MRC Medical Research Council

Max Perutz Science Writing Award 2016

Shortlisted essays

Winner

Liza Selley, MRC-PHE Centre for Environment and Health

Braking perceptions of traffic pollution

It's been splashed across the papers – traffic pollution is a menace. Striking 30,000 of us each year with heart disease, respiratory illnesses and lung cancer, vehicle fumes kill four times as many people as car accidents and hospitalise a great many more.

At the beginning of my PhD my supervisor asked me to conjure up an image of traffic and tell him where I thought those fumes came from. Picturing a trail of lorries trundling up the motorway, I confidently answered that they came from the exhaust pipe.

Now I wasn't wrong – those lorries would have produced half a kilogram of exhaust per mile travelled – but I really wasn't considering the full picture. I hadn't thought about the wear and tear that occurs each time the clutch is released or the brakes are squeezed, the friction that shears at the tyres and the road surface or the dust that the wheels kick up. I certainly hadn't realised that the particles that these processes create represent more than half of vehicle emissions.

The problem is that neither have my colleagues and neither have our policy makers. Think of all those headlines warning of the dangers of exhaust emissions: ‘Diesel is killing thousands!’, ‘Exhaust causes cancer!’. Have you ever read that about brake dust or tyre wear? No, because air pollution scientists are caught in a diesel storm, and despite knowing that non-exhaust particles have toxic properties, haven’t got round to seeing what that other pollution does to people’s lungs.

That is what my research is about: discovering the other half of the story and providing the policy makers with evidence that we need to regulate wear particles as well as exhaust fumes. Otherwise it’s like removing the nest but leaving the wasps behind – as diesel emissions decrease, non-exhaust particles will remain in the air and our hearts and lungs will keep getting stung.

Our lungs are defended by macrophages – caretaking cells that hoover up inhaled germs and particles, protecting us from chest infections and keeping us breathing smoothly. In the lab I sprinkled brake dust, particles produced when brakes and wheels press together, onto these cells and found that they could only hoover up a quarter of the germs that they usually can.

I also noticed that brake dust encouraged the macrophages to release alarm signals called cytokines, which call the rest of the immune system for assistance, and damaged energy production, forcing the caretaker cells to enter self-destruct mode. The most important discovery however, was that brake dust impacted all of these functions to the same extent as our old friend, the diesel exhaust particle.

Worryingly, this means that brake dust is as capable of causing what I call ‘London Throat’ – the constant froggy feeling and string of coughs and colds that city dwellers endure – or the same deadly asthma attacks as diesel exhaust. It also means that brake dust contributes to the £62 billion that we spend each year on pollution-related healthcare.

As a non-exhaust enthusiast, my supervisor was very excited to hear this and through mutterings of “I told you so!” suggested we delve further to see why brake dust is so toxic. We found that brake dust is made predominantly from metals and that blocking those metals chemically was like bacon to a hangover. Without its metals, brake dust had no impact on germ hoovering, cytokine production or cell survival. This showed that metals are responsible for brake dust toxicity and suggested that we ought to be worrying about other metallic pollutants like clutch and road wear too.

The importance of these findings are easiest to understand when you consider all of the improvements that stemmed from matching investigations into exhaust toxicity. Policy makers responded by introducing diversions for the fumiest vehicles, surcharges for diesel car parking, fleets of ‘green’ buses to replace the older polluting ones, and charging points for electric vehicles popped up like daisies.

But like a pessimist at a party, my research has shown that these interventions aren’t enough. People who live in low-exhaust areas will still be inhaling dangerous pollutants and unless we tackle those emissions too, our health and our economy will continue to feel that sting.

Runner-up

Katie Ember, MRC Centre for Regenerative Medicine at the University of Edinburgh

Cholangiocarcinoma: The cancer you've never heard of

It's just as vital to our survival as our hearts. But the first time I watched a human liver being dissected, I realised how little I knew about this incredible organ. Wei – the post-doc carrying out the procedure – was sitting in front of a sterile cabinet, a scalpel in one purple-gloved hand and forceps in the other. Unfortunately, I'm not a biologist by training and was about to make this painfully obvious.

"How many livers have you got there?" I asked.
From what I could see, he was working on about three livers all piled together on a stainless steel tray. He looked momentarily confused.
"Half," he replied. "This is half a liver."

I was astonished. Admittedly, this liver wasn't surrounded by bones, muscles, fat and other organs to keep it compact, so it had expanded. Even so, I couldn't imagine how the half-a-liver could fit inside a body along with heart, lungs, intestines, pancreas and stomach. Let alone a *full* liver. "Yeah, it's actually the largest internal organ," Wei explained. "It takes up most of the middle of your torso."

Weighing approximately 1.5kg with a diameter of 14cm, the liver is responsible for detoxification of harmful substances in your body; including alcohol, drugs and toxic by-products of normal biological processes. It assists blood clotting, synthesises hormones and stores energy. It's a fascinating, complex organ and we can't live without it, but what I'm interested in is something inside the liver that can put the rest of it at risk.

