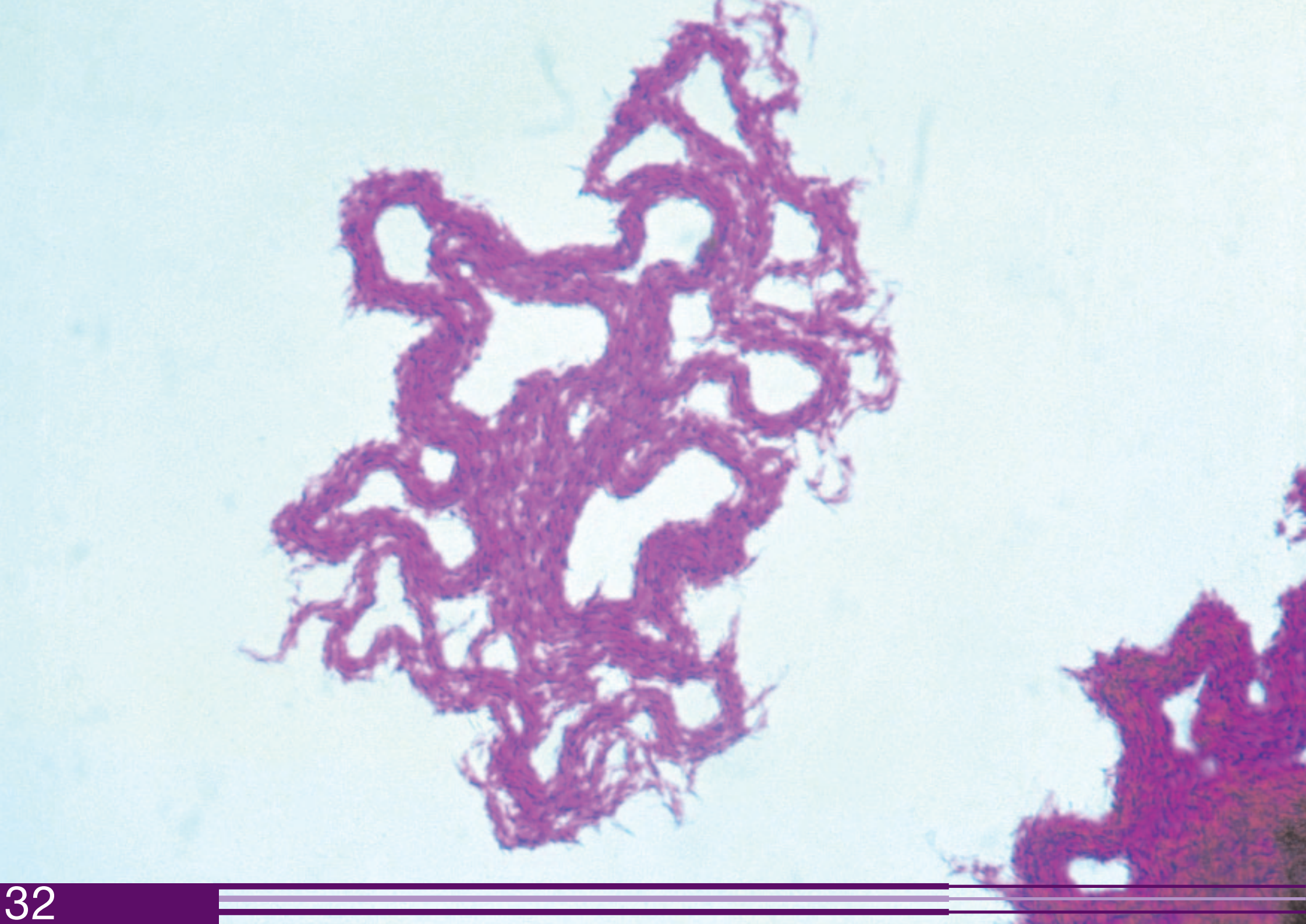
Source: The Alzheimer Society of Ireland

Parkinson's disease

Parkinson's disease is a slowly progressive condition, which occurs when the brain produces insufficient quantities of the chemical dopamine. This results in many changes relating to movement, balance and co-ordination.
Parkinson's disease affects about one person in every 1,000. It is more common in later years. The cause of Parkinson's disease is not yet known, but significant progress in understanding Parkinson's has been made in recent years.
There is no known cure at present, but medication can usually control symptoms to a marked degree.

Source: Parkinson's Association of Ireland

Microbes, parasites and your immune system



FIGHTING DRUG-RESISTANT YEAST INFECTIONS

Prof David Coleman, Dr Derek Sullivan, Dr Gary Moran, and students Sarah Gee and Emmanuelle Pinjon (School of Dental Science, TCD) are hunting for new drugs to treat *Candida dubliniensis*

It's not every day you discover a new organism but, in 1995, our group discovered a new species of yeast, now called *Candida dubliniensis.* It causes distressing mouth infections in elderly people, for instance, or people with cystic fibrosis or AIDS, and in the rare cases when it gets into the bloodstream, it can be fatal. Yeast infections are treated with the antifungal azole drugs, but *C. dubliniensis* quickly becomes resistant. So we are studying drug resistance in *C. dubliniensis,* as a prelude to developing new antifungal drugs.

***C. dubliniensis* was discovered in Dublin**, but is found worldwide and has probably been around for centuries. We believe it came to prominence in the 1990s when AIDS patients were given azole drugs as a precaution against fungal infections. Ironically, this practice probably encouraged the emergence of drug-resistant *C. dubliniensis.*

We have now found that, if you give azole drugs to *C. dubliniensis* in the laboratory, it quickly becomes resistant, switching on a 'drug pump' protein that moves the drug molecule out of the yeast cells. The behaviour of this particular drug pump differs to those found in other yeasts. Our next task is to have the *C. dubliniensis* genome sequenced (hopefully during 2004). This information will allow us to identify the yeast's weak points, and hopefully lead to the development of a new generation of antifungal drugs.

HOW VIRUSES ESCAPE THE IMMUNE SYSTEM

Better vaccines and a better understanding of our immune system could come from research being done by Prof Luke O'Neill and PhD student Elisabeth Brint (Biochemistry TCD)

It is a humbling thought, but a tiny virus knows more about our immune system than we do. The virus in question is Vaccinia, a pox virus widely used to vaccinate against smallpox, and which is particularly good at evading the immune system. We hope that, if we can discover how Vaccinia operates, it will shed light on our immune system, and lead to better vaccines.

We focused on the immune cells' early warning alarm system. These are the toll-like receptors, a group of 10 recently discovered molecules which alert your body to the presence of an invading microbe. Normally, these trigger the immune system to wage war on any invader, but Vaccinia can disable the alarm, and so survive to cause an infection. This also explains why, very occasionally, a Vaccinia vaccine can make some people sick.

Initially, scientists thought the toll-like receptors recognised only bacteria, but we showed that they also have a role in eliminating viruses. And we have now found a Vaccinia protein, A52R, that can disable toll-like receptors, effectively switching off the body's alarm. When we modified some Vaccinia so that it lacked this protein, and then infected mice with it, we found that the disabled virus was eliminated by the mice's immune system much faster than the normal virus. We believe this modified virus might make a more effective smallpox vaccine, and that our work has improved our understanding of how the immune system deals with viruses.

NEW DRUGS TO FIGHT TB

How do TB bacteria survive inside your body? Dr Wim Meijer (Industrial Microbiology, UCD) and PhD student Donal Wall are investigating

TB infection is notoriously difficult to cure. This is partly because most TB strains are now resistant to all the available antibiotics, and partly because the TB bacterium, *Mycobacterium tuberculosis*, can actually hide out within the very cells of your immune system that are supposed to detect and kill the infection. If we could understand how the bacteria survive inside these macrophage immune cells, it might help scientists to design more effective TB drugs. Unfortunately, *M. tuberculosis* is difficult to work with in the laboratory. So instead, we are studying a close cousin, *Rhodococcus equi*. This bacterium, which also hides out in our macrophage cells, causes a potentially fatal pneumonia in foals, and a TB-like disease in some people.

To date, we have discovered that, to survive inside the cells, the invading *R. equi* rely on two enzymes which allow them to feed on the cells' lactate and lipids. When we disable these two bacterial enzymes, the bacteria become weaker and are much less virulent. Our next step is to see what else is crucial for the bacteria's survival in the cells, and we are already looking at iron.

Of course, what is true for R. *equi is not* necessarily true for *M. tuberculosis.* But if we can identify enzymes that are crucial for the bacteria's survival, and if chemists can design drugs that block these enzymes, then we might just have an effective new drug for TB.

HOW FOOD POISONING CAN AFFECT YOUR NERVES

Dr Martina Prendergast and Dr Anthony Moran (Microbiology, NUI Galway) are studying how a food pathogen causes Guillain-Barré syndrome

The symptoms start with a tingling in the fingers and toes that can rapidly progress to full-blown paralysis. Fortunately, most people who develop Guillain-Barré syndrome (GBS), make a full recovery. But the intriguing thing is that three-quarters of GBS cases are triggered by an infection. And 66% of those are caused by *Campylobacter jejuni*. Found in undercooked food and contaminated milk, *C. jejuni* is the leading bacterial cause of food poisoning. But how does food poisoning trigger GBS?

The problem arises because *C. jejuni* cunningly disguises itself as a human nerve cell, camouflaging itself in the same sugars found on nerve cells, and fooling the immune system into treating it as a friend, not a foe. Eventually, however, the system notices and attacks the invading bacteria, but unfortunately often attacks the nerve cells too.

We have now proven that GBS is indeed an autoimmune disease: taking the surface sugars from the bacteria, we produced antibodies which acted against both the bacterial sugars and those found on nerve cells. Significantly, our new understanding of the mechanism involved, has enabled us to perform safety tests on **a new vaccine** against *C. jejuni* which the US Navy is testing, and to ensure that the vaccine would not cause GBS. As well as protecting military personnel from 'travellers diarrhoea', such a vaccine could benefit other high-risk groups who are frequently exposed to infection.

NEW DRUGS TO TREAT MALARIA?

Why are some immune suppressant drugs also effective against malaria? Dr Angus Bell and PhD student Paul Monaghan (Microbiology, TCD) are investigating

Strange, but true: some **immune suppressor drugs,** such as those given to people receiving organ transplants, are also effective against malaria. The world badly needs new malaria drugs, but clearly immune suppressors won't do, because they depress people's immune system.

In the early 1990s, researchers in Switzerland, among them one of us (Angus Bell), found derivatives of these drugs which were anti-malarial, and which did not suppress the immune system. The company holding the patents on these drugs did not want to develop them as anti-malarials at that time, however. Our idea now is to find out how these compounds work, by identifying what they target in the malaria parasite, then design different drugs aimed at the same target.

We are interested in one immune suppressant drug, called FK506. This, we discovered, interacts with a protein found only in the malaria parasite, and which we call the FK binding protein (FKBP). We have now characterised the protein, and its functions in the parasite.

Hopefully, we can use this information to design a drug to target the FKBP and kill the malaria parasite, but not suppress people's immune systems. Already, we are working with several new compounds derived from FK506 and given to us by a US biotech company. So the next generation of anti-malaria drugs may yet come from Irish medical research.

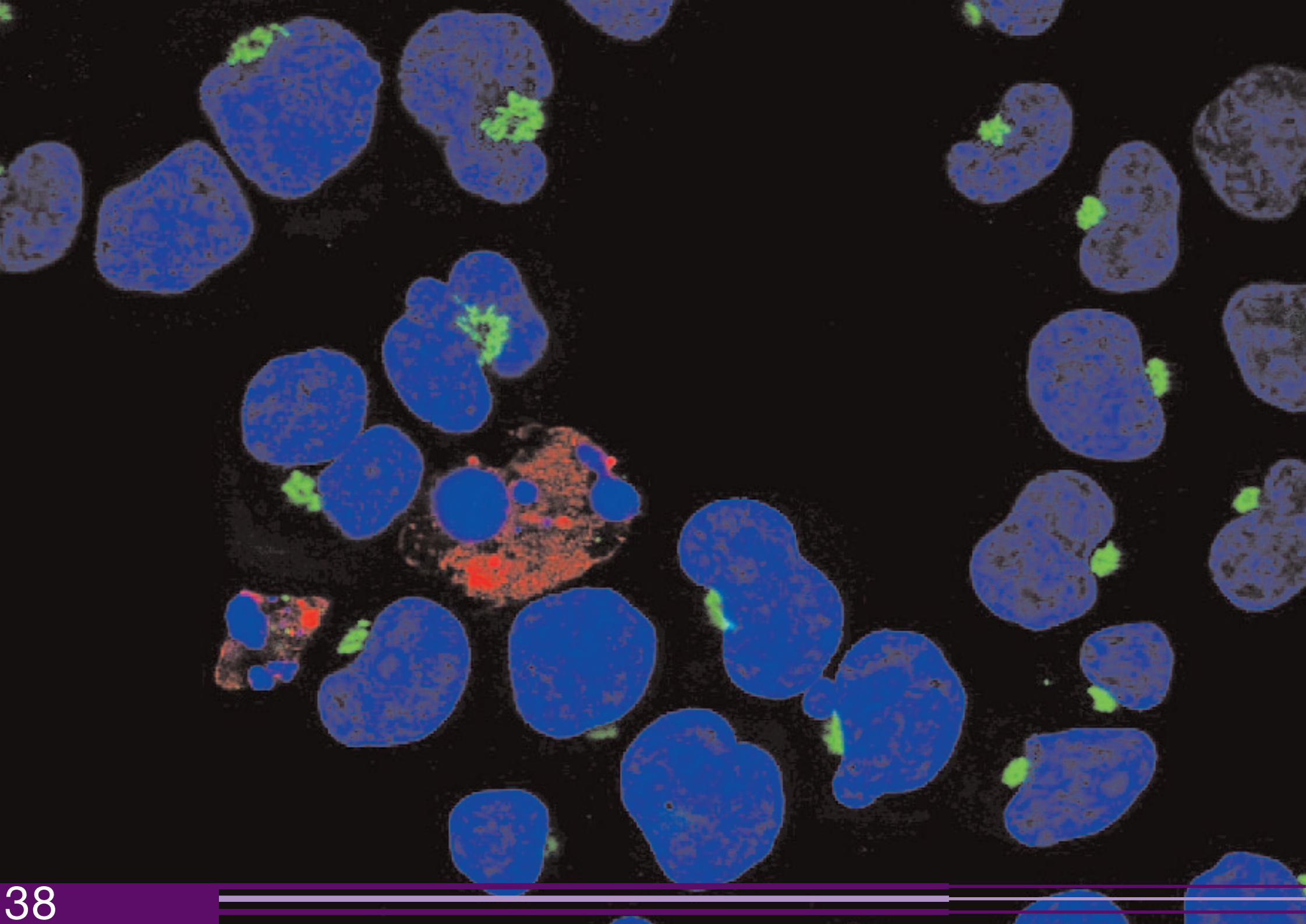
REDUCING THE RISK OF ABDOMINAL ADHESIONS

Ronan Cahill, Prof HP Redmond and Dr J Wang (Surgery, Cork University Hospital) are looking at ways to minimise the complications of abdominal surgery

Abdominal surgery always produces some internal scarring. This is a natural reaction and it can be a good thing, helping to limit any infection and to support the tissue as it heals. Frequently, however, the scars become 'sticky', forming adhesions that glue bits of abdominal tissue together. And when that happens, problems can rise: acute problems, such as bowel obstruction; and long-term problems, such as infertility in women, if the fallopian tubes are affected. Clearly, we need to minimise the risk of these peritoneal adhesions occurring, but without eliminating scarring altogether.

From previous studies elsewhere, we know that adhesions are more likely if there is some infection (as might happen with a burst bowel). We also know they are due in part to inflammation at the site; the mechanism was not clear, but it was thought the immune system's mast cells were involved. Working on special laboratory mice which have almost no mast cells, we have now shown that they seldom develop adhesions. This confirms the role of inflammation and mast cells, and suggests that we might be able to minimise adhesions if we could find a way of damping the action of the mast cells. In a separate study, again on laboratory mice, we found that applying special anti-bacterial solutions during an operation will significantly reduce the risk of adhesions. These solutions are occasionally used in transplant operations, but following this study, a US company is now looking at their wider use in abdominal surgery.

Life and death of cells

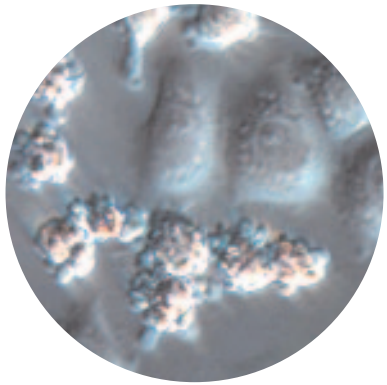


WHAT CONTROLS WHEN CELLS DIE?

Prof Seamus Martin and PhD student Helen Conroy (Genetics, TCD) are studying the chain of events involved in apoptosis

You have spaces between your fingers because, when you were developing in the womb, the cells that filled those spaces selectively died off, leaving the individual digits. The missing cells did not die haphazardly, but through a process of programmed cell death called **apoptosis.** This process, involving the controlled demolition of cells with minimal disturbance to neighbouring cells, is used to eliminate cells that are no longer required or that are a potential threat. We see it not just in development, but also where cells are undergoing constant renewal (all dividing tissues), and where cells are damaged, infected or simply aged.

Apoptosis is controlled by a family of proteins called caspases, that are present in all cells and activated at the onset of apoptosis. Once the caspases are activated, the cell is committed to dying and there is no going back. In this research, we identified two new proteins (called NAC and ASC) that activate caspases and hence trigger cell death. Our next step is to identify the conditions in the cell that activate these proteins, and so initiate the chain of events that ends with the cell's death.



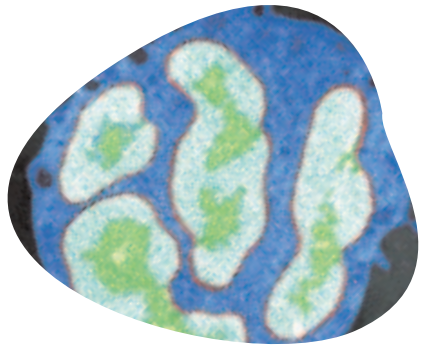
TOO MUCH OF A GOOD THING CAN BE BAD FOR YOU

Dr William Watson and PhD student Belinda Doyle (Mater Hospital, Dublin and the Conway Institute of Biomolecular and Biomedical Research, UCD) are studying why some blood cells don't die when they should

Wounds normally come with infections, so our body's 'wound response' includes a massive attack on any invading bacteria. This attack is mounted by neutrophils, a type of white blood cell that produces toxins to kill the pathogens. Unfortunately, some people undergoing major surgery find that their body perceives the operation as a wound and, though there is no infection, responds with a flood of neutrophils. This can lead to potentially fatal disorders, such as systemic inflammatory response syndrome, triggered partly by the toxins the neutrophils produce.

To understand why this can arise, we need to understand a neutrophil's life cycle. This short-lived cell normally survives in the blood for about six hours, then dies by a process of controlled suicide, called apoptosis. We believe that inappropriate inflammatory responses happen if apoptosis is delayed, and the cells are prevented from dying. The proteins that control apoptosis include inhibitors, which prevent it happening too early, and caspases, which actually trigger apoptosis. The balance between these determines whether a neutrophil lives or dies, and for apoptosis to happen, production of the inhibitors must be switched off, and the caspases switched on.

Working with neutrophils taken from patients who have suffered an acute inflammatory response, we discovered a particular protein that is important in inhibiting apoptosis in these cases. It seems these neutrophils don't die because they have not matured properly, information which may be useful in helping us to treat these inflammatory diseases.

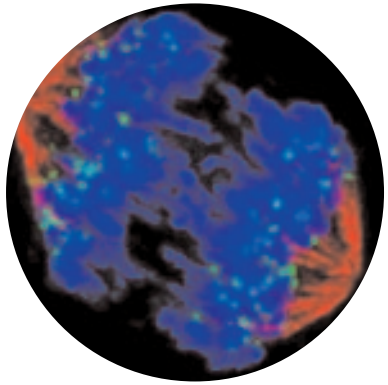


THE FREIGHT CONTROLLERS OF THE CELL

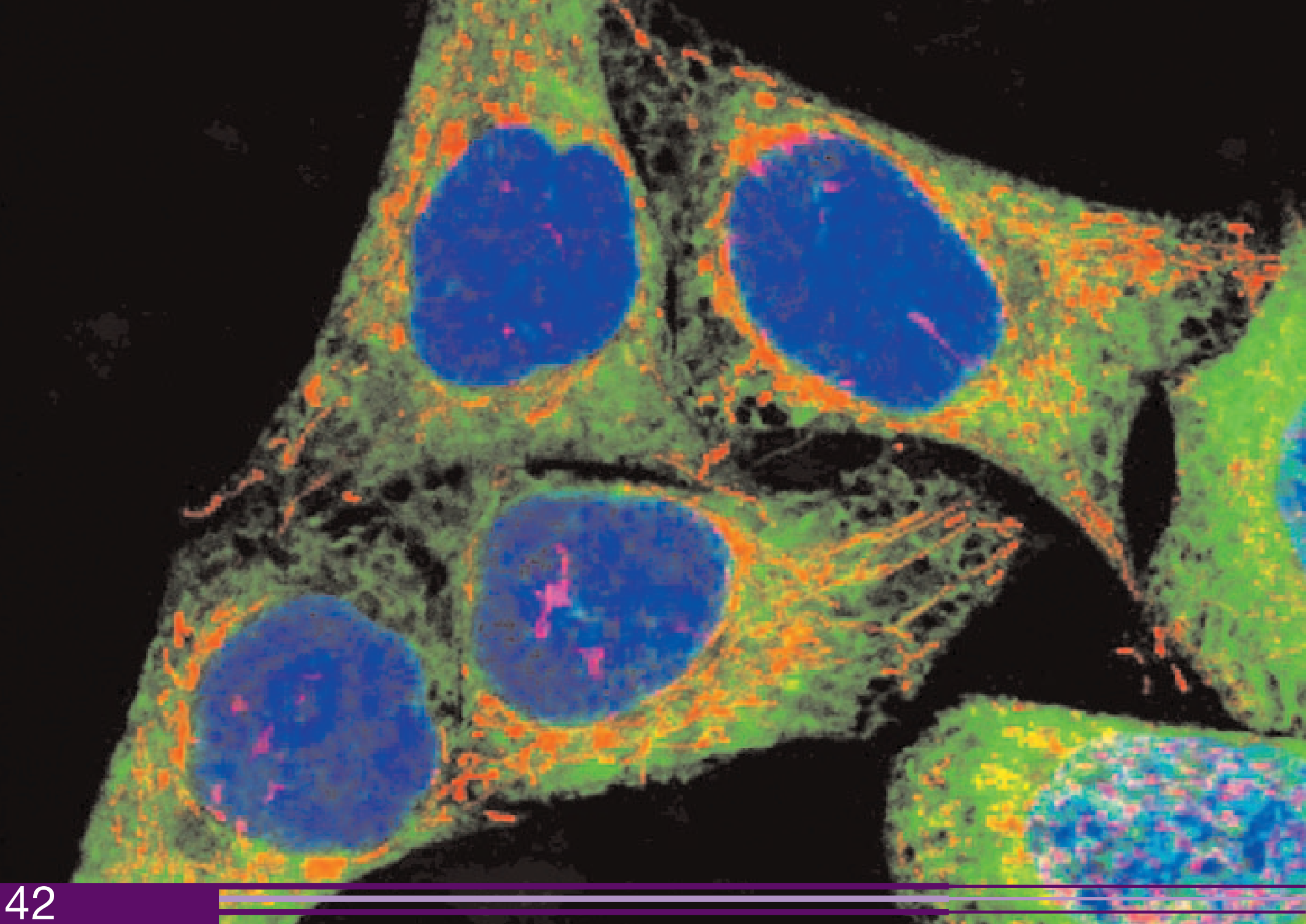
Dr Mary McCaffrey, Dr Deborah Wallace and Andrew Lindsay (Biochemistry, UCC) study how nutrients are transported in and out of cells

Haemochromatosis is a disease that develops when too much iron is absorbed through the gut. Our bodies can't cope with the excess, so unless blood is removed or lost, the iron will accumulate leading to complications. It's just one example of what can happen when the machinery that controls the transport of nutrients in and out of cells becomes faulty. To discover what is going on, we study the proteins involved in controlling these transport processes.

The main controllers are the Rab proteins, 60 or so enzymes that regulate the transport of 'cellular freight'. Rab4, for instance, helps sort through the molecular freight that has arrived in the cell; and Rab11 controls the transport of appropriate freight back to the cell surface (recycling). By studying these enzymes, we have identified six other proteins involved in this process, called the 'Rab11-family interacting proteins' (FIPs). Sophisticated biotechnology techniques allow us to pinpoint where in a cell the proteins are active, and we are now characterising the FIPs, most of which interact with Rab11 at the recycling depots. It has also become clear that Rab11 and FIP4 are also involved in the upheaval that happens when a cell divides to form two daughter cells. New cell membrane must be put in place then, and we believe the Rab and FIP proteins play a role in controlling this movement. Our next step is to understand what is happening at the molecular level, work which may ultimately help us to understand diseases such as haemochromatosis.



Genes, cells and disease



HOW DO ANAESTHETICS WORK?

Why do some anaesthetics occasionally cause a potentially fatal side effect? Work by Prof Kay Ohlendieck (Biology, NUI Maynooth), Prof James Heffron (Biochemistry, UCC), and PhD student Louise Glover, could lead to safer anaesthetics with fewer side-effects

Anaesthetic gases are wonderful drugs that make modern surgery possible. Unfortunately, some of these narcotics occasionally cause severe, even life-threatening side effects. And because scientists still don't know how they work, we also don't know what causes these dangerous side effects.

Our research team is interested in halothane, an anaesthetic which can trigger a rare, but potentially fatal problem called **malignant hyperthermia;** about one person in a thousand is at risk. In malignant hyperthermia, the patient's temperature rises quickly, and their muscles become very rigid; hopefully, they will survive, but their heart, lungs and kidneys will probably be damaged.

To understand how malignant hyperthermia happens, we looked at halothane's effect on muscle cells, comparing muscle samples taken from normal people and from people who are sensitive to halothane (and at risk of developing malignant hyperthermia). We discovered that the drug activates a muscle protein which is involved in converting nerve signals into muscular contractions: when the drug activates the protein, it releases a flood of calcium ions, triggering severe contractions and the malignant hyperthermia. The difference between 'sensitive' and 'normal' muscle is clear-cut: sensitive muscle reacts at very low doses of the drug whereas normal muscles react only to very high doses.

Our discovery is an important step in understanding how anaesthetics work, and explaining malignant hyperthermia. The result, which has just been published internationally, will hopefully lead to the design of safer drugs with fewer side-effects.

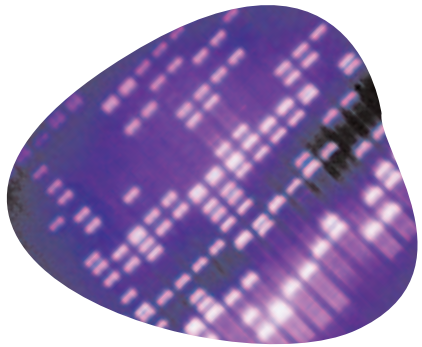
A 10,000 YEAR OLD DISEASE

When Prof David Croke and his PhD student Jonathon Flanagan (Biochemistry, Royal College of Surgeons in Ireland) studied the genetics of galactosaemia, they discovered it arrived here with the first settlers

Every child born in Ireland is tested at birth for a number of genetic diseases, including galactosaemia. About 1% of Irish people carry a galactosaemia mutation, and people who inherit a mutation from both of their parents cannot convert galactose (one of the milk sugars) into glucose. This serious and potentially fatal disorder must be detected early, hence the infant screening programme.

There are, however, several forms of galactosaemia, each caused by a different mutation. The most common one in Ireland, Q188R, is due to a mutation in the GALT (galactose-1-phosphate uridyltransferase) gene on chromosome 9. We know from other European studies that the various mutations arose at different times in history. By studying the DNA sequences that surround the Q188R mutation, we sought to learn more about its history, and hence also **the genetic history of the Irish people.**

Comparing DNA samples donated by 350 galactosaemia patients from all over Europe, we discovered that the Q188R mutation is about 10,000 years old, so it probably arrived here with the first settlers from Europe about 9,000 years ago. This kind of genetic information is increasingly useful, first, in designing screening programmes, and second, because scientists now know that some drugs for certain diseases work best in people with a particular genetic make-up. Our work here continues, and we are now studying why some forms of Q188R are more severe than others.



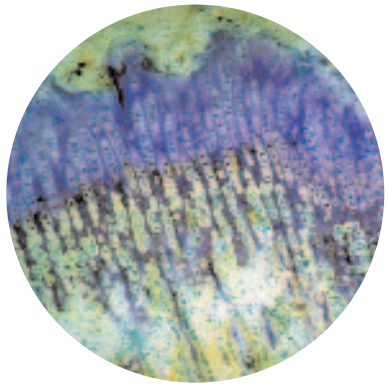
NEW WAYS TO TREAT A BRITTLE BONE DISEASE?

Dr Jane Farrar, Prof Pete Humphries, Dr Paul Kenna, Dr Sophia Millington-Ward and PhD student Danny Allen (Genetics, TCD) are hoping to develop a treatment for an inherited form of brittle bone disease

Osteogenesis imperfecta (OI) is a genetic disease that results in brittle bones. The root cause is a fault in **a gene that codes for collagen**, which is essential for the body's skeleton. The severity of OI varies widely, however: some people are so badly affected that they die young, while others develop only a mild form of the disease. As yet, there is no effective treatment.

The reason OI is so variable, and so difficult to treat, is because there are actually many different forms of the disease: to date, scientists have identified over 150 different mutations in the collagen gene in question. Each one is different, yet each one produces faulty collagen and the net result is brittle bones. Developing a separate treatment for each mutation would be unrealistic, not to say uneconomic, so we are experimenting with a more generic technique that would hopefully treat a large number of the OI variations.

The approach uses something called a 'hammerhead ribozyme', essentially a special type of RNA molecule designed to detect and destroy the transcripts produced by most forms of the collagen gene. When we added our ribozyme to cells growing in culture in the laboratory, we found that it successfully suppressed 50% of the abnormal collagen genes. This is a very promising result, and our next step will be to test our compound in mice that have osteogenesis imperfecta.



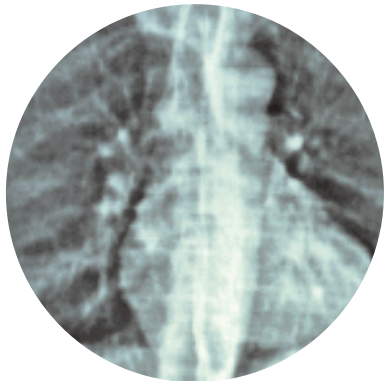
WHEN DENTAL PULP IS INFLAMED

A better understanding of how teeth function may come from research by Dr Michael O'Sullivan, Prof Keith Tipton and PhD student Jeff O'Sullivan (Dental School, and Biochemistry TCD)

The dental pulp inside your teeth contains nerves, blood vessels, and specialised pulp cells that carry out the normal metabolic processes and also synthesise dentine, the hard coating on teeth. Being surrounded by hard tissue, the pulp cells have problems if they ever become inflamed ('pulpitis'), because they have little room to expand. We might find ways to prevent the problem if we could understand what happens when dental pulp is inflamed.

One potentially toxic compound involved in inflammation is an amine called serotonin. In dental pulp, serotonin is removed (oxidised) by a specialised amine oxidase enzyme (SSAO). This SSAO is doubly interesting because, in many tissues it also promotes inflammation to fight infection, by directing white blood cells to the infected site. We have shown that these two activities are connected: to redirect white blood cells SSOA must oxidise amines, such as serotonin. SSOA activity may also be necessary for normal dental pulp development.

Intriguingly, SSOA is also of interest in diabetes, because its amine oxidation function seems to be important in stimulating cells to utilise glucose, at least in some tissues. Like the white blood cell trafficking, this glucose stimulation happens only when the enzyme oxidises amines, and the activity of SSAO is increased in diabetes. Thus, SSAO is multifunctional, playing various important roles. Developing ways to alter its activity could help in dealing with inflammatory conditions such as pulpitis, and in reducing the consequences of diabetes.



WHEN LESS IS MORE

Dr John Laffey and Prof Paul McLoughlin (Physiology, UCD) are studying how best to treat lung failure

It's counterintuitive, but sometimes a ventilator can harm a patient's lung. Ventilators help patients with lung failure to breathe; otherwise, their blood oxygen level would fall, carbon dioxide (the waste product of breathing) would accumulate, and their blood would become more acidic. This **hypercapnic acidosis** (HA), was generally considered 'a bad thing'.

Recently, however, studies showed that a ventilator forcing a 'full breath' into a damaged lung can injure what is left of the lung. In 2000, researchers proved that lowering the intensity of ventilation actually saves patients' lives. Intensive care doctors now reduce the volume, and 'tolerate' the resulting HA. But some scientists, among them Prof Brian Kavanagh in Toronto, and one of us (John Laffey), wondered what the HA was doing, and if it was part of the body's attempts to alleviate the lung damage?

We set out to explore this in a system resembling the acute lung failure that results from serious infections, which is the commonest and most severe form of acute lung failure. When we induced lung failure in rats in the laboratory, put them on a ventilator and gave them carbon dioxide, we found that the acidosis reduced the inflammation in their lungs, improved blood oxygen levels and decreased lung damage. We now think the HA reduces the production of the toxic chemicals that occur during lung injury. These encouraging results have major implications for how patients with acute lung failure are treated, and we plan to extend our studies to other types of lung injury.

Mother and baby: pregnancy and health

FAECAL INCONTINENCE FOLLOWING DELIVERY

Rhona Mahony and Prof Colm O' Herlihy (Obstetrics and Gynaecology, UCD, and the National Maternity Hospital) are studying the causes of and treatment of faecal incontinence after women give birth

Injury to the 'back passage' or anal sphincter is a recognised complication of vaginal delivery, and it can lead to faecal incontinence. In about 3% of vaginal deliveries, the anal sphincter can tear, for instance, or the nerve supplying the muscle can be damaged. This probably accounts for the fact that, while 4% of people develop some faecal incontinence during their life, the problem is eight times more common in women than men.

To identify women who might be at particular risk, we studied a group of women expecting their second baby and who had evidence of anal sphincter injury following their first vaginal delivery. We found that women with an identifiable defect in the sphincter were indeed at risk of developing symptoms of faecal incontinence following further vaginal delivery. Diabetic women, however, who because of their diabetes have subtle nerve abnormalities which might affect muscle function, did not appear to be at any additional risk. We also studied 400 women whose anal sphincter had torn during delivery and found that, while 56% of patients had some symptoms, only 7% had severe problems with faecal incontinence.

Finally, we compared different ways of managing anal sphincter injuries, and found it was better to use a laxative than a constipating agent in the days immediately following the delivery. Biofeedback physiotherapy, a form of 'pelvic floor' exercise, was also effective and helped 80% of the women in our study to reduce their symptoms.

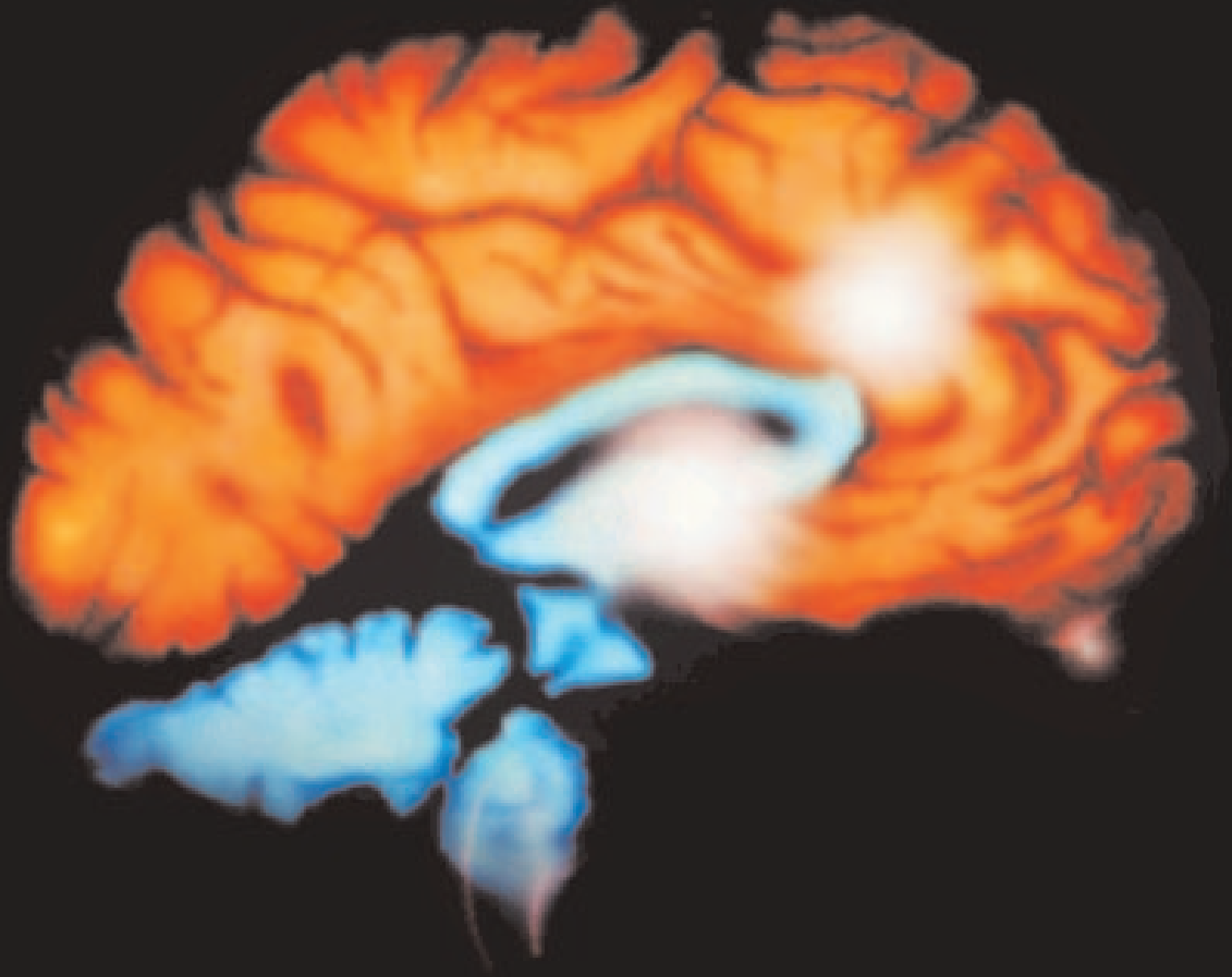
TESTING FOR PRE-ECLAMPSIA IN PREGNANCY

Dr Bridgette Byrne and MSc student Aoife Crowley (Coombe Women's Hospital, and Royal College of Surgeons Ireland) are trying to identify women at risk of developing pre-eclampsia

Pre-eclampsia is relatively common in pregnancy, with symptoms that include high blood pressure and oedema (swelling) in the mother. Fortunately, most cases are mild, but in severe cases, the baby might be born small, or must be delivered prematurely. On occasion, the disease may be severe enough to threaten the mother's life. No one yet knows what causes the condition, and this makes it all the more difficult to identify women at risk. But there is one clue: women with pre-eclampsia have more of their baby's cells circulating in their bloodstream than other women.

All pregnant woman have some foetal cells crossing into their bloodstream, a phenomenon called **'foetal trafficking'**. We think the foetal cells are important in teaching the mother's immune system to recognise the foetus as 'friend' and not 'foe', and so ensure a healthy pregnancy. Some studies found that this foetal trafficking increases before pre-eclampsia develops, which suggests we could use it to predict women at risk. However, when we measured foetal trafficking in pregnant women during the first three months of pregnancy, we found no significant difference between those who later developed pre-eclampsia and those who did not. This suggests that the increased foetal trafficking seen during pre-eclampsia might be a consequence of, and not a cause of the condition.

Mental health



THE GENETICS OF SCHIZOPHRENIA

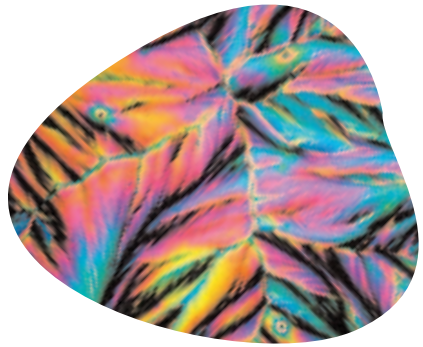
Dr Aiden Corvin, Prof Michael Gill and colleagues (Psychiatry/ Genetics, St James's Hospital, Dublin and TCD) have identified a gene that is associated with schizophrenia

Schizophrenia and bipolar affective disorder (sometimes called manic depression) are important psychotic disorders that together affect about 2% of people. We know that genes can play an important role in illness and that there is often a strong family susceptibility to becoming ill. However, little is known about which genes are important or whether the same genes might be involved in these two diseases.

Research from Iceland suggested a gene, Neuregulin-1, might be implicated in schizophrenia, so we decided to look for this gene in the Irish population. Over 300 people who have schizophrenia and/or bipolar affective disorder (and 250 healthy blood donors) helped us by donating blood, which we analysed for neuregulin-1.

Our results confirm that **neuregulin-1 is indeed associated with schizophrenia** (though not with bipolar affective disorder): about 21% of people with schizophrenia have the gene, compared with 15% in the general population. Interestingly, we found the same form of the gene contributes to susceptibility in Ireland and in Scotland, but that this is subtly different to that seen in Iceland.

There has been considerable international interest in our findings, and we are now investigating other genes involved in schizophrenia and bipolar affective disorder, as well as studying what neuregulin-1 does. Current schizophrenia drugs target the body's dopamine pathways, but neuregulin-1 is involved in a different pathway, the glutamate system. So, if we can learn more about neuregulin-1 and glutamate, it might lead to a new generation of schizophrenia treatments.



THE BENEFITS OF LEADERSHIP TRAINING

Michael Watts and Trudy Meehan (GROW Mental Health Organisation, Kilkenny) found that training group leaders benefits all group members

Mutual-help groups are a cost effective element in the health service. But to be successful, it is essential that every group member feels psychologically safe within their group. This means that those who lead the group meetings must be skilled in noticing and responding appropriately to participants needs. To help ensure this, GROW has developed a training programme for group leaders. The programme was monitored and evaluated by the Department of Applied Psychology at UCC, who helped us to refine the final version of the course manual.

We found that people who took the course developed a greater awareness of the psychological vulnerability of group members, and learned ways to deal with difficulties that can arise, either directly themselves or by referring the person to mainstream services. An unexpected but very positive outcome was that those who took the course gained the confidence to go back to further education in work-related areas.

This project was co-funded by the Calouste Gulbenkian Foundation.

In the community: public health

A CHANGE OF HEART

Changing your lifestyle after a heart attack is not easy. Carol Condon and Prof Geraldine McCarthy (School of Nursing and Midwifery, UCC) investigate the challenges

Over-protective family members, and difficulty managing stress . . . just some of the problems facing people who are trying to change their lifestyle after a heart attack. It is essential that people succeed in making these changes, to minimise their chances of another attack. So we thought it was important to hear from the patients themselves about the problems they faced.

We interviewed ten people six weeks after they were discharged from hospital. Although in the early days after their heart attack all had been enthusiastic about making changes, they were finding it harder than they had expected. Quitting smoking and managing stress were particularly difficult. There was the added problem of trying to change too many things at once. Overprotective family members were a major source of frustration. Significantly, those interviewed had little knowledge about community support services, and even where they were aware of such services, did not feel these would be of benefit, believing they had to cope with making lifestyle changes on their own. On the plus side, all ten were looking forward to the future and trying to resume normal life.

Based on this survey, we recommend: more primary care services providing professional support in the community; a nurse-led telephone support service (which does not wait for the patients to call); stress management programmes; improved cardiac rehabilitation services; an individualised approach to care based on assessing each patient's needs; and long-term follow-up of patients.

NEW NEEDS MEAN NEW SERVICES

Mary McCarron, Dr Cecily Begley and Prof Michael Gill (School of Nursing & Midwifery Studies, TCD) looked at the special needs of people who have Down's syndrome and dementia

Thanks to improved healthcare, people with Down's syndrome are living longer. But there is a problem: as people with Down's syndrome age, they are more likely to develop dementia – indeed, as many as 40% of those aged over 35 show some signs of dementia. Existing healthcare services are not yet aware of or able to meet the particular needs of these people.

To assess this growing problem, we monitored the daily assistance needed by people who have both Down's syndrome and dementia. We found that those with even moderate dementia need on average eight hours assistance each day (those with no dementia need less than three hours). As the dementia progresses, their needs also change: at mid-stage, they need someone to monitor their wandering, for instance; later they will need considerable nursing care. Existing resources for people with Down's syndrome (e.g. community group homes) are not equipped or designed for people with dementia. Equally, conventional dementia support services lack the expertise to treat people with Down's syndrome (e.g. communication difficulties, and assessing someone with underlying intellectual disability).

We therefore urgently recommend: early screening and dementia assessment for people with Down's syndrome; education and training for staff, families and other health care professionals; and the immediate provision of additional resources to reorient and redesign care facilities and services, both day and residential, to ensure humane and appropriate care for this increasingly at risk population.

NURSES, MOTHERS AND THE PUBLIC HEALTH SERVICE –1

Sinead Hanafin looked at some of the factors that can influence the quality of the public health nursing service

Good relationships are essential in life, and the dealings public health nurses have with families are no exception. To look at the factors that can influence relations between public health nurses and mothers, I surveyed nurses and managers working across the Irish public health services, and I also interviewed a number of mothers with babies.

Most new mothers have their first contact with a public health nurse in the days after they return home following the birth of their child. However, if the nurse does not hear about the birth in time, or does not contact the family until later, it can influence all future interactions. Significantly, I found that if the first contact comes early, the family usually views the service as helpful. But if the first contact is late, families frequently conclude that the service is interested only in ensuring that children are not neglected or ill treated.

I also identified other issues that can affect the quality of the service provided. These included, for example, home visiting; having a suitably equipped, warm, clean, safe, child-friendly, local health centre; having up-to-date, relevant and specific advice and information; and, finally, following up problems that arose. Significantly, I found that although some families had many needs, almost all families had some needs, and that these can change as the infant develops. Perhaps most important of all, is that these needs can be met through the public health nursing service.

NURSES, MOTHERS AND THE PUBLIC HEALTH SERVICE – 2

Helen Mulcahy and Prof Geraldine McCarthy (Nursing Studies, UCC) looked at some of the issues that can arise for nurses and mothers of vulnerable families

Some mothers, especially first-time mothers, may need extra support after their baby is born. The local public health nurse might class such a family as "vulnerable", a term that is used in legislation and public health reports. But could such a label compromise relations between the nurse and the client? And could that affect the quality of service delivered?

We studied the relationships between ‘mothers of vulnerable families’ and public health nurses, to see if there were differences in attitudes, perceptions, needs and expectations, interviewing 44 mothers of infants who had been identified as ‘vulnerable’, and their nurse. The overall response from nurses and mothers was positive, and most valued the relationship and found it "highly participatory". Most mothers said they felt comfortable with the nurse and were glad of the support. Some suggested they would have appreciated additional visits, however, and for the nurse to be more available in the weeks immediately following the child’s birth. Nurses, though they might see a need for, and want to give additional help, reported being constrained by a lack of resources. Our recommendations include, for instance, that nurses should consult families about their needs; and they should not assume mothers will make contact in the event of a problem, especially by telephone. Given the importance of first impressions, we recommend special training for those in community work. We suggest further studies to follow nurse-mother relationships over time, and to investigate why so many of those classed as ‘vulnerable’ are first-time mothers.

TO FLUORIDATE OR NOT TO FLUORIDATE

Dr Paul Beirne (University Dental School, Cork) considers the public health and policy implications of opposing viewpoints

The debate over public water fluoridation has run for over 50 years, with strong ‘pro’ and ‘anti’ fluoridation camps holding entrenched views. Supporters describe fluoridation as ‘one of the ten great public health achievements of the twentieth century’. Opponents, on the other hand, label it as ‘the greatest scientific fraud, possibly of all time'. To understand these opposing viewpoints I analysed the scientific, popular and alternative media reporting on the issues. I sought to understand how opponents and proponents perceive the risks of fluoridation and interpret the scientific evidence. I also considered approaches to making public policy decisions under conditions of uncertainty advocated by opposing sides of the conflict.

My analysis of the media reporting reveals that the interpretation of scientific evidence is subjective and heavily influenced by the interpreter’s preconceived beliefs. People for and against fluoridation have, it seems, very different ‘world views’: it is not just fluoridation they disagree on; they also have very different attitudes to hierarchies and social structures, and towards the merit of ‘expert’ opinions. The implications of these findings are that these opposing perspectives will never be reconciled. Yet, these differing viewpoints must be understood and taken into account if we are to have real dialogue and public involvement in decision-making. This would be an important first step in developing public health policies that are widely supported. The findings of this analysis also apply to other areas of public policy which are hotly debated, from vaccination to incineration.

Health services

COMPARING CANCER SERVICES ACROSS IRELAND

Dr Harry Comber, Dr Marie Reilly and researcher Salah Mahmud (National Cancer Registry, Cork) have studied cancer statistics for the various health board areas

The National Cancer Registry has been collecting data on the incidence and treatment of all cancers in Ireland since 1994 and on cancer deaths up to the end of 2000, which has resulted in a valuable database. We decided to analyse this information to investigate whether the survival rates for cancer patients were significantly different in different parts of the country, and if so, whether this was related to the type of cancer, perhaps, or the type of patient (perhaps rural patients are more likely to be older, for instance), or different forms of cancer treatment that regional health boards provided.

For this study, we looked at the four most common cancers in Ireland (breast, colorectal, lung and prostate), and analysed all cases newly diagnosed by the National Cancer Registry in the five years 1994-98. Almost half of all the cancer patients were treated in the Eastern Region Health Authority (ERHA), so we took this as our baseline for the comparisons. We found significant differences in the survival rates of patients with breast or colorectal cancer between the ERHA and the rest of the country, even after taking account of other risk factors such as patient age and stage of cancer. The differences in survival for prostate and lung cancer patients were slight, however. This is as expected because these two cancers are not as sensitive to treatment differences as breast and colorectal cancers are.

IMPROVING HOSPITAL OUTPATIENT SERVICES

Orla Keegan and Prof Hannah McGee (Psychology, Royal College of Surgeons Ireland), are helping hospitals to assess the service they provide

Anyone who has waited for an outpatient appointment, knows that the system can usually be improved. The problem is that, though outpatient appointments are a scarce resource, they are difficult to manage efficiently because they are influenced by so many factors, such as patients who don't show, and consultants' timetables. To help hospitals examine the system they operate, we have developed outpatient questionnaires (one for those who attend, one for those who fail to show).

Testing these at several outpatient clinics in the eastern region, we found general satisfaction with the level of medical care, but considerable dissatisfaction with the outpatient 'system'. For instance, over half waited an hour longer than they deemed acceptable. Significantly, we found that most people are prepared to wait within reason, but want to know in advance how long they might be waiting and, having waited, expect a reasonable consultation time. One-quarter said the physical conditions were poor (e.g. quality of waiting area), and people also resented being told to return a second time for other tests. Up to one-third of patients don't attend for their appointment, whether because they have recovered, are too ill or simply forget. Knowing their views, and encouraging them to cancel their appointment in advance, can help a hospital improve its service and release appointments for others in the waiting list. Our questionnaires can therefore yield valuable information for hospitals, and we have now produced a training manual so that managers can conduct their own surveys.

PROVIDING NEUROPHYSIOLOGY SERVICES IN REMOTE AREAS

Mary Fitzsimons and PhD student Lisa Ronan (Neuroscience Division, Beaumont Hospital, Dublin) believe that telemedicine could provide a valuable service

The northwest of Ireland has no clinical neurophysiological service. So patients who need electroencephalography, for instance, must travel to Dublin or Galway. Understandably, people sometimes decide that the long round trip is just too much. While the equipment needed is minimal (just a computer, amplifier and electrodes), you do also need a technician and, to provide a full service, a consultant neurophysiologist. There are only a handful of these in Ireland, however, mostly in the main cities. With 'telemedicine', local doctors could gain access to these experts, but are there enough patients in the northwest to warrant a telemedicine service?

To estimate the likely demand, we conducted a thorough audit of patients who use the eastern region's neurophysiological services (including patients travelling from the northwest), and we compared the numbers with those seen in Britain. We discovered that there is considerably less use of neurophysiological services here, even in the eastern region, and even more so in the northwest. The Association of British Clinical Neurophysiologists recommends services for 640 patients per 100,000 population per year. Our audit revealed that current clinical neurophysiology activity in the Eastern Regional Health Authority reaches only about half that level, and for the Northwest Health Board it is half that again (23% of the British recommended level). This suggests that, if a telemedicine service was available in the northwest, many more people would avail of it than currently make the journey to Dublin. Clearly, such a service would greatly improve patient care in remote areas.

This project was co-funded by the North Western Health Board.

THE BELIEFS AND BEHAVIOUR OF CARDIAC PATIENTS

Dr Molly Byrne, Prof Andrew Murphy and Dr Jane Walsh (Department of General Practice, NUI Galway) have studied how people's perceptions can affect how they manage their disease

Primary preventive care targets people who have not yet become ill, while **secondary preventive care** is aimed at preventing ill people from getting worse. So, for heart disease patients, secondary prevention might be aimed at preventing another heart attack, and could include measures such as medication, and lifestyle changes. Secondary prevention could make a tremendous difference to someone with coronary heart disease, but do all patients comply with the recommended measures? And do a person's beliefs and perceptions play any part in this?

To assess secondary prevention measures among cardiac patients, we gathered data on 1,611 patients in the Western and Northwestern Health Board Regions, including information on medication, diet and exercise. As an example of our findings, 53% were following the recommended low-fat diet, but 22% were still on a high-fat diet. We also interviewed the patients to determine their perceptions about their illness and treatment, to see if we could relate their behaviour to their perceptions.

We found that people who believed their medication was necessary and had few concerns about side-effects, were more likely to take the drugs. But we found little association between people's perception of their disease, and their willingness to make lifestyle changes: many of those who realised their disease was serious, had not yet changed their behaviour. This could be because heart disease is a chronic condition that for many people does not result in many symptoms. Clearly, secondary prevention programmes will need to take account of this if they are to be effective.

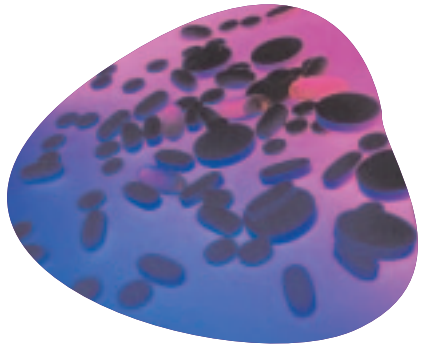
KEEP TAKING THE TABLETS

Dr Martin Henman, Lisa Vivero (Pharmacology, TCD) and Kate Mulvenna (NEHB primary care pharmacist) looked at how community pharmacists can help patients to take their medicine

Imagine for a moment that you have a chronic coronary condition. Your GP has prescribed drugs that will minimise your chances of a heart attack in years to come but, right now, you have no symptoms. Question: would you take the full prescribed dose every day? Or would you sometimes decide you didn't need to?

Increasingly, it's recognised that people with chronic conditions, such as high blood pressure, do not always take their medication as prescribed. To investigate whether community pharmacists can help improve people's knowledge of their medicine, we ran a pilot scheme with several pharmacists. They contacted a sample of their regular customers who were taking at least two cardiac medications, and offered advice about the medication. They also gave the customers a short questionnaire to ascertain their understanding of the medicine and their general compliance with the prescription. This revealed that while some patients were well-informed, others had limited information. In these latter cases, the pharmacist was then able to provide information and advice. Crucially, our questionnaire also revealed that many people take less of their medication than is recommended. In these cases, the pharmacist was able to ascertain why (the person might have been concerned about side-effects, for instance), and if need be refer them to their GP for further help. To this end, the pilot project worked well, and we now have plans to expand it.

This project was co-funded by the North Eastern Health Board.



APPENDIX – IMAGES

The following images were supplied by the Wellcome Trust photographic library:

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