

PICTURE OF HEALTH

2011

A snapshot of HRB funded research

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FOREWORD

I strongly believe in the value of health research. Health research can contribute to delivering a better healthcare system and improved standards of well-being.



The Picture of Health 2011 report describes, in easily understood language, the latest developments in health research in Ireland supported by the Health Research Board (HRB).

Health research involves many stakeholders. I am pleased that this publication aims to communicate the outcomes of HRB-funded research to these key stakeholder groups including health practitioners, the research community, policy-makers and the general public. It focuses on the relevance, value and potential impact of this research on people's health, the delivery of health services and the formulation of health policy.

The 2011 report captures just some of the achievements that flowed from HRB-funded researchers, who completed research projects in 2010. The stories illustrate that Irish health research is making an impact locally and globally.

The Health Research Board promotes excellence and provides our healthcare system with the evidence on which better services, better care and better outcomes depend.

A handwritten signature in black ink that reads "James Reilly". The signature is written in a cursive, flowing style.

Dr James Reilly TD
Minister for Health

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INTRODUCTION



Health research affects our daily lives. It develops our understanding of health and human diseases. It provides the evidence to help us to tackle health challenges, to improve our health care system, while at the same time it creates opportunities for economic benefits.

The Picture of Health captures just some of the immediate achievements that flow from the Health Research Board's (HRB) investment in health research.

In 2010, a total of 105 HRB grants were completed, resulting in:

- 105 new international collaborations
- 669 patients enrolled on cancer clinical trials across 14 hospitals
- 18 new products and interventions in development
- 38 PhD students trained across many health disciplines
- 59 influences on policy and practice
- Leverage of over €11m in additional research funding

This edition shows the active involvement of dentists, doctors, midwives, nurses, physiotherapists, psychologists, social workers, statisticians, and others in Irish health research, alongside the more traditional academic researchers.

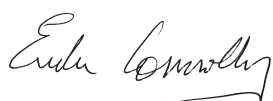
It shows how research is helping to develop the necessary skills to transform our health service, providing evidence to understand what works best, changing national health policies and/or practice guidelines, and promoting active collaborations with partners in research, industry, government and the wider community to deliver positive change.

It reports on promising new drugs, devices, treatment strategies and delivery systems which fuel our clinical and translational research systems and potentially yield huge benefits to patients and the public.

It features research designed to improve the quality of health care, reduce its cost, evaluate its effectiveness, improve patient safety, and broaden access to essential services, as well as focusing on the prevention of ill-health.

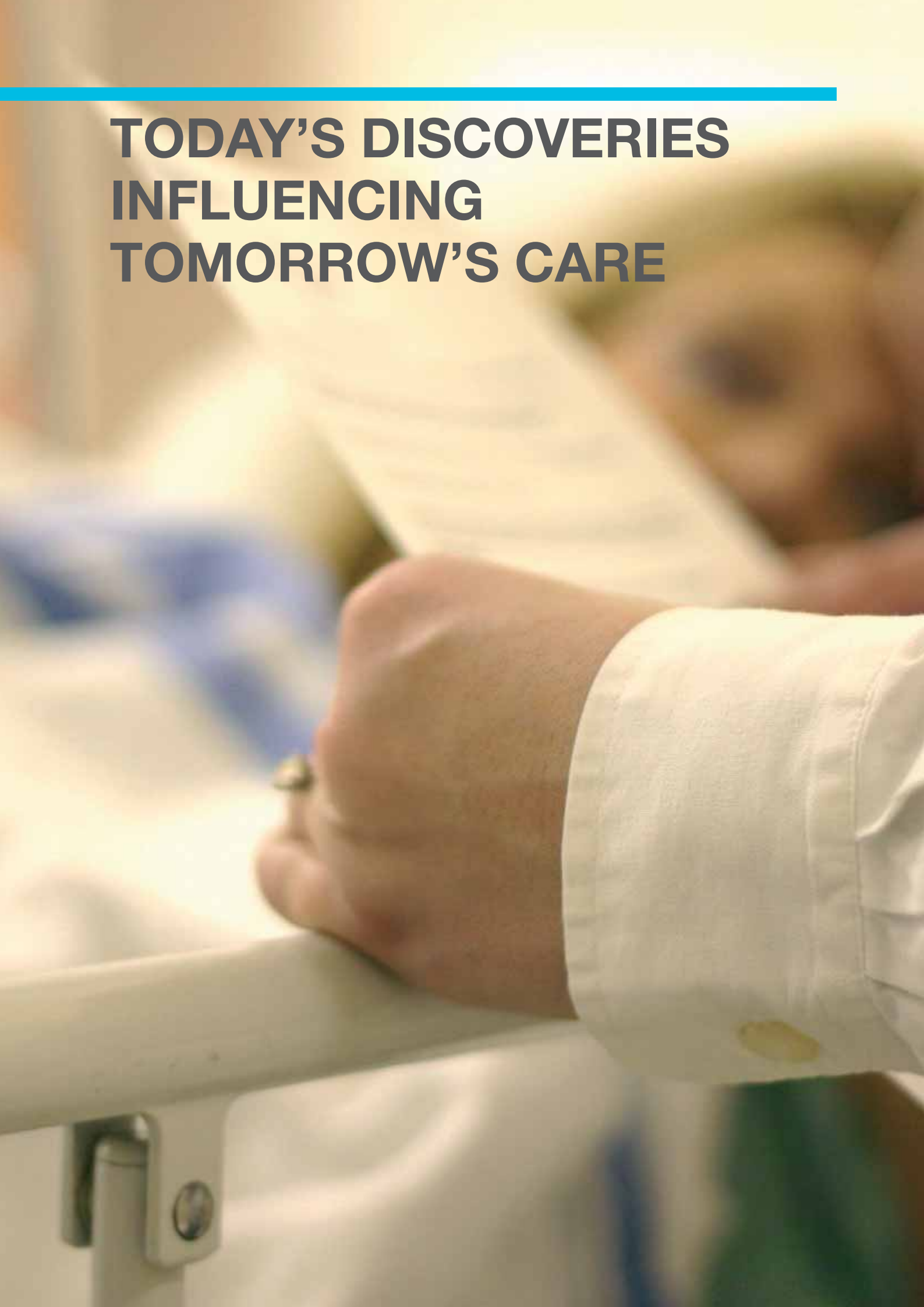
It highlights the important role of patient involvement in health research and gives voice to patient and staff experiences within our health system.

The Health Research Board continues to evolve and adapt to the changing environment. This Picture of Health 2011 endorses our new strategic direction and provides a snapshot in time of research which will continue to deliver new and improved health products, services, policies and practices over the coming years.



Enda Connolly
Chief Executive

**TODAY'S DISCOVERIES
INFLUENCING
TOMORROW'S CARE**



HOW TO GROW EYE TISSUE TO RESTORE SIGHT

Patients with damage to a part of the eye called the cornea can suffer sight loss and irritation. So HRB-funded research has developed a way to grow replacement tissue in the lab that can restore the cornea and fix the problem.

“The cornea is the clear dome of the eye,” explains Dr Finbarr O’Sullivan, a Post-doctoral Researcher at the National Institute for Cellular Biotechnology at Dublin City University. “It’s providing both a window into the eye - it focuses about 70 per cent of the light coming in - and also a barrier to protect the eye from the outside environment.”

Injury or disease can damage the cornea, meaning a patient may develop blindness, and the eye can feel painfully irritated. For some patients, transplanting a small piece of tissue from an area of the eye called the limbus can do the trick and the cornea grows back, but it doesn’t work for everyone, explains Dr O’Sullivan.

The team at DCU has been working with the Royal Victoria Eye and Ear Hospital and the Irish Blood Transfusion Service to develop and validate a method of growing sheets of suitable cells in the lab that can then be transplanted into the eyes of patients.

These sheets can be grown up from donor material, or from the patient’s other eye if it is healthy, says Dr O’Sullivan.

“Clinical trials involving stem cell transplant for corneal repair are in progress in several countries, but the technique is still highly experimental and results, while promising, have been variable,” he explains. “As a result of our research over the past four years on the culture and fundamental cell and molecular biology of human limbal stem cells, a new optimised protocol has been developed which will now for the first time make this exciting new treatment available to Irish patients, as part of a clinical trial.”

Achievements

- » Developed a way to grow tissue from the eye in the lab.
- » To provide better transplant options for patients with corneal eye damage in Ireland.

Dr Finbarr O’Sullivan, DCU



SILENCING THE ALARM SIGNAL FOR ALLERGIES

Our immune systems work hard for us every day, fighting off bugs and kick-starting the body's clean-up and healing process if we get injured.

But sometimes the immune system can see threats in everyday things: for some people, breathing in pollen, dust or pollutants in the air can set off an immune response that leads to an allergic reaction.

Stopping that inappropriate response could help to treat allergic disease, and HRB-funded researchers at Trinity College Dublin have come up with a way to literally cut that alarm signal and halt the immune response.

It centres on a molecule called interleukin-33 (IL-33), which normally tells the immune system to switch on. And IL-33 has a strong association with allergic disease, explains Prof Seamus Martin, Smurfit Professor of Medical Genetics at Trinity.

His group discovered that a type of molecular scissors called caspases, which occur naturally in the body, can snip IL-33 and inactivate it. In addition they have developed a system that loads such a scissor molecule onto a specially-designed antibody that can find IL-33 in the body and latch on to it so the scissors can do its work.

It's the first system of its type and Prof Martin believes that being able to inactivate IL-33 could be an important future step in managing allergic responses.

"I would be quite optimistic that in the next five years IL-33 therapy may be very desirable in allergy," he says.

Achievements

- » Discovered a possible new approach to stopping immune responses linked to allergies.
- » Patented technology to inactivate biologically important molecules.

Prof Seamus Martin, TCD



NEW APPROACHES TO KEEPING AIRWAYS HEALTHY

Whooping cough and allergies can cause breathing problems, but HRB-funded research is paving the way to a more effective whooping cough vaccine - and along the way the study has also discovered a potential route to protect against allergies.

We already use a childhood vaccine against whooping cough - which is caused by the bacterium *Bordetella pertussis* - but it can't be given to newborns, and they remain vulnerable to the disease, which is back on the rise in Europe and the US.

"We need better vaccines, ones that can protect much earlier and where the protection afforded by immunisation lasts a lot longer than the current one," says Dr Bernard Mahon, a Senior Lecturer in the Institute of Immunology at NUI Maynooth.

Working with collaborators in France, the Maynooth group tested a new vaccine in the lab, using a weakened version of the bug that has been modified so it doesn't cause disease but gives strong immunity.

That work led on to an EU-funded project, Child Innovac, to develop the vaccine - which is designed to be delivered as a nasal spray to newborns - and run early clinical trials in Sweden.

The Maynooth group also discovered that the weakened whooping cough bug appears to educate the immune system in early life and protect against allergies.

They ran with that idea and found that stem cells can also offer a similar protection in the airways, by switching off a type of immune cell that could lead to an allergic response, explains Dr Mahon.

Achievements

- » New potential vaccine for whooping cough developed.
- » Could inform new therapies to prevent allergies.

Dr Bernard Mahon, NUIM



EARLY MATERNAL CHANGES THAT WARN OF FOETAL GROWTH RISK IN PREGNANCY

If a baby's growth is restricted as it develops in the womb, this can lead to problems such as stillbirth, low birth weight and medical problems later in life.

Growth restriction often goes undetected during pregnancy, but new findings suggest there are measurable changes in the mother's blood as early as 15 weeks into the pregnancy that signal increased risk of later growth problems for the baby.

HRB Clinical Research Fellow Dr Richard Horgan carried out a study of blood samples from women whose babies were small for their age during pregnancy and at birth, and he compared them with samples from women whose babies had grown normally. He also looked at an animal model that mimicked what happens in growth restriction in the womb.

Together the findings pointed to a set of 19 biochemicals in blood samples just 15 weeks into the pregnancy. The relative levels of these 'metabolites' could be linked with the risk of later growth complications.

"If these metabolites were found in early pregnancy, you were 44 times more likely to have a growth restricted baby than normal growth," says Dr Horgan, who worked with

HRB Clinician Scientist Prof Louise Kenny and conducted the study at University College Cork and The University of Manchester, UK.

The markers are now being validated in around 3,000 pregnant women through SCOPE, a major international study that has received support from the HRB.

Ideally the outcome would be a routine screening test in early pregnancy that can identify women who may need closer monitoring, according to Dr Horgan, which could reduce the risk of later complications in the pregnancy.

Achievements

- » Identified markers in the blood in early pregnancy that seem to signal increased risk of growth complications later on.
- » Links with major international study of pregnancy.

Dr Richard Horgan, UCC



DELIVERING MEDICINES FOR EASIER BREATHING

Even if you have the most effective medicine in the world, it is of little use unless it gets to the place in the body where it needs to work.

That's why scientists at the Royal College of Surgeons in Ireland and Beaumont Hospital have come up with new ways to deliver medicines right into the lungs - where they can pack their direct punch against disease.

New genetic-based medicines for chronic airway conditions like chronic obstructive pulmonary disease (COPD) and cystic fibrosis will look to address not just the symptoms, but also their causes, explains Dr Sally-Ann Cryan, a Lecturer in Pharmacy in RCSI.

But in order to work, the genetic material needs to get into the correct cells in the lung. So the HRB-funded project has come up with two new systems for delivering genetic material into a type of cell called a macrophage, deep in the lung.

Macrophages usually gobble up bacteria or foreign material like dust in the lung, so in one system the researchers successfully camouflaged genetic material called RNA in a particle that could enter the macrophage like a Trojan horse.

"We disguise the RNA so that these macrophages think they are clearing, say, a dust particle and in fact what they are doing is taking the RNA in," says Dr Cryan.

Once inside the cell the RNA works to stop inflammation in the lungs and this technology therefore offers a new way of treating patients suffering with a range of respiratory diseases.

The researchers have been working with Irish medical devices company Aerogen to develop the technology, and preclinical trials are now underway to further test out the inhaled delivery systems.

Achievements

- » Developed new technologies that could allow patients to inhale medicines directly into specific lung cells.
- » Developed a high-throughput screening method suitable for industry to identify when medicines are delivered to cells.

Dr Sally-Ann Cryan, RCSI



LIFE-SAVING MEDICINES IN UGANDA - THE LOCAL INFLUENCE

Medicines are an important part of the fight against diseases such as malaria and HIV/Aids. But an Irish Aid-funded study, managed by the HRB, has been finding that in Ugandan populations, the local food can have an effect on how those medicines are absorbed, as can taking the different types of drugs at the same time.

Factors such as genetics, weight, malnutrition, food, pregnancy, herbal medicines, other diseases and other medications can influence drug levels after we take medicines, explains Dr Concepta Merry, a Senior Lecturer in Global Health at Trinity College Dublin.

“An African lady who is HIV positive, malnourished, pregnant, co-infected with TB and who takes traditional medicines may need a different dose of anti-HIV drugs to their male counterpart in the developed world,” she says.

Dr Merry’s team looked at how the local food in Uganda can affect the body’s uptake of anti-HIV drugs.

“We studied different diets with a number of HIV drugs and were able to simplify the dietary recommendations for a commonly prescribed HIV drug so that it can be taken safely with or without food,” she says.

Patients who are taking anti-HIV drugs daily and for life may also need to take short courses of anti-malarial drugs too, and the researchers found that in a Ugandan population, taking both types of drugs

simultaneously could cause changes in the drug levels of both the malaria and HIV treatments.

“We also studied the effect of prescribing drugs for TB and drugs for malaria at the same time and found major reductions in the levels of the commonly prescribed drugs for malaria suggesting that we may need to rethink our approach to co-treatment of these diseases,” says Dr Merry.

Achievements

- » Taking certain anti-HIV and anti-malarial drugs together can affect their absorption into the body.
- » Simplified dietary recommendations for patients in Uganda taking anti-HIV drugs.

Dr Concepta Merry, TCD



A NEW WAY TO TIE DOWN PAIN

We've all experienced pain at some point - but how do you classify that feeling? HRB-funded physiotherapist Dr Keith Smart identified the clinical symptoms that link into three broad types of pain, and the approach could help ensure patients are put onto appropriate treatments.

Classifying pain as simple, acute or chronic may not be the best route to understanding how to treat it, says Dr Smart, who is based at St Vincent's University Hospital.

"Those classification labels might not be the most useful in helping clinicians to know which patients might be most likely to recover, or which treatments they might benefit from."

Over the last 20 years, research into how our bodies register and process pain has pointed to three broad types that could be more useful: the 'nociceptive' pain you feel when you stub your toe, the 'peripheral neuropathic' pain that shoots down the leg in nerve injuries such as sciatica and finally a type of pain called 'central sensitisation', where the body seems to process pain in a way that makes relatively small injuries hard to bear, as in fibromyalgia.

Dr Smart asked clinicians about clinical symptoms they linked with those types of pain, then co-ordinated a study that looked at those symptoms among 460 patients with leg and back pain in Ireland and the UK.

The research identified lists of clinical criteria for each pain type that could pave the way for more formal guidelines to help healthcare professionals identify what their patients are suffering and how best to treat them.

Achievements

- » Identified clinical symptoms of different pain types.
- » Will inform the development of guidelines for classifying and treating pain.

Dr Keith Smart,
St Vincent's University Hospital



MAKING STEM CELLS SAFER TO USE

Stem cells hold the promise of treating Parkinson’s disease, but they can also raise the risk of tumours developing. Now HRB-funded researchers at University College Cork have come up with a system to help avoid that unwanted side-effect.

Dr Aideen Sullivan and Dr André Toulouse engineered the solution to work in mouse stem cells, which can be coaxed to replace lost brain cells that normally produce an important chemical called dopamine.

“The loss of dopamine-producing brain cells is what causes the motor symptoms of Parkinson’s disease,” explains Dr Sullivan.

“Introducing transplanted stem cells can make connections with the host brain, and therefore replace the lost circuitry.”

Because such stem cells can renew themselves, in theory a single stem cell could provide a limitless supply of replacement cells for transplantation, but this ability to grow and change is what can increase the risk of tumours forming.

So the study put a set of instructions into the cells to tell them to die if they start growing rapidly after they have transplanted.

“We can modify the stem cells so that if they continue to grow after transplantation they kill themselves,” says Dr Sullivan.

The system, which the researchers have validated in cells in the lab, could also be applied to therapies looking to use stem cells to tackle other diseases, she adds.

“What we have developed is really very widely applicable. The same problem exists no matter where you are putting the stem cells.”

Achievements

- » Developed a system that could make stem cells safer for transplanting.

Dr Aideen Sullivan, UCC



Dr André Toulouse, UCC



MOVING TO A BETTER NIGHT'S SLEEP WITH BACK PAIN

Monitoring sleep can be a tricky business, but a HRB-funded feasibility study has been figuring out how physiotherapy treatment for back pain can have an impact on how patients sleep.

“Back pain is a widespread problem, it affects 80 per cent of the population, and poor quality sleep is a common problem affecting over 50 per cent of the population,” says Dr Deirdre Hurley, a Senior Lecturer in the School of Public Health, Physiotherapy and Population Science, University College Dublin.

“But we had no idea of the relationship between back pain and sleep, and of the effects of physiotherapy on that relationship.”

To examine how you might set up a study to investigate these relationships, the team at UCD and Beaumont Hospital Physiotherapy Department recruited 60 patients with back pain and followed them up at intervals for six months.

Patients filled out questionnaires about their sleep, and they also used devices in the home to record details of their sleep quality. The technology included a non-contact sleep and breathing monitor developed by UCD campus company BiancaMed Ltd.

The results showed that physiotherapy was linked with some sleep improvement, but Dr Hurley explains that the focus of this small-scale study was more about working out the logistics of how to monitor sleep in the home over time.

BiancaMed's sleep-monitoring technology has since been acquired by multinational company ResMed, and the UCD/Beaumont team is now running a larger trial to monitor the effects of physiotherapy for patients with back pain.

Achievements

- » Pilot study on the effects of physiotherapy for back pain on sleep quality.
- » Helped to validate patented non-invasive sleep-monitoring technology developed in Ireland.

Dr Deirdre Hurley, UCD



ONE-TO-ONE MOTIVATION SESSION CAN HELP HEART ATTACK PATIENTS BEAT THE CLOCK

If you are having a heart attack, getting medical treatment quickly can improve your chances of surviving and doing well afterwards - yet many people who have symptoms delay in getting to hospital.

However a HRB-funded study has found that in patients who had a heart attack, a short and timely education session made them more likely to rapidly seek appropriate help when they experienced heart attack warning symptoms again.

“Getting to the emergency department within that first hour after the onset of symptoms saves lives,” explains Dr Gabrielle McKee from the School of Nursing and Midwifery, Trinity College Dublin.

It’s recommended that patients who think they are experiencing a heart attack should act promptly and call an ambulance.

However this study of nearly 2,000 patients found that people waited a long time before deciding what to do or whom to tell, and many patients made their own way into hospital or phoned the GP first. The project found that a one-to-one motivational educational session, which provides further education, including information on the range of symptoms of a heart attack, and develops a personalised plan about what patients should do if they had symptoms again, had an impact.

McKee and her team found that those who received this session and had subsequent heart attack symptoms managed on average to reduce their time of getting to hospital from 4.6 hours down to a zippier 1.7 hours.

She says the findings suggest that patients who have had a heart attack need specific education regarding prompt response to heart attack symptoms before they leave the hospital – “we have fixed you as best we can, and if it happens again let’s work out the best actions for you to take.”

Achievements

- » Confirmed that people with heart attack symptoms often delay in getting to hospital, reducing survival opportunities.
- » A short, personalised educational session makes it more likely that in the event of a reoccurrence, patients will get to hospital faster.

Dr Gabrielle McKee, TCD



EARLIER EXPOSURE TO FLUORIDE PLEASE - PROTECTING TEETH IN PRE-SCHOOL CHILDREN WITH DISABILITIES

Pre-school children with disabilities should have their teeth cleaned with fluoridated toothpaste in order to protect them, according to the largest study of its kind carried out in Ireland.

This HRB-funded research looked at separate groups of pre-school children with disabilities and found that decay started to become evident after the age of three.

“Up to three years of age there was virtually no dental decay in these children,” explain researchers Prof June Nunn and Dr Darius Sagheri, of the Special Care Dentistry Unit at the Dublin Dental University Hospital, Trinity College Dublin.

“But once you got over that threshold that’s when decay started to develop, and when they have decay it tends to remain untreated. Protecting these children needs to start earlier. The recommendation here in Ireland is that children under the age of two shouldn’t be using fluoridated toothpaste. However given the vulnerability of these children, and the fact that dental caries can take years to develop, we need to start protection early. This is especially as for many of them co-operation would be compromised - they may even need a general anaesthetic to have dental care - so protecting them is a priority. Our recommendation is that they should be using the fluoridated toothpaste.”

The study of almost 350 children found that an intensive educational programme with parents had little impact on the dental health of the children. Follow-up work with focus

groups suggested that parents might engage better with a more motivational approach, where healthcare professionals would tailor the information to the individual family and encourage the parents to want to change behaviours.

“Parents wanted more ownership of how they access information,” says Prof Nunn. “They don’t want someone on their doorstep telling them how to clean their child’s teeth or what their child should be eating. Motivational interviewing engages the individual more with ownership of the problem for themselves.”

Achievements

- » Recommended a change to the current policy and the use of fluoridated toothpaste in preschool children with disabilities.
- » Identified the need for more motivational approaches in dental health education.

Prof June Nunn and Dr Darius Sagheri,
Dublin Dental University Hospital



MINING CENSUS DATA TO IMPROVE HEALTH SERVICES

The way in which breast cancer screening services are organised strongly influences how many women will take them up.

That’s an important finding from a HRB-funded study that has shown how analysing population data can help reshape the provision of breast cancer screening services. The research linked the health registration data of around 500,000 people with information from the Northern Ireland Census prepared by the Northern Ireland Longitudinal Study.

HRB Health Services Research Fellow Dr Heather Kinnear from Queen’s University Belfast looked at the uptake of breast screening in the dataset, and found strong evidence that how the services are organised influences whether uptakes are high or low.

“This research has clearly established for the first time that organisational factors can have a large effect on breast screening uptake rates,” she says.

Those findings are now informing efforts to reshape the provision of breast cancer screening services in Northern Ireland to help increase uptake rates. Other types of cancer screening are now being explored in the datasets.

Another outcome from the project is that it developed methods for linking the health services and Census data while safeguarding patient privacy, she explains.

“By establishing the methodology for linkage of health services data to the Census data, we have opened up a whole new stream of health services research,” she adds.

Achievements

- » Evidence of how supporting population studies can make an impact on how services are delivered.
- » New methods established for linking health registration data and Census data in a secure and confidential manner for addressing important research questions.

Dr Heather Kinnear, QUB



GETTING A BETTER UNDERSTANDING OF HIV INFECTION IN DUBLIN

The Dublin HIV Cohort Study is a major HRB-funded study that has tracked over 1,700 people with HIV in Dublin - including details of the viruses - since 2006.

There are two distinct types of HIV in circulation in Dublin, explains Prof Bill Powderly, Professor of Medicine at University College Dublin.

“There’s an endogenous Irish infection with the classic northern European type of virus; then among immigrants who are mainly from sub-Saharan Africa, there’s the classic subtype C HIV,” he says. “But there’s little evidence of mixing between the two epidemics.”

The study also found that around five to 10 per cent of cases newly diagnosed in Dublin show drug resistance, notes Prof Powderly. “You can’t assume the drugs you are going to use will always work and it’s very important that physicians test the virus of a particular patient before they start the treatment, it may need to be tailored.”

And as treatments improve and people live longer with the virus, other issues are emerging - the study’s findings emphasise that a HIV infection increases the risk of cardiovascular disease and bone thinning.

“We have some data that suggests the active HIV infection has important effects on bone metabolism and can contribute to problems such as osteoporosis, so it means even if the person’s immune system is still pretty stable it would be often to the advantage of the patient to treat earlier and prevent some future complications,” says Prof Powderly.

Achievements

- » Detailed analysis of HIV infections in Dublin shows some drug resistance.
- » Evidence that HIV infection increases the risk of long-term complications such as heart disease and weakening bones.
- » Highlights need for early and appropriate treatment of patients with HIV.

Prof Bill Powderly, UCD



GETTING THAT BLOOD PRESSURE DOWN

Chronically high blood pressure, or hypertension, can lead to serious medical problems such as heart disease and stroke, so keeping blood pressure under control is an important public health issue.

However, blood pressure goals are achieved in only 25 to 40 per cent of the patients who take anti-hypertensive drug treatment - a figure that has remained unchanged for the last 40 years. So how might we best improve results in a community setting, where most blood pressure management takes place?

A HRB-funded Cochrane review study led by Dr Liam Glynn reviewed 72 randomised controlled trials in the published literature.

The idea was to identify ways that can help improve the numbers of patients who can reach their blood pressure goals, thereby reducing the risk of heart attack and stroke, explains Dr Glynn, a Senior Lecturer in General Practice at NUI Galway and GP in Ballyvaughan, Co. Clare.

Overall, the review found that education aimed at patients or healthcare professionals does not appear to be effective - what works best is good organisation that sees patients regularly followed up and recalled for appointments.

Other strategies for success encourage patients to monitor their own blood pressure or involve other health professionals such as nurses and pharmacists in blood pressure management in the community.

“It has direct translation to everyday clinical practice,” says Dr Glynn.

“We need to improve organisation in terms of diagnosing, treating and following-up patients with hypertension; and that can include nurse-led care, the use of technology such as text messages to remind patients to take their medication or come to appointments and also getting patients more involved in the monitoring of their own illness.”

Achievements

- » Efficient patient recall and follow up for GP appointments helps reduce blood pressure.
- » Self-monitoring of blood pressure can help patients control hypertension.
- » Nurse- and pharmacist-led schemes for blood pressure control hold promise.

Dr Liam Glynn, NUIG



SHEDDING LIGHT ON NEW THERAPIES FOR BLINDNESS

New transplant therapies are being developed to restore sight in forms of blindness where cells in the back of the eye have died. Little is known about what happens to those transplanted cells early on, but a HRB-funded study has been shedding light on that crucial first phase, and particularly how the recipient's immune system reacts to those new additions.

Transplanting cells behind the retina at the back of the eye can restore sight in animal models of degenerative blindness. However after you graft hundreds of thousands of cells in, pretty soon the bulk of those grafted cells disappear.

Few people have looked at why this massive cell loss happens, explains Mr David Keegan, a consultant vitreo-retinal surgeon at the Mater Misericordiae Hospital.

So Mr Keegan and the team at the retinal transplant lab in University College Dublin took a close look at what happens to those transplanted cells within the first few days. They found a pronounced type of immune response that saw cells from the host literally gobble up the transplanted cells.

The study identified some of the immune system's molecular pathways that are switched on in this phase, and knowing more about the process could help to optimise transplants and potentially overcome this initial hurdle, explains Mr Keegan.

"It's about asking how best can we suppress that early immune response without compromising the transplant - rather than using a blunderbuss treatment like steroids, you might be using a more targeted therapy for just a few weeks and then the graft settles in."

The findings would be relevant for emerging transplant therapies for a range of conditions in humans, including retinitis pigmentosa, macular degeneration and glaucoma, explains Mr Keegan. "If you are going to use a cell-based therapy you have to look at these issues."

Achievements

- » Identified early events when cells are transplanted into the eye to combat blindness in animal models.

Mr David Keegan,
Mater Misericordiae Hospital



DIGGING INTO DISEASE



FIGURING OUT HOW BONES WEAKEN EARLY IN OSTEOPOROSIS

What happens to bones early in osteoporosis, before they become brittle enough to break? Are there ways of spotting the disease in those earliest stages, long before the conventional tests can pick it up?

HRB-funded research has been peering deep inside bones, and has figured out those key early steps towards osteoporosis. Using a sheep model, a team led by Prof Fergal O'Brien at the Royal College of Surgeons in Ireland looked at what happens at various levels in the bones as they become weaker.

First they spotted that particular bone cells die off, and that the levels of minerals - some of which are important for strength - change over time. The bones became weaker first at a small-scale level, then on a larger scale, and the likelihood of fracture increased.

But the clinical test commonly used to detect osteoporosis - the DXA scan - could pick up only the later changes.

"When changes begin to manifest themselves in the patient they are monitored by DXA," says Prof O'Brien. "But really we need to look at new ways to try and diagnose the disease in its earlier stages."

This new understanding of how bone weakens over time may explain why current treatments for established osteoporosis do not always reduce the risk of fracture, according to Prof O'Brien.

He adds that the knowledge generated by the research stand to inform new approaches to earlier diagnosis and possibly treatment in humans, and it will feed into efforts to grow bone in the lab that can be grafted to replace damaged or diseased bone in patients.

Achievements

- » Identified how bone weakens over time as osteoporosis develops.
- » Paves way to earlier diagnosis and treatment of the disease in patients.
- » Will help develop better ways to grow bone tissue for grafts.

Prof Fergal O'Brien, RCSI



PROTECTING THE BRAIN IN STROKE

Stroke is one of Ireland's biggest killers and causes of disability, and most of us know someone who has been affected by this 'heart attack in the brain'. HRB-funded research has been looking to minimise the damage.

During a stroke, vulnerable brain cells are starved of vital oxygen and nutrients, and they die. Depending on where the stroke happens in the brain, and how widespread the damage is, a stroke may kill the person, or leave them paralysed, with speech difficulties or unable to live independently.

When a stroke hits, a core area of brain tissue dies quickly and is probably not rescuable, explains Prof Jochen Prehn, Professor of Physiology at the Royal College of Surgeons in Ireland.

But perhaps there could be ways to limit the damage by protecting the brain cells just outside that immediately hit zone.

These nearby cells die at a slower rate, so there could be time to create a protective environment for them, says Prof Prehn.

That's why his team has been looking closely at what happens in a lab-based model of stroke, and they discovered that enzymes called calpains become active in these nearby cells as they die off slowly.

This finding could point to a way to protect at-risk brain tissue by blocking the action of the calpains after a stroke and sparing these brain cells from death, explains Prof Prehn. "Our research provides hope that inhibition of these enzymes could potentially be employed to protect the brain cells in the treatment of stroke."

Achievements

- » Identified a key biochemical event in brain cell death during stroke.
- » Provides a basis for developing brain-protecting drugs in stroke.

Prof Jochen Prehn, RCSI



LEAKY GUTS - THE CHOLESTEROL CONNECTION

Having a leaky gut is as bad as it sounds: in inflammatory bowel disease, the wall of the intestine stops being an effective barrier and can lead to flare-ups of pain and inflammation.

New HRB-funded research suggests that cholesterol changes in the cells of the intestinal barrier could be an early step in how this leakiness develops.

“In order to be healthy the intestine needs to have a functional barrier between the food passing through and the inner tissues and blood of the body,” explains Dr Ann Hopkins, a Research Lecturer at the Royal College of Surgeons in Ireland.

“But under conditions where people have disrupted intestinal function, such as inflammatory bowel diseases like Crohn’s Disease and ulcerative colitis, it’s known that the intestinal barrier gets leaky. Having a leaky barrier means stimulation of the immune system, which can result in pain and further disruption of the barrier.”

Dr Hopkins and her team looked at substances that make up the ‘glue’ between that barrier of cells that line the inner surface of the intestine - that glue is much like the mortar between bricks of a wall.

And they found that if they interfered with the cholesterol levels in the intestinal barrier, the glue became disrupted, and the barrier stopped working as efficiently. “The cells start to break apart and the barrier starts to get leaky,” explains Dr Hopkins.

These early changes in gut leakiness could offer a warning signal that a flare-up is likely, or it may even suggest that diet could affect the integrity of that all-important gut barrier, says Dr Hopkins.

Achievements

- » Identified the importance of cholesterol in the gut wall barrier.
- » Possible new warning marker for early-stage inflammatory bowel disease.

Dr Ann Hopkins, RCSI



NEW GENE LINKS IMPLICATED IN LUNG DISEASE

Health studies can create mountains of data, and how you use that information counts. By mining into results generated by a large European study on chronic obstructive pulmonary disease (COPD), a HRB-funded project has discovered new genetic links to the progressive lung disease.

The 'COPD Gene Scan' project collected clinical data and genetic information from 1064 people with COPD and from more than 900 healthy controls in centres throughout Europe. The EU-funded study was the largest of its kind ever undertaken at the time, explains Prof Leslie Daly, Professor of Epidemiology and Biomedical Statistics at University College Dublin.

When the EU-funded project ended, a vast amount of data was still available in a biobank of stored tissue and information. So Prof Daly worked with Dr Clare O'Connor and Dr Juzer Lotya to develop new ways of looking at the data and to dig into it for new clues about COPD.

"There is one known genetic determinant of COPD and we suspected for a long time there are other genetic determinants," he says.

Their hunch was right: they discovered various new genetic links, including a gene that helps our bodies to regulate iron, another gene that plays a role in the degeneration of lung tissue and a protective combination of two other gene variants.

The results will need further study to be validated, but the analysis could shed light on the causes of COPD, according to Prof Daly, and could inform future genetic therapies for the illness.

Achievements

- » Identified new gene links implicated in the lung condition COPD.
- » Developed new statistical methods to analyse genetic data in patient samples.

Prof Leslie Daly, UCD



A SUGAR THAT'S NO TREAT FOR CANCER CELLS

Scientists funded by the HRB have created a new type of sugar-like compound that can kill cancer cells in the lab.

The new molecules are not the types of sugars we might spoon into our tea or eat as part of an apple, they are modified and chemically more complex, explains Prof Declan Gilheany, Associate Professor of Chemistry at University College Dublin.

"We have a new way of making a type of sugar called branched hexoses - we had the tools to make ones that had never existed before," he says.

His team made a suite of different modified hexoses and related molecules, and then collaborated with Prof William Watson at UCD's Conway Institute, to look at their effects on prostate cancer cells in the lab.

They hit the jackpot with one of the modified sugars: "One was extremely good at inducing cell death in the cancer cells, and it showed high anticancer activity at relatively low concentrations," says Prof Gilheany

The molecular structure of the new modified sugar is unlike other molecules that are known to induce this type of cell death in cancer cells, suggesting that the study may have revealed a new type of cancer-killer, explains Prof Gilheany: "It could be a whole new class of anti-cancer drugs, though that remains to be investigated."

Achievements

- » Created a new type of modified sugar molecule that killed cancer cells in a lab model.
- » Could represent a new class of anti-cancer compounds.

Prof Declan Gilheany, UCD



SEVERE BRAIN SEIZURES IN EARLY LIFE COULD BE LINKED TO ADULT EPILEPSY

Severe brain seizures in early life may cause damage that's linked to epilepsy in adulthood - that's according to a new animal model developed by HRB-funded scientists at the Royal College of Surgeons in Ireland.

Neonatal seizures -seizures during the period from birth until the end of the first month - are caused by abnormal electrical activity in the brain, but not enough is known about their long-term consequences, explains researcher Prof David Henshall.

His group designed a model to look at the link between very prolonged seizures in the developing brain and temporal lobe epilepsy in adulthood, a disorder that affects over 35,000 people in Ireland.

What they found was that severe seizures in that early neonatal period could, under some circumstances, cause the type of damage to brain tissue that in later life is a hallmark of temporal lobe epilepsy, explains Prof Henshall.

He describes how the model offers a new angle on understanding how epilepsy develops: "There's a need to have a number of different types of animal models of neonatal seizures," he says. "We think our new model can fill a particular gap - it models consequences of the most severe neonatal seizures that we think no other model has managed to do before."

The findings also highlight the urgent need for better drugs to treat seizures in the neonatal period, says Prof Henshall, and their model is now being used to help identify appropriate drugs that could calm abnormal electrical activity in the developing brain to dampen down potentially damaging seizures.

Achievements

- » Links found between severe brain seizures in early life and later damage associated with epilepsy.
- » New model for screening drugs to help newborns having brain seizures.

Prof David Henshall, RCSI



UNCOVERING THE SECRETS OF AGEING IN CARDIOVASCULAR DISEASE

What do wrinkles, cataracts and stiff arteries have in common? They are features we associate with older age, and they all involve a build-up of rigid molecules called 'Advanced Glycation End-products', or AGEs.

Now a HRB-funded study has identified that people with chronic high blood pressure have high levels of AGEs in their bloodstream.

Rigid, cross-linked molecules are very much a feature of ageing, explains Dr Azra Mahmud, who conducted the project with the late Prof John Feely at Trinity College Dublin and St James's Hospital.

"If you cut an apple and leave it open, you see the browning reaction as molecules cross-link together," explains Dr Mahmud. "The same process happens in our skin when we get wrinkles or when we get cataracts in our eyes, that's about AGEs being deposited in the tissues."

Recently it has come to light that deposited AGEs are a feature of stiff arteries, and in this study Dr Mahmud found a link with chronic high blood pressure. "We showed that AGEs in the bloodstream are increased in patients with high blood pressure, and they also correlate quite strongly with arterial stiffness," she says.

The study also found high levels of AGEs and stiffness in tissue samples from the aorta - a major blood vessel that serves the heart - in patients with coronary artery disease. "We believe our work will establish the role of AGEs in hypertension and coronary artery disease," says Dr Mahmud, who adds the findings could be an incentive to search for therapeutic agents to target AGE buildup in arteries. "We need something like an AGE-breaker, which de-stiffens the artery."

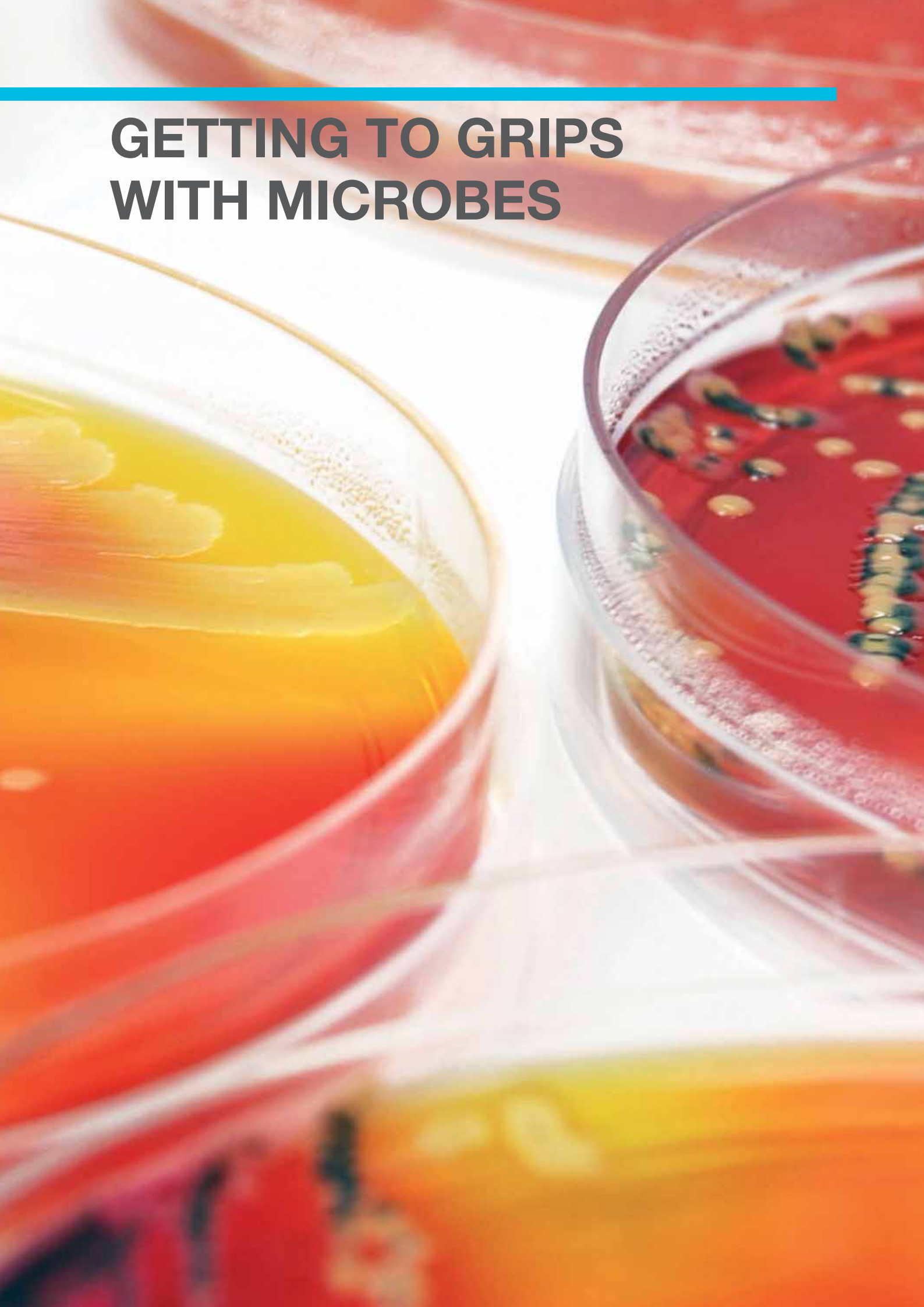
Achievements

- » Identified importance of AGEs in cardiovascular disease.
- » Could be a new target for drugs to keep arteries healthy and lower blood pressure.

Dr Azra Mahmud, TCD



GETTING TO GRIPS WITH MICROBES



REDUCING DIARRHOEAL DISEASE - WITH SUNLIGHT

Putting bottles of drinking water in the sun kills off harmful bugs in the water and can dramatically cut the rates of diarrhoeal disease and dysentery in young children, a study has found.

Over a billion people in the world have no access to safe drinking water on a daily basis, and this results in the deaths of around 1.5 million children under five each year from diarrhoeal disease, explains Dr Kevin McGuigan, who heads the Solar Disinfection Group at the Royal College of Surgeons in Ireland.

“We are trying to address that problem in a way that is affordable and easy to use,” he says, describing the solar disinfection (SODIS) method, where UV rays from the sun and an increase in water temperature can kill bacteria.

“It’s very simple - you fill a plastic bottle with whatever water you have available. Then you place that in direct sunlight for a minimum of six hours, and by then the water is biologically safe.”

The group, which runs projects in Asia and Africa, recently worked with CARE Cambodia on a 12-month study involving almost 1,000 young children in Cambodia, which was funded by Irish Aid through the HRB.

If a participating family used SODIS to clean their drinking water, there was a 50 per cent reduction in dysentery and a 63 per cent reduction in non-dysentery diarrhoea among the children under five, compared to families who did not use SODIS.

“In each case we found the count in the solar disinfection bottles were over 10 times less than the count in the test bottles,” says Dr McGuigan.

Even after the trial ended, many families there continued to use SODIS to clean their drinking water, he adds.

Achievements

- » Dramatic reduction in diarrhoeal disease among young children in developing countries.
- » Validates cheap and effective way to disinfect water.

Dr Kevin McGuigan, RCSI



PROTECT YOUR HEART AS WELL AS YOUR SMILE

Unhealthy teeth and gums can put you at increased risk of heart attack and stroke, and a new study funded by the HRB has identified a possible reason for that link.

“Your mouth is home to over 600 different species of bacteria, some of which help you break down food. But if you don’t keep your teeth clean, your gums can get inflamed and bleed, and that means bacteria can get into your bloodstream”, explains Dr Steve Kerrigan, who heads the Cardiovascular Infection Group at the Royal College of Surgeons in Ireland.

If bacteria from your mouth end up in your bloodstream, your immune system typically tries to wipe them out. However, if that doesn’t work the bacteria can stick to blood cells called platelets and make them sticky. The sticky platelets can form a clot around the bacteria, which if it gets large enough may then block blood flow to the heart or brain.

“This HRB-funded study identified a protein on the common mouth bacterium *Streptococcus gordonii* that seems to help activate stickiness in the platelets. Ultimately this could lead to a new method for stopping the clot formation without relying on conventional antibiotics”, explains Dr Kerrigan.

But prevention is better than cure, he notes: “A general education programme adopted by the government to teach people - especially children - the importance of brushing their teeth and attending their dentist regularly to avoid potential cardiovascular complications later in life would be of enormous benefit to the Irish population, as all of this can be avoided if people exercise proper dental hygiene, brush and floss regularly.”

Achievements

- » Identified a protein that could link blood infection with increased risk of heart attack or stroke.
- » Could point to new therapies for blood infections by oral bacteria.
- » Highlights the importance of oral hygiene education.

Dr Steve Kerrigan, RCSI



USING BAD BUGS TO DO GOOD THINGS

Probiotic strains of bacteria can deliver health benefits in the gut, but how do you get them there in large numbers? A HRB-funded project has engineered friendly bacteria to be more robust in the body - by stealing a few secrets from not-so-friendly bacteria.

“One of the major failings of wild type probiotics, the ones you would find in yogurts and other foods, is that while they are very beneficial they pass through the gut very quickly, so their beneficial effect is quite short,” says Dr Roy Sleator, who carried out the project at the Alimentary Pharmabiotic Centre in University College Cork.

To figure out how to get greater numbers of good bacteria in the gut, Dr Sleator looked at disease-causing bacteria and identified genes that allow those bugs to withstand the body’s defences.

Inserting these stress-tolerance genes into the good bacteria meant they could survive for longer and in higher numbers in the gut, as Dr Sleator explains.

“We were able to upgrade the probiotics and we found they were better able to protect against infection. The beneficial effect is due to the probiotics themselves and if you increase their numbers you increase the dose, and therefore the therapeutic effect.”

The robust probiotics could now have clinical potential as delivery systems for drugs or vaccines into the gut, he adds.

Achievements

- » Engineered probiotic bacteria survived more effectively in the gut and offered greater health benefits.
- » Developed potential new delivery systems for drugs and vaccines.

Dr Roy Sleator, CIT



HOW DO DANGEROUS BACTERIA MANIPULATE OUR IMMUNE DEFENCES?

Your nose is home to an array of bacteria, and your immune system can usually keep them in check. But sometimes disease-causing bacteria in the nose can dodge those defences, and research jointly funded by the Medical Research Charities Group (MRCG) and the HRB has discovered clues about how they do it.

The study focused on *Neisseria meningitidis* serogroup B, a bug that can cause meningitis.

“Although many people carry these bacteria in their nose some get sick, but some don’t. We are trying to understand what part the immune system plays,” says Dr Ed Lavelle, an Assistant Professor in Immunology at Trinity College Dublin.

The research found that the bacteria make several proteins that steer the immune responses in particular directions so the bacteria don’t get killed off.

“Some of these proteins turn the immune response up, others down, but they all seem to be able to regulate immune responses,” says Dr Lavelle.

The findings can help scientists in the search for vaccines against *Neisseria meningitidis* serogroup B, because if we know what the bacteria need to survive in the nose and go on to cause infection, then a potential vaccine could block those processes.

“If it’s important in helping the bacterium to cause disease then it’s potentially useful as a vaccine target,” says Dr Lavelle.

More generally, understanding how our immune system interacts with bacterial proteins could help us to develop drugs to therapeutically dampen down our own immune responses where they are causing trouble in inflammatory or auto-immune diseases, he adds.

Achievements

- » Identified how a meningitis-causing bug could evade the immune system.
- » Will inform vaccine and immune-based therapies.

Dr Ed Lavelle, TCD



GUT BUGS COULD AFFECT RADIATION DAMAGE

Could altering bugs in the gut help reduce the side-effects of radiation treatment for cancer in the pelvis? That's a possibility raised by a HRB-funded study, which found that gut bacteria could help trigger radiation damage to the normal, healthy gut cells that line the intestine.

"Radiation used to treat cancer can injure normal, non-cancer body tissues such as the intestinal tract," explains researcher Prof Larry Egan, Professor of Clinical Pharmacology at NUI Galway. "When that happens, it causes significant suffering for patients and, if severe, can compromise the efficacy of the anti-cancer radiation if it has to be stopped or reduced."

To examine the role that bacteria in the gut could play in that damage to healthy cells, Prof Egan and colleagues tested the effects of antibiotics and specific genetic factors on the susceptibility to radiation injury in an experimental model.

And what they found was that gut bacteria are required in the gut for radiation to induce damage to the normal cells.

"When gut bacteria were lowered, or the ability of the body to sense them was reduced, less intestinal radiation injury occurred," says Prof Egan.

It raises the possibility, which needs further testing, that changing the population of bacteria in the gut could have a protective effect during radiation treatment that targets the pelvis, as Prof Egan describes.

"The results indicate that manipulation of the host gut bacteria could minimise unwanted damage to the intestine during anti-cancer radiotherapy."

Achievements

- » Discovered in a model system that bacteria in the gut can help trigger radiation damage to healthy intestinal cells during cancer treatment.
- » Manipulating gut bacteria may help minimise radiation damage.

Prof Larry Egan, NUI Galway



A close-up photograph of a woman with short, light-colored hair smiling broadly. She is looking towards the left. In the foreground, a person wearing a blue medical scrub top is holding a dental mirror, reflecting the woman's teeth. The background is a soft, out-of-focus blue. A solid blue horizontal bar is at the top of the image, containing the text.

A BIGGER PICTURE OF PATIENT AND STAFF EXPERIENCES

SEEING THE EVERYDAY IMPACTS WHEN MANAGING LUNG DISEASE

How can clinicians help patients with lung disease whose lives are ruled by breathlessness and fatigue, to the point of being housebound?

A HRB-funded study has found we need a fresh mindset to understand the everyday issues being faced by patients with the progressive lung condition chronic obstructive pulmonary disease (COPD). The work has also been opening up new dialogue around their palliative care needs.

Patients with severe COPD typically experience breathlessness and pain, weight loss and fatigue, explains Dr Geralyn Hynes from the Royal College of Surgeons, who carried out the study at Trinity College Dublin.

But while policies were in place to provide palliative care for such symptoms, there was also evidence of unmet palliative care needs.

Dr Hynes collaborated with respiratory nurses to carry out the study, recruiting 26 patients who had come into hospital with a severe attack of COPD. She later interviewed the patients at home. "Their whole lives were controlled by breathlessness," says Dr Hynes. "And where we focus on the physical needs, the breathlessness, the weight loss or the weight gain, what was really concerning

the patients was they had lost the ability to engage with communities and extended families: they were housebound. So we came to understand palliative care as being about addressing these illnesses or life experiences as integral to managing breathlessness."

An inquiry group set up through the study identified the need for greater focus on planning discharge from hospital and for the nurses to remain in contact with patients following discharge.

Achievements

- » Identified strategies to focus care on the broader experience of patients with severe COPD as well as dealing with acute symptoms.
- » Highlighted the importance of collaboration between palliative and respiratory nurses for care of COPD patients.

Dr Geralyn Hynes, RCSI



FATIGUE IS A SYMPTOM OF ARTHRITIS TOO

Patients with inflammatory arthritis experience not only swelling, pain and tenderness, but also fatigue, and it should be measured alongside the more routinely recognised symptoms.

That’s the finding of a study that tracked the experiences of patients as they underwent treatment for the condition.

“Fatigue is a long-reported symptom of rheumatoid arthritis, but it’s not one that is necessarily well recognised,” explains Dr Patricia Minnock, an Advanced Nurse Practitioner in Rheumatology at Our Lady’s Hospice and Care Services.

To examine fatigue in rheumatoid and psoriatic arthritis, Dr Minnock worked with 130 patients from St Vincent’s University Hospital as they underwent treatment with biologic drugs for the illness.

Her study, which was funded by the National Council for the Professional Development of Nursing and Midwifery and the HRB, looked not only at their clinically measured signs, but also used questionnaires, one short and one long, to rate their fatigue levels.

Overall, the patients showed improvements in clinical signs over six months, and most reported they were not as tired. But for some patients the fatigue persisted, and

Dr Minnock found that they had greater levels of pain and a lower self-belief in their own ability to manage their arthritis.

The study pointed to the need to acknowledge fatigue and include it in regular measurements. It also highlighted the need to empower patients to become better managers of their own arthritis symptoms, says Dr Minnock, who carried out the research through Trinity College Dublin.

“My study has shown the short-form questionnaire is very feasible for use in a clinical setting for the assessment and hopefully improved management of fatigue.”

Impacts

- » Identified the need to measure fatigue when patients are treated for inflammatory arthritis.
- » Validated a short, convenient way to measure fatigue at patient check-ups.

Dr Patricia Minnock,
Our Lady’s Hospice



FACING UP TO NEGATIVE ATTITUDES ABOUT MENTAL ILLNESS

People who have spent time in hospital for mental illness face stigma when they return to the community setting, a HRB-funded study has found.

Around 70 per cent of total admissions to psychiatric hospitals are readmissions, suggesting that many people do not transition well back into the community. To look into the issue, Dr Brian Keogh interviewed 31 service users about their experiences of going home from hospital and what came through in the interviews was the stigma and negative attitudes they face.

“The main problem for the participants overall was how other people viewed them now they were labeled as ‘psychiatric patients’,” says Dr Keogh, who is a Lecturer in Psychiatric Nursing at Trinity College Dublin.

“The participants felt ashamed that they were admitted to hospital, and when they came home from hospital this sense of shame was often reinforced by other people.

Mostly they managed this through concealing their mental health problems. They didn’t tell anyone about them, and often they avoided other people completely and often other people avoided them.”

Dr Keogh also found that the participants had not been prepared for discharge or to manage the stigma that most of them encountered, and he sees an opportunity for improvement here.

“I think there needs to be a more formalised way of assisting people to cope with stigma when they are going home from hospital,” he says.

“People who use the mental health services need to be made aware that stigma is an issue and they need to be given skills and strategies to be better prepared to react or cope with stigma.”

Achievements

- » Identified stigma as a major problem for people who have been hospitalised for mental illness.
- » Better preparation needed for service users before discharge from hospital.

Dr Brian Keogh, TCD



CHILDREN WANT TO BE SEEN AND HEARD WHEN PARENTS SEPARATE AFTER A HISTORY OF DOMESTIC ABUSE

Children in families where the parents have separated after a history of domestic abuse - perpetrated by their father against their mother - want to be included in discussions about contact with the abusive parent, their father.

That is one of the findings of a HRB-funded study that examined the experiences and the concerns of children in Ireland where there has been a history of the father abusing the mother before separation.

“I was asking how do children experience contact with their fathers after the parents have separated, what are their particular emotional needs and physical safety needs and are they being met,” says researcher Dr Stephanie Holt, a social worker based at Trinity College Dublin.

Crucially, Dr Holt involved children directly in the process of finding out more about their experiences by listening to what they and their parents had to say.

And what she heard from 16 children and young people who took part was a mix of responses.

“Some were desperate for contact with the fathers who had no interest in them, while other children wanted no contact,” says Dr Holt. “But for me the overriding consideration was that very few people, including their parents, actually sat down with the child and asked ‘what do you want?’.”

Problems then arose in the court setting, where decisions were being made on behalf of the child’s best interest, but without taking into account the individual child’s wishes.

This is the first time a study in Ireland has looked at the issue of post-separation contact in the context of domestic abuse from a child’s perspective, but the findings resonate with international studies, says Dr Holt.

Her research also highlighted the continued abuse of mothers and children by the mother’s ex-partner through the facility of child contact.

Achievements

- » Children want a stronger voice in post-separation contact arrangements following abuse.
- » Abuse of the mother and children can continue through post-separation contact.

Dr Stephanie Holt, TCD



ASYLUM-SEEKERS AND REFUGEES MEET BARRIERS TO MATERNITY SERVICES

Asylum-seeking and refugee women in Ireland experience difficulties using Irish maternity services for several reasons, including communication barriers, dispersal policies, perceived racism and the predominance of technological modes of delivery.

Those are among the findings of a study by HRB Clinical Midwifery Fellow Dr Carolyn Tobin, who carried out interviews with 22 women in accommodation centres in Ireland.

While at Trinity College Dublin, Dr Tobin organised and conducted interviews with asylum-seeking and refugee women who had given birth here, and several issues came to the fore.

“The biggest one was communication and lack of access to interpreters,” says Dr Tobin. “That increased anxiety, and had a knock-on effect on informed consent.” Other obstacles included the technological birth culture that predominates in Ireland - this can be a source of fear for someone coming from an environment where an operative delivery can mean maternal death, explains Dr Tobin.

Loneliness, perceived racism and barriers to breastfeeding were also cited in the interviews, she adds. The policy of dispersal, which saw families being moved at short notice to other regions within Ireland posed problems for women who had recently had a C-section, had medical or post natal complications that

required follow up or whose infants needed post-natal medical follow up - women reported waiting up to three months to have medical records transferred to their new doctor, the study also found.

“There’s a need for more of a community based social model of midwifery that would provide relationship and support and improve communication and continuity of care,” says Dr Tobin. “There should be dedicated on-site antenatal education for pregnant women seeking refuge and asylum in Ireland, as this group have a set of very specific needs that are currently not being met.”

Achievements

- » Communication, birth culture and dispersal policies create barriers for asylum-seeking and refugee women giving birth in Ireland.

Dr Carolyn Tobin, TCD



HOW THE SMOKING BAN EXEMPTION AFFECTS NURSING HOMES

Nursing homes that freely allow smoking indoors show high levels of staff exposure to nicotine, and particulate matter in the air is on a par with Irish pubs before the smoking ban was implemented, according to a joint Medical Research Charities Group (MRCG) and HRB-funded study.

The ban on smoking in workplaces in Ireland came into effect in 2004, but there were some exemptions. One was nursing homes, because for residents, that's where they live.

A study of 20 nursing homes in the Meath/Kildare area found that individual homes have different policies: two premises banned smoking completely, two allowed smoking anywhere indoors and the remainder tended to restrict smoking to a dedicated common room.

The study, conducted by Dublin Institute of Technology and the Tobacco Free Research Institute, measured particulate matter in the air in the homes - some of which would originate from smoking. They also asked staff to wear badges that measured nicotine levels in the environment, and nicotine badges were placed in the nursing homes.

What did they find? Particle levels measured in smoking areas in nursing homes were about eight times higher than in the nursing homes where smoking was completely prohibited, and those high levels were similar to those observed in pubs prior to the smoking ban.

Meanwhile staff in 'smoking' homes were exposed to levels of nicotine that were around four times higher than were similar staff in the non-smoking homes.

The results of the study should inform policies to help minimise the exposure of non-smokers, both staff and residents, to tobacco smoke in nursing homes, explains researcher Prof Pat Goodman from DIT.

Achievements

- » First direct measurement of how the smoking ban exemption affects nursing home environment.
- » Will inform policies to reduce tobacco smoke exposure in nursing homes.

Prof Pat Goodman, DIT



LEARNING FROM THE EXPERIENCES OF SUICIDAL MEN

What helps young men to overcome feelings of suicidality? HRB-funded research has found that more open discussion about suicidal feelings can help suicidal young men rebuild their sense of value.

The study, carried out by Dr Evelyn Gordon and Prof Chris Stevenson at Dublin City University, interviewed 17 men aged 18 to 34 about their experiences of feeling suicidal and how they overcame their suicidality.

“Through the assistance of people in their social and professional network, these young men managed to regain a sense of value in themselves as individuals who were worthy of life,” says Dr Gordon, a Lecturer in Psychotherapy and Mental Health at DCU.

“The key practices that enabled that transition included being treated as a person of value - being listened to, being asked about their fears and concerns, and being asked what their wishes were for their own care and treatment for those in the mental health services. This helped them to take more control of their lives and to develop a sense of empowerment.”

The study found that social stigma pushed many of the men into concealing their suicidal feelings from those close to them and from health professionals, explains Dr Gordon.

“They felt ashamed and they could not talk about it - it was a mechanism to protect themselves and others,” she says. “But often

what helped was a positive response or a simple act of human kindness - that often served as a turning point for these young men.”

The study - and the wider literature - shows that healthcare professionals often feel ill-equipped to discuss suicidal feelings with their patients, according to Dr Gordon.

“Simple things could help - for example being open to enquiring about the feelings of a young man arriving at the surgery. What our study shows, contrary to some common myths, is that if you talk openly with the person about their feelings and anxieties, it helps them feel more normal.”

Achievements

- » Identified the need for more open discussion about fears and concerns that exacerbate suicidality among young men.
- » Generated awareness leaflets for health professionals, families and the suicidal person.

Dr Evelyn Gordon, DCU



SHOULD I STAY OR SHOULD I GO? A STUDY OF NURSE MIGRATION IN IRELAND

In recent years, Ireland has actively encouraged an influx of nurses from outside the EU, and migrant nurses play an important role in our health service. But will they stay?

A HRB-funded study has gathered key data about migrant nurses in Ireland, and has highlighted crucial issues around retaining their expertise here.

The Nurse Migration Project combed through registration and work authorisation data and found that between 2000 and 2009, 38 percent of nurses newly registered in Ireland came from outside the EU, with the majority coming from the Philippines and India.

The study, which was carried out through the Royal College of Surgeons in Ireland, also interviewed more than 300 migrant nurses in 2009, and found a significant proportion had actively considered onward migration and only 19 percent (65) of respondents were planning to remain in Ireland.

Issues highlighted include the lack of career progression of migrant nurses in Ireland, and factors cited as potential reasons to leave Ireland included uncertainty over residency and citizenship, the impact of the recession in Ireland and careers opportunities overseas.

“Health workforce planning projections for Ireland suggest an ongoing need for migrant nurses,” states a policy document prepared by researcher Dr Niamh Humphries, Prof Hannah McGee and Prof Ruairi Brugha from RCSI. “Health workforce planners need to carefully consider the implications of the potential loss of significant numbers of migrant nurses from the Irish health system.”

Achievements

- » Highlighted issues around retaining migrant nurses in Ireland.
- » Developed a series of policy briefs detailing the origins, experiences and issues faced by migrant nurses in Ireland.

Prof Ruairi Brugha, RCSI



PROBLEMS FOR INJECTING DRUG USERS WHO NEED HEPATITIS C CARE

Hepatitis C is a serious problem among injecting drug users, where the chronic infection damages the liver. Yet only a small proportion of infected drug users access health services for the virus. A HRB-funded study sought to find out why.

The researchers interviewed problem drug users and healthcare professionals across a range of services in the eastern region of Ireland. They included GP practices, addiction clinics, community agencies, and specialist liver and infectious diseases units.

So what barriers emerged? “Perceptions of hepatitis C and competing priorities are important reasons why problem drug users do not access treatment,” says lead researcher Dr Davina Swan from University College Dublin. “Meanwhile, relationships with health care providers, education and if they develop symptoms of liver disease are reasons that motivate them to access treatment.”

The findings from the research team - which included staff from HSE Addiction Services, Canal Communities Drugs Task Force, Community Response and St James’s, Mater and St Vincent’s Hospitals - can now inform the provision of hepatitis C care for problem drug users.

“This research highlights a need for interventions which raise awareness of hepatitis C among at-risk groups and which help problem drug users with hepatitis C infection access treatment and reduce alcohol use,” says Principal Investigator Prof Walter Cullen, now at the University of Limerick.

“The study recommends that education and further integration between primary and secondary care are likely to be key elements of such interventions.”

Continuing work is exploring problem alcohol use among problem drug users, which affects liver and mental health among people infected with hepatitis C.

Achievements

- » Identified reasons why many injecting drug users with hepatitis C do not access services to treat the condition.
- » Findings are informing policies on the provision of hepatitis C services.

Prof Walter Cullen, UL and
Dr Davina Swan, UCD





FOCUS ON BREAST CANCER RESEARCH

CELL MOLECULES LINKED WITH AGGRESSIVE BREAST CANCERS

Cell molecules called MAGE-D4B and NCS-1 are present in many aggressive breast cancers, and they could offer a potential 'biomarker' to help identify which patients need harder-hitting treatment.

"Breast cancer doesn't have a 'one-size-fits-all' solution and so better ways of diagnosing, prognosing and treating patients as individuals are essential," says Prof Lorraine O'Driscoll, a Principal Investigator in the School of Pharmacy & Pharmaceutical Sciences at Trinity College Dublin.

Her HRB-funded group looked at tumour samples from patients, and also at cells growing in the lab, and they found that MAGE-D4B and NCS-1, which are gene products, are detectable in many breast tumours, but are generally undetectable in normal breast tissue.

In particular, where the MAGE-D4B is present, the tumour tends to have more 'dangerous' characteristics such as rapid growth, spread to lymph nodes and earlier relapse and death of the patient, according to Prof O'Driscoll.

And looking at cells growing in the lab, MAGE-D4B appears to be associated with cancer cells that would have the capacity to move to other sites in the body.

"Our results suggest that MAGE-D4B and NCS-1 have potential as biomarkers for sub-groups of cancer patients; where they are associated with poor outcome in terms of both time to relapse and death from breast cancer," says Prof O'Driscoll. "They may help to prognose outcome and so contribute to treatment decisions - whether a patient should be prioritised for treatment or just undergo on-going observation."

Achievements

- » Found two genes that appear to be associated with aggressive breast cancer.
- » May have potential as biomarkers to identify which patients need more rigorous treatment.

Prof Lorraine O'Driscoll, TCD



USING COMPUTER TECHNIQUES TO FIND CANCER GENES

Researchers at University College Dublin have discovered a gene that gets switched on in aggressive breast cancer - and they found it initially by trawling through publicly available computer databases.

The study looked to help solve the puzzle of why some breast cancers respond well to treatments while others don't, explains Prof Des Higgins, one of the researchers on the HRB-funded project.

"We were trying to find clues at the genetic level, at the level of gene expression," he says.

It's a commonly taken approach, and because hundreds of studies have already been carried out on the genes that are expressed in breast cancer, publicly available databases of genetic information are available from patient samples from around the world.

"We looked at various datasets using some of the techniques we had developed in our lab - this was purely computational, running computer programmes and doing data analysis," explains Prof Higgins.

And the results highlighted a molecule - a type of 'microRNA' - that was of interest.

"It stood out - it seemed to be highly expressed in one lot of patients and not in another."

To zone in on that molecule, Prof William Gallagher's group at UCD went to look for its

expression in banks of real tissue samples, and used lab models to see what happens when the gene is switched on strongly.

The results linked this microRNA with more aggressive types of cancer and, if validated, it could possibly act as a measurable signal to help identify patients in need of specific treatments.

"It would be potentially a red flag," says Prof Higgins. "The initial use of this would be as a marker to help subdivide patients into categories, but in the longer term it could give you possible targets for therapies."

Achievements

- » Identified a gene that is switched on strongly in samples from breast cancer patients with more aggressive disease.
- » Project methods provided foundation for Molecular Therapeutics for Cancer Ireland, a Science Foundation Ireland Strategic Research Cluster.

Prof Des Higgins, UCD



A 'STICKY' CLUE IN BREAST CANCER SPREAD

A HRB-funded study has pinpointed a protein that helps breast cancer to spread to other sites in the body in a process called metastasis.

The protein, CD44, appears to help cancer cells 'stick' at remote sites where they can then grow and form secondary tumours.

"Metastasis is the leading cause of cancer deaths worldwide and the process itself is massively understudied," says Post-doctoral Researcher Dr Suzanne McFarlane from Queen's University Belfast. "We need to understand it at the cellular and molecular level."

Dr McFarlane's project looked at breast tumour biopsies from patients and found that if the tumours showed high levels of CD44 they were associated with poorer survival outcomes and more formation of distant tumours.

Next she looked at how breast cancer cells behave in the bloodstream, and used a mouse model to work out that if CD44 levels are high in the cancer cells, they tend to reduce survival time and increase tumour burden. But if the cells had low CD44 levels, the outlook was better.

"If the tumour cell had CD44 the animal got sicker much quicker, the rate of metastasis was higher," she describes. "But when we stopped the cells expressing CD44 we found increased survival and decreased burden of tumours."

Dr McFarlane also found that CD44 plays a role in the wandering cancer cells sticking to normal cells that line the bloodstream, and she worked out how it affects the cell's biochemistry to increase this stickiness.

Ultimately the finding could point the way to using CD44 to help identify tumours that are at high risk of spreading elsewhere in the body, or even identify targets where drugs could intervene and stop the cells sticking, she says.

Achievements

- » Identified possible role for CD44 protein in breast cancer cells spreading to other sites in the body.
- » Potential marker to identify at-risk patients, or drug target for treatment.

Dr Suzanne McFarlane, QUB



BREAST CANCER SIGNALS IN THE BLOODSTREAM

A biopsy of tissue taken from a tumour can tell doctors much about a patient's breast cancer. But what if you could also get information about the tumour from a straightforward blood sample?

A HRB-funded project at NUI Galway has been looking at how measuring levels of specific molecules called chemokines that are circulating in a patient's bloodstream can offer clues about the characteristics of breast cancer tumours.

"Chemokines are produced by cells and released into the bloodstream," explains Dr Roisin Dwyer, who worked on the project with Dr Shirley Potter and Prof Michael Kerin.

"They play an important role in controlling cell behaviour and in the context of breast cancer, are thought to be involved in stimulating tumour growth and spread to other organs."

The researchers found high levels of a chemokine called SDF-1a in the bloodstream of patients with breast cancer compared with healthy controls.

And when they looked at samples of the corresponding tumours, they found an interesting pattern: "While the tumour cells were shown to release chemokines, it was found that the cells surrounding them secreted even higher levels," says Dr Dwyer.

"This in turn stimulated the breast cancer cells to migrate or move, indicating a potentially important role in the spread of tumour cells to other organs. Further understanding of the elements controlling chemokine secretion will clarify their role in breast cancer and may support the development of new therapeutic agents."

Achievements

- » Found high levels of a 'chemokine' molecular signal in the bloodstream of breast cancer patients.
- » Points to possible new ways of diagnosing or monitoring breast cancer from blood samples.
- » Identified potential role for chemokine molecules in breast cancer spread.

Dr Roisin Dwyer, NUIG



PREDICTING CHEMO DRUG RESPONSE IN BREAST CANCER

Many women with breast cancer are treated with the drug paclitaxel (Taxol®), and for some, the drug works well. But not for everyone: some tumours have or develop resistance to the drug, and a HRB-funded project has been finding out why.

The research looked at a molecule called MAD2, explains Dr Amanda McCann, Senior Lecturer at the UCD School of Medicine and Medical Science, and Dr Fiona Furlong, now a Cancer Research Ireland Fellow, who worked together on the project.

“Currently, there is no way of knowing if a patient’s tumour is resistant to paclitaxel based regimens,” says Dr McCann. “And we would like to prevent a patient from suffering the unwanted side effects of a drug which they ultimately will not respond to.”

The project found that if breast cancer cells growing in the lab had high levels of MAD2, they died if exposed to the drug. But if the researchers engineered the cells to have lower levels of MAD2, then the cells became resistant by going into a senescent or non-dividing state and the drug could not have an effect. The study also found that low levels of oxygen in the cancer cells diminished MAD2 and led to resistance to paclitaxel.

The findings have implications for characterising tumours and deciding the best course of treatment for the patient, says Dr Furlong: “The measurement of MAD2 at the time of cancer diagnosis has the potential to identify which tumours may be efficiently eradicated with paclitaxel and thereby guide the clinical management of the cancer at the outset of patient care.”

Achievements

- » Showed that a molecule, MAD2, may mediate resistance to a drug commonly used to treat breast cancer.
- » Low oxygen levels in cancer cells increases resistance to the drug.
- » Findings can help identify optimum treatments for patients.

Dr Amanda McCann, UCD



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