Wei indicated a tiny pale vessel, running like a string through the surrounding rust-coloured tissue.
“Here’s a branch of the bile duct.” This small tubule is the focus of my research. The bile duct carries bile from the gall bladder, where it’s stored, through the liver to the small intestine. Here, bile is critical for the digestion of fats.

All the thread-like branches of the bile duct connect to a main ‘trunk’ in the liver, the common bile duct, which is about 1.5cm wide. But compared to the size of the liver, it is minuscule and this is the challenge I’m facing. This seemingly innocuous vessel is the source of a rare but incredibly lethal form of cancer – cholangiocarcinoma.

In general, cancer survival rates are improving dramatically: now half of those diagnosed with cancer survive at least ten years after diagnosis. However, if you’re diagnosed with cholangiocarcinoma, your chance of still being alive in five years is 5 per cent. That’s one of the worst prognoses for any cancer out there and it hasn’t changed in decades.

One of the main problems is that conventional medical imaging techniques such as magnetic resonance imaging (MRI), X-ray and positron emission tomography (PET) scanning all rely on detecting rays of light or radiation passing through the patient – whether these are radio waves, X-rays or gamma radiation. These methods are brilliant for imaging large organs or diseases that cause significant internal changes, such as coronary heart disease. But light is absorbed by tissue: if there is a lot of tissue between the source and the detector, the resolution of the images produced is much lower. As the bile duct is embedded in our enormous liver which is in turn surrounded by more tissue, tumours arising from this area are only detected when they’re about 2cm in diameter. And by then, it’s almost always too late.

Although considered a ’rare cancer’ thousands die annually from cholangiocarcinoma and research is hampered by a lack of awareness and funding. We need early diagnosis. Bile duct biopsies are possible, but they’re painful for the patient and there’s the danger that samples could be taken from the unaffected area alone. The aim of my research is to develop a way of detecting

cholangiocarcinoma as early, accurately and non-invasively as possible, and to do this I'm also using light. But unlike standard scanning methods, I'm going to be detecting as much light as possible by both shining it and collecting it inside the bile duct via endoscopy.

Endoscopes are formed of bundles of optical fibres – glass cables that can transmit light with incredible accuracy. These are identical to the cables used to channel internet data at high speeds, except I'll be using them to shine light into the bile duct and then collect light scattered back by the same bundle. Light scattered by cells tells us about their chemistry, because different molecules absorb and scatter light to different extents. Cancer cells are chemically very distinct from healthy cells: they direct their chemical reactions into growing and dividing rapidly, rather than carrying out normal cellular functions. My hope is that we can sense these molecular changes using endoscopy.

Maybe then we will be able to diagnose this most lethal of cancers in time to do something about it.

Commended

Paul Cowling, University of Edinburgh

Shedding some real light on lung cancer

It is June, and twilight sets in over the bustling beer garden. I take a drink from my pint before returning my attention to my friend Chris who is ranting about the state of affairs at Newcastle Football Club. He finishes venting his anger over the team's lacklustre performances and proceeds to light a cigarette.

I watch the embers glow at the tip as he inhales over 4000 chemicals into his lungs, 43 of which cause cancer. I look around the beer garden to see dozens of other people doing the same thing. With every cigarette they smoke, they typically lose eight minutes off their lifespan.

For smokers, those 43 chemicals significantly increase the risk of developing lung cancer. This lethal cocktail reacts with your DNA and causes mutations on the molecular level. Over time, the numbers of these mutations grow, until your cells morph into out-of-control growth machines – cancerous tumours. Cancer is such a deadly disease because bits of these tumours often break away, travel around the body to other organs, and establish new growths.

Statistically, one in two UK citizens born after 1960 will get some form of cancer – that's three out of my six friends at the pub). Of every diagnosis, one in five will be lung cancer, which is predominantly caused by tobacco smoking. Lung cancer survival rates are equally daunting: for every 100 diagnoses, only 15 patients will survive to five years following diagnosis. This could be improved through earlier detection; if patients are diagnosed in the earlier stages of the disease, their survival rate can be as high as 50 per cent after five years.

My research is about finding a faster and more reliable way to diagnose lung cancer. Unfortunately, it's not always easy to diagnose lung cancer early enough. The most common symptoms – persistent cough, tiredness and shortness of breath – might seem trivial and are commonly associated with many other lung diseases. Additionally, more serious symptoms don't present themselves until it is too late. Another problem is that our current diagnosis methods are 'one-size-fits-all'.

So I am trying to find out what is cancerous and what is healthy with a targeting agent. I use proteins, called antibodies, which are produced by the immune system to help fight off infections. Once made, antibodies are designed to have a single, specific target; they are essentially the 'homing missiles' of the body. Nowadays, we can make and select an antibody that will only target lung cancer cells.

Next, I attach the metal palladium to the antibodies. Palladium acts like a light switch, essentially 'switching on' the properties of certain chemicals. Finally, I introduce one of these certain chemicals into the lung to be switched on by palladium: a fluorescent molecule, which absorbs light and then spits it back out again as a different colour. And there you have it: a big, glowing sign marking the location of cancerous cells.

What you may not know about the human lung is that it has its own fluorescent glow, which is caused by the same proteins that make the tissue stretchy so that your lungs expand when you inhale. This means that when I use fluorescent molecules to distinguish between healthy and cancerous cells, they need to glow differently from the lung itself so that I can generate some contrast. Think of it like trying to see the stars when the moon is out: the moonlight swamps the light from the stars, obscuring them.

It's the same with using fluorescent molecules in the lung. My solution for this is to use a series of fluorescent molecules, like a firecracker or a chain of fairy lights. The palladium 'light switch' will cause these molecules to glow simultaneously and more brightly than the lung's own fluorescence. It's essentially like having 10 stars glowing in the exact same place so that you can see them.

When my research comes to fruition, I hope to provide a new method for earlier diagnosis of lung cancer, which means that treatments will be more effective. So, the five-year survival rate has the potential to increase from 15 to 50 people out of 100. However, what it really means is that my friend Chris has a chance at a longer life and may one day be sitting in that same beer garden boasting about the triumphs of Newcastle Football Club.

Commended

Edie Crosse, MRC Regenerative Medicine at the University of Edinburgh

Back to blood's beginning: searching for the cure for leukaemia

Blood, both vital and sinister, is tied so closely to our ideas of what it is to be human, warm and alive. Throughout history people have felt connected to their families, tribes and countrymen imagining that the same blood flows through their veins – as if more than just cells but spirit is circulated. Nordic people often allude to their Viking blood making them hardier and stoic; the ancient Mayans believed blood was given by the Gods to bestow them with life, and frequently gave ritualistic blood-letting ceremonies to return it to them.

These cultural perceptions of blood are perhaps why the word leukaemia is so evocative – as if the essence of the afflicted person has been polluted. Blood cancer. The UK alone saw 9,300 new cases in 2013 and on average 13 deaths each day. There is clearly important work to be done and my PhD plays a part in that.

Leukaemia arises from the blood stem cells which reside in the bone marrow. In normal healthy conditions these stem cells, termed haematopoietic stem cells (HSCs), divide to either create a new version of themselves or to generate cells of the blood and immune system. In leukaemia, a genetic change causes uncontrolled proliferation of one of the blood cell types, disrupting the balance of the blood dynamics and resulting in increased susceptibility to infection as well as reduced ability to clot and heal wounds and bruises. The effects are devastating.

Current treatment sees patients receiving chemotherapy and/or radiotherapy to kill the cancerous cells. They are then transplanted with HSCs deriving from the bone marrow either harvested from themselves at an earlier stage or from a donor. These cells have the amazing ability to find their way from the blood

vessels to the bone marrow of the recipient, set up camp there and start a production line of all the cells of blood and immune system.

But it is a far from perfect solution. Transplants deriving from the patient's own cells may contain contaminating cancerous cells and remission is a frequent occurrence. Cells from the patient would recognise donor transplanted cells as foreign and vice versa prompting a two-way immune attack. This means immunosuppressive drugs are required in a patient whose immune system has already been nearly wiped out from the radiation and chemotherapy. The result is an extremely sick patient at high risk of further disease and infection and mortality rates remain high.

This is where my PhD project comes in. What if it were possible to generate an unlimited source of healthy HSCs from the patient's own cells thus avoiding the immunosuppressive drugs that weaken the patient so much? Nobel Prize winning techniques have shown it's possible to turn back the time on cells, reprogramming them to a powerful stem cell state capable of generating any cell type in the body simply by altering the expression of a few critical genes. If we could then direct these cells to become an HSC, scan and correct them for cancer causing abnormalities, we've got ourselves some transplantable, patient-specific stem cells.

Simple right? In practice, in order to reprogram these cells you have to understand in great detail how these cells are generated naturally in the body. This involves an extraordinarily complex network of signals, spanning from the far-ranging down to communication between neighbouring cells. This lets the cell know that it is in the right place at the right time and it changes its identity into that of a blood stem cell. Some of these critical signals are known but they have not been sufficient to make the perfect HSC in the lab.

This process first occurs early in embryonic development, so it is this time that we study so meticulously in our lab group. We know the region in the embryo where HSCs first arise, in the central blood vessel, and we know the type of cell that they morph from. It is my job to screen this region for signals that are likely to turn them into HSCs. This takes a bit of detective work. Certain clues, such as changes in

cell shape, indicate a cell changing into an HSC. This transition involves different genes being switched on or off so comparison of differences between shape-changing cells and their unchanging neighbours may reveal critical signals that were previously unknown.

The very first HSCs are extremely rare but we are constantly whittling down the population of cells in which we know they reside. It is not too far a distant notion in which we crack the code of their identity. Then it's a short hop to generating them for clinical use and using them to treat leukaemia as well as other blood disorders. So perhaps as well as giving people back their health we can give them back their spirit.

Commended

Ainslie Johnstone, University of Oxford

Practice – not miracles – makes perfect

On 8 January 2011 Gabrielle Giffords, a US congresswoman, was shot in the head at point-blank range. The bullet struck Giffords' forehead on the left-hand side and travelled straight through her brain, destroying everything in its path.

Though this assassination attempt ultimately failed, the congresswoman awoke from a medically induced coma, unable to speak, move, or breathe unassisted. Different regions of our brains are responsible for performing different functions, and the incident had damaged parts of Giffords' brain controlling movement of the right side of her body, vision on the right, and areas responsible for speech and language.

Yet in August of the same year, less than eight months after the attack, Giffords walked back into Congress. She still had impaired vision on the right, and trouble moving her right arm and leg; but she could walk unassisted, understand language as normal, and was speaking in short sentences. The media reported the congresswoman's miraculous recovery – but this was no miracle, just an example of neuroplasticity, which we study in my lab in Oxford. Neuroplasticity describes the way in which, even as adults, our brains can modify and adapt according to our needs.

Here in the UK there are around 1.1 million people who have survived some form of brain injury. These injuries can be caused by accidents, as in the case of Ms Giffords, or by a stroke, where the blood supply to a group of neurons is cut off, causing them to die. Whatever the cause of brain injury, once fatal damage to neurons is done, it cannot be undone. The skills that these neurons were once responsible for will, at least temporarily, be lost.

This sudden loss of ability takes an emotional, as well as a physical toll: around two-thirds of people with brain injury go on to experience depression or anxiety. However, with rehabilitation and intensive practice of her lost skills, such as speaking and walking, our brains can reorganise their functions, as happened for Ms Giffords. Healthy brain cells, known as neurons, which were close to the damaged areas, had taken on the roles of their dead neighbours. This neuroplasticity is critical for allowing sufferers to regain full and independent lives, yet it is a process that is not very well understood.

My research focuses on how we can enhance neuroplasticity within areas of the brain that control our movements. This is particularly important for improving recovery after a stroke, where around 80 per cent of survivors are left with movement problems. I am trying to identify the best way for people to learn a new skill, and investigate how different methods of learning change the brain. As well as testing things like the effect of giving different instructions, I have also been experimenting with something a little more unusual. In an attempt to boost neuroplasticity I have been using tiny electric currents to stimulate the brain.

My technique of choice is called transcranial direct current stimulation, known as tDCS, which is not nearly as terrifying as it sounds. During my experiments, volunteers have two rubber electrodes attached to their head, one close to the movement control areas of the brain, and another on their forehead. tDCS works by sending a very low electric current through the brain, between the two electrodes – most people don't feel anything. Participants in my experiments have either real or placebo tDCS while they practice a new skill. Those people who have real tDCS tend to learn skills faster, and remember them for longer, than people who have placebo.

While it's pretty amazing that tDCS benefits skill learning, I am more interested in what it does to the brain. Using magnetic resonance brain imaging (MRI), and magnetic brain stimulation, I study how tDCS changes the amounts of certain natural chemicals within the brain. In my lab, we think that changing the amount of these neurochemicals is the first stage in allowing new connections to form between neurons. By creating these connections, areas of the brain are able to take on new roles as they are needed. This change in neurochemicals occurs

when people intensively practice something, and when they receive tDCS. For this reason, we think that tDCS is boosting the natural neuroplasticity process.

Although most of my experiments are performed on healthy volunteers, the principles are just the same in an injured brain. In proof of this, researchers in my lab have recently demonstrated that tDCS improves arm movement training after a stroke. Stroke patients who received tDCS also maintained these improvements for longer after rehabilitation had ended.

While this finding is extremely exciting, understanding how tDCS causes these enhancements is crucial. By identifying the exact changes that must occur in the brain to allow neuroplasticity, we can develop the best rehabilitation techniques. We don’t need a miracle!

Holly Wilkinson, University of Manchester

Testing the ‘metal’ of chronic wounds

If I said the phrase ‘wound healing’, what would that mean to you? You could imagine anything from applying a small plaster to a paper cut, to frantically trying to stem excessive bleeding from a traumatic bullet wound.

I'm willing to bet that your first thought wasn’t an elderly, hospitalised woman with a bed sore, or a middle-aged diabetic man with a foot ulcer. While less immediate than trauma surgery, these non-healing chronic wounds can be just as life-threatening and debilitating. Unfortunately, getting them to heal is often far more complicated than simply patching them up with plasters and bandages.

Were you to Google the term ‘chronic wound’ you would find horrific pictures of pressure sores, leg ulcers and diabetic foot ulcers. You would probably also read that those most likely to suffer from chronic wounds are the elderly and diabetic. The sad reality is that we live in an era where the elderly ‘at risk’ population is rapidly expanding. Our fast food culture and sedentary lifestyle means diabetes is also reaching staggering levels. The figures are frightening!

Ten years ago, managing chronic wounds was estimated to cost the NHS £3 billion per year. By 2013 the yearly cost had risen to £5 billion; 5 per cent of the total NHS budget. If this trend continues, by 2020 chronic wounds will cost the NHS well over £8 billion every year. For the patients, day-to-day life becomes incredibly challenging. Their wounds often become so severe that they are left with just one unthinkable option, amputation. But this is extremely risky and could even lead to death.

So what can we do about this unseen epidemic?

Surprising new findings from my PhD now suggest that something as unlikely as metals may hold the key to combating chronic wounds. Conventional remedies, such as dressing the wound or providing antibiotics, frequently fail because the causes of chronic wounds are so complex. For example, we know that defects in the patient's own cells, combined with deadly antibiotic-resistant bugs, like MRSA, provide an environment that delays healing.

But the Romans and Greeks knew that specific metals could preserve drinking water. By the 20th century, people realised that metals such as silver, gold and copper killed bacteria and could reduce infection in the clinic. The advent of antibiotics in the 1940s however, put silver firmly on the back-burner. However, in recent years an explosion of antibiotic-resistant bacteria has led us back to Grandma's medicine cabinet, with silver wound dressings now showing great promise in the clinic.

Metals don't just kill bacteria. In fact, our bodies contain a range of different metals that are essential to keep us alive. Metals, like calcium and magnesium, are the reason our hearts beat and our minds think. They orchestrate the behaviour of every cell in our body, and all of the bacterial cells that live on our bodies. Yet amazingly, little is known about the roles that these essential metals play in wound healing. In my PhD research I'm using a special technique to accurately determine the role of metals in normal wound healing, and comparing this to chronic wounds in the elderly and diabetic. Already we have found important differences in the metal composition of chronic wounds.

My current research is exploring how these specific metal changes could lead to poor healing. To do this, I've broken the complex wound environment down into individual cell types in the laboratory. Here, I'm testing the effect of metals on each cell type in turn. What's truly fascinating is that the same metal often has very different effects on each type of cell. For example, a metal that promotes growth in cells that fill the wound gap also regulates the activity of cells designed to kill wound bacteria. As these effects are beneficial for healing, the next step will be to go back to the clinic. Here, I will develop and test methods to actively and selectively manipulate the most exciting metals in order to promote healing.

So what does the future hold? High levels of diabetes and an ageing population mean that developing a debilitating chronic wound at some point in our lives remains a very real possibility. My research into metals could change this. I hope that, in just a few years, effective new treatments for chronic wounds will substantially improve the quality of life of your elderly neighbour, your uncle, or one day even yourself.

Charlotte Spicer, MRC Centre for Neuromuscular Diseases

The bigger picture

You'll find me in the lab at my bench, lab coat on, pipette in hand. Today I'm growing cells in tiny dishes, tomorrow I'll be on the microscope taking pictures. Zoom out from this image and you'll see the other researchers in the lab.

Some are extracting DNA from human cells whilst others are trying to make sense of their data. Zoom out further still and you'll see the doctors and nurses in the hospital next door. They're working with patients, running trials and exploring new treatments.

My work is part of a big picture. Laboratory scientists, doctors, nurses, patients, we all work together as part of a 'translational' research team. Translational research is a two-way bridge between basic lab science and clinical trials. In the lab, we investigate diseases at a cellular level and attempt to turn our findings into effective treatments that can be tested in patients.

Meanwhile, doctors make observations about diseases in patients and this insight can further guide our research. It is thanks to this translation and the cooperation of a team of investigators at University College London (UCL) and the University of Kansas that we are now able to give hope to patients with a rare, muscle disease called inclusion body myositis, IBM for short.

When I tell people I study IBM, most are unaware of its existence. IBM is a debilitating disease that affects people in mid to late life and causes their muscles, particularly those in their arms, legs, wrists, fingers, and neck to become weak and waste away. As you can imagine this can make even the simplest of everyday tasks like walking up stairs or even getting out of a chair an endless struggle and patients can end up reliant on a wheelchair to get around. As the

disease progresses, they may even have difficulty swallowing and breathing as these muscles deteriorate.

Being diagnosed with a disease that even medical professionals know so little about can be a daunting experience. Think how it must feel to then find out that there is no treatment, as is the case with IBM. But what can we do to change that?

Muscles of IBM patients contain ‘inclusion bodies’. These are abnormal clumps of excess proteins which are thought to be harmful to the muscle cells. Normally cells are able to get rid of excess proteins by switching on a process called the heat shock response. The main players in this process act as bin men, helping dispose of old, damaged and excess proteins, thus protecting the cells from damage. In IBM however, this process does not function as effectively. We wondered whether giving muscle cells a helping hand with the disposal of these excess proteins would protect the muscle and keep it healthy. We could do this by boosting the heat shock response with a drug called Arimoclomol.

Sounds promising? Yes, but how do we know if this drug works in practice? To answer this, we needed models that replicated the disease. We started by growing muscle cells from rats in a petri dish and encouraging them to make excess protein, mimicking the muscle cells of IBM patients. When we treated these cells with Arimoclomol, the excess protein levels were reduced and the cells were healthier and survived longer than the untreated cells.

Next we used genetically modified mice to see how the drug worked in a whole living system. These mice had symptoms resembling IBM in patients, including muscle weakness and damage associated with inclusion bodies. Would Arimoclomol have the same benefit in this animal model as in the cell model? Remarkably, treating these mice with Arimoclomol reversed signs of the disease and improved their muscle strength.

Our findings in the lab proved that Arimoclomol is beneficial in both cell and animal models of IBM so where does this lead next? Will Arimoclomol work in patients? A safety trial in a small number of patients has shown that Arimoclomol

is tolerated and a full clinical trial will soon be underway to see if it can slow the disease progression and improve muscle strength in people with IBM to ultimately improve their quality of life. Meanwhile I'll be delving deeper into the mechanisms causing IBM.

It is exciting that Arimoclomol has the potential to be the first effective treatment for patients with IBM and I am proud of the contribution I have made to this research. I am motivated, like all those in my field, by the desire to change the outlook for patients with incurable diseases. Most importantly, this story highlights the power of translational research. Hard work, persistence, teamwork and communication can help address such considerable challenges as finding treatments for debilitating diseases like IBM.

David Allsop, University of Dundee

Chewing the fat – new approaches to tackle the obesity crisis

Returning from work or school after another dull day, you wearily switch on the TV. The news is on, and suddenly your attention is caught by the headline story. There is an epidemic. In countries west and east, rich and poor, it is spreading. Over 10 per cent of people in the world are sufferers and thousands in Britain have succumbed this year alone. There is no vaccine.

You'd be forgiven for thinking this is the first page of script from a clichéd Hollywood blockbuster, but hidden among the melodrama there are real headlines and a serious story. The affliction in question? Obesity.

Obesity occurs where too much energy is put into the body from the food we consume and not enough is used up, mainly through exercise. Fats are valuable fuel sources, so the body readily stores it whenever it can.

Nevertheless, many don't consider it a disease. Most people would prescribe a dose of self-control to prevent over-indulgence, or perhaps an injection of motivation to get out and exercise more. But whilst both these would doubtless help, the issue isn't one that's going away any time soon. Some have estimated obesity costs an eye watering £8 billion to the NHS every year, a figure that is increasing all the time. This problem creates a huge financial drain on our society – so the incentive for cutting levels of obesity in the general population is strong.

Piling on the pounds is not, in itself, usually the primary concern – rather, it's the myriad of problems that can stem from obesity. Type 2 diabetes is the most well-known example of a condition that often starts with obesity, but it has also been strongly linked with many other health problems – from liver disease, to high blood

pressure and even some forms of dementia. From complication to complication, a seemingly simple condition can be the first step onto a slippery slope that causes so many of us to require medical attention year after year.

In my PhD research, I am particularly interested in investigating how obesity relates to Type 2 diabetes and Alzheimer's disease. It's known that all three are linked, but we don't yet know exactly how.

So how do you go about understanding the ways in which so many different interconnecting conditions are related? One solution is to look for the common factors. I work on one, a type of protein which is known to be active in the brain and is involved in the processes that ultimately cause brain cells to die in Alzheimer's. Its name is Beta site APP Cleaving Enzyme 1. This is a bit of a mouthful, so we shorten it to BACE1- pronounced 'base 1'.

Besides the brain, BACE1 is also found in many other parts of the body, where its function has been largely ignored. Interestingly, by removing BACE1 from the whole body – that is, preventing it from being produced – we can prevent mice from putting on excessive weight, even when they are fed a high fat diet. These mice, which normally would also be diabetic, are protected from developing the disease.

But how is BACE1 working? And in which organs beyond the brain is it most important? My research can be thought of as detective work, and the case can be solved through the process of elimination. Modern genetic techniques enable us to make precise models in which we can remove almost any protein from specific cell types or tissues in mice.

Because of the obvious importance of adipocytes (fat cells) in obesity, I am using genetically modified mice that lack BACE1 in their fat cells. The protein continues to function normally everywhere else, so if preventing BACE1 from being made in adipocytes also prevents obesity and diabetes in the same way as removing it from the whole body, then we will know that the adipocytes are amongst the most critical cells in which BACE1 operates.

Ultimately, the aim of my research is to find a way of lowering BACE1 levels with a drug that would make it harder for the body to put on weight in the first place, before any serious health problems arise. If we know that altering BACE1 in adipocytes could impact upon the progression of obesity, then we will have uncovered a target for such a drug.

Sadly, we don't envisage a world whereby targeting levels of BACE1 in the body will allow you to eat 10 bags of crisps a day whilst remaining slim – no drug is likely to be this effective! The story of obesity is complex, but by trying to understand the biology behind the various processes involved, we can begin to reduce the burden – on our health services, our economy and our waistlines.

Thomas Crowley, University of Birmingham

Joints remember, for better or for worse

Think about the last hour. How busy was it? We may feel fairly relaxed for hours at a time, but inside your body, every day, every hour, every minute in fact, microscopic cells are fighting a colossal battle. This war, for the most part, is fought silently and without you even noticing, but it is there, making that relaxed hour actually one of the most exciting events in the natural world.

The battle is inflammation, a natural activity involving an immense arsenal of cells, toxins, chemical signals and communication, held in balance between two dangerous opposites. Too little inflammation is akin to surrender, making you susceptible to microbial infection. Too much turns into friendly fire, producing diseases characterized by constant inflammation.

This might sound like a tightrope walk, but the overwhelming majority of inflammatory episodes are a brief nuisance you are barely aware of. An itchy spot where an insect has bitten you, the red welt when you're scalded, these represent a carefully orchestrated war held perfectly in check beneath your skin.

Inflammation is based on communication between white blood cells circulating in your blood and tissue-resident cells, which live permanently in one area of your body. White blood cells are the soldiers of the immune system, patrolling the blood until a danger signal alerts them to infection or injury. This danger signal allows them to home in, arriving en masse in the damaged area, releasing toxins to kill microbes and infected cells, or engulfing them whole to destroy them internally.

This homing system couldn't work without tissue-resident cells, like fibroblasts. These cells used to be thought of as structural, just bricks and mortar giving tissue

shape. We now know that they not only recruit white blood cells, but also activate them, keep them alive, and tell them when they can leave the inflamed site. They act as commanders to the soldier white blood cells, and understanding how commands go wrong could help produce new drugs targeting chronic inflammatory diseases.

Rheumatoid arthritis affects hundreds of thousands of people in the UK. It causes constant joint inflammation and pain, eventually destroying joint cartilage and bone. To combat this disease, I research the fibroblasts living in the joint. If cells receive a danger signal once, this will trigger the usually short-lived inflammatory episode we all experience. This includes release of alarm calls that recruit white blood cells. Repeated exposure is much more like the start of a friendly fire scenario of too much inflammation.

I repeatedly expose healthy and rheumatoid joint fibroblasts to danger signals to search for differences in how healthy and diseased cells regulate the inflammatory episode. Do they carefully maintain the balance of ‘just enough’ inflammation? Or do they respond with ever greater strength, until friendly fire pushes the joint to become permanently inflamed?

One danger signal causes fibroblasts to release alarm signals. If however, cells are exposed to a danger signal, allowed to recover, then exposed to another danger signal, their response is much greater. Several of the alarm signals I have studied are released in three times greater quantities when cells are stimulated the second time. This means fibroblasts remember danger and learn from it, so when they experience it again their response is several times greater.

If you called for help, people nearby would hear you and respond. Now imagine after that first time you started carrying a megaphone. The next time you need help you could shout three times louder, so many more people would hear you and respond.

This is exactly what the joint fibroblasts do. Interestingly, the joint is not alone. Fibroblasts from the tonsil also show this memory, whilst those from the skin do not. The increased volume sounds like a good thing, but remember that the silent

war of inflammation is a careful balance. Will shouting too loud attract too much of a crowd? Will too many soldiers mean an overreaction to the situation? And why is it that some areas get a megaphone and others don't?

The truth is, I don't know, but I'm working on it. If I can answer these questions we may better understand why friendly fire occurs. If we can understand that, we can develop new drugs to bring it under control. By studying other areas of the body, we may also see the same pattern in other chronic inflammatory diseases, and develop a drug not just for rheumatoid arthritis, but one that can treat inflammatory diseases in different areas of the body.

The joint remembers, and whether this is good or bad is yet to be understood. Its memory, and that of other areas of the body, may be the key to peace in the silent war. Maybe it could be the answer to chronic inflammation. Maybe your last hour could be as relaxed as you thought it was after all.

Victoria Allan, The Farr Institute of Health Informatics Research

Preventing a heart that goes ba-boom, ba-, ba-, ba- , -boom, ba-boom

Your heart is a mighty engine. Sitting in the centre left of your upper chest, it beats tirelessly to ensure that your brain, kidney, liver and lungs are all adequately fuelled. Size-wise, it's about as small as two clenched fists. Structurally, it consists of pumping chambers, values, and pipework, and is powered by a series of electrical impulses. Each component of the heart's system works together in an orderly sequence: ba-boom, ba-boom, ba-boom, ba-boom.

Unfortunately, as with all great feats of engineering, the heart malfunctions sometimes. A blocked pipe: heart attack. A weakened pump: heart failure. An electrical fault causing the heart to beat in a rapid or disorganised manner … ba-boom, ba-, ba-, ba- , -boom, ba-boom: Atrial Fibrillation.

Yet despite being the world's most common heartbeat disorder, atrial fibrillation is less well known to people than other cardiovascular diseases such as heart attack and heart failure. Indeed, the first time you are likely to hear of atrial fibrillation is when either you or your family member are diagnosed with it. Atrial fibrillation is so common that the risk of developing it in your lifetime is one in four.

Sadly, living with atrial fibrillation doesn't just mean having a heart that goes ba-boom, ba-, ba-, ba- , -boom, ba-boom. Living with atrial fibrillation means living with debilitating symptoms like chronic fatigue, shortness of breath, and heart palpitations. Living with atrial fibrillation means living with a leading risk factor for suffering a stroke. Living with atrial fibrillation means living with lifelong medications.

Atrial fibrillation can devastate lives and therefore preventing people from developing it is a public health priority. Public health campaigns aimed at quitting smoking, improving diet, and increasing exercise have been hugely successful in cutting the number of people who have heart attacks. But where are the public health campaigns for atrial fibrillation? How can you or I reduce our own personal risks of developing atrial fibrillation?

The truth is there aren't any public health campaigns for atrial fibrillation. The risk factors for developing atrial fibrillation are not very well defined. There have been no clinical trials testing prevention strategies for atrial fibrillation, as researchers do not know which interventions to test, nor the types of people to recruit to take part.

Current understanding about risk factor factors for atrial fibrillation is based on findings from cohort studies. Typically, these studies involve several thousand people who volunteer information about their health behaviours, environment, and medical history; they might be screened for a range of physical and biological measures and then they are followed forward through time to see who develops the disease of interest.

My research takes a different approach to investigating risk factors for atrial fibrillation, and involves the use of electronic health records. Electronic health records concern the digital collection of people's health and health-related information. They are collected routinely each time you or I visit our doctor or attend a hospital appointment. Electronic health records can contain symptoms, diagnoses, drug prescriptions, operations, procedures, results of pathological tests, anthropometric measurements, and health behaviours.

Instead of recruiting several thousand people to take part in a cohort study, electronic health records allow a whole country to become a cohort. Instead of being limited to the information collected as part of a cohort study, electronic health records allow a much wider array of factors to be studied, as well as how these factors may develop and progress over time, and how multiple factors may be interrelated.

Traditionally, researchers have formed study hypotheses based on what they think they know and what they expect to find. However, it could be that the risk factors for atrial fibrillation remain unclear because researchers have been looking in the wrong place entirely.

My research therefore aims to use electronic health records to refine understanding about existing risk factors for atrial fibrillation, as well as to discover novel factors that researchers hadn't thought to consider previously. In this way, I hope to stimulate greater awareness about atrial fibrillation, contribute knowledge to help shape atrial fibrillation prevention strategies, and ultimately lead to a future where fewer people suffer from atrial fibrillation, and more people's hearts keep on beating healthily: ba-boom, ba-boom, ba-boom, ba-boom.

Alex Hendry, King's College London

Risk, resilience and Peppa Pig: How studying toddlers at risk for autism could help us understand how to improve their future

Autism makes life harder: harder to communicate effectively with people, harder to deal with the sights, sounds and smells that the world throws at us, and harder to respond to change. Adults with autism experience higher than average levels of unemployment, social isolation, anxiety and depression.

I became a researcher because I would like to change this, but I have no desire to 'cure' autism. Even if it could be achieved (and better minds than mine have all but concluded it can't, not least because autism is a spectrum condition that affects people in different ways), I believe that alongside the difficulties that autism brings, come benefits. I'm not just talking about cognitive advantages, such as the findings linking autism with enhanced attention to detail and a systematic thinking style. I mean the benefit to all of us that comes from a world populated by individuals with diverse ways of seeing and being.

The challenge then, is to work out how to make the lives of people with autism less hard without quashing their individuality. To find out what supports optimum outcomes for a person with autism (mechanisms of resilience), and to see whether we can spot early signs of the difficulties that could hamper their chance to fulfil their full potential (mechanisms of risk).

But human development is messy. We are the product of a billion interactions between our biology and our environment. So our best chance at identifying mechanisms of risk and resilience is to observe children in their first few years of life, before such mechanisms become entangled with, and changed by, those complex interactions.

That is the approach we take with the British Autism Study of Infant Siblings project: we closely monitor the early development of children with a higher than average chance of developing autism (because they have an older brother or sister with an autism diagnosis) and look for signs – or markers – of differences in areas that evidence suggests might be related to the development of autism.

We then investigate how these markers correspond to a range of factors, including early symptoms of autism, general ability level, language skills, and how well the child copes with the age-appropriate demands of life. This is a collaborative effort, involving hundreds of families and researchers with all kinds of specialisms. Our methods range from the low-tech (toys and nursery rhymes feature highly) to the super high-tech (recording brain activity and eye movements to millisecond accuracy).

The area I'm focusing on in my research is executive function. Executive function is an umbrella term for the skills and behaviours involved in problem-solving. These include the ability to focus, stay on track and keep calm, as well as to plan and adapt to new situations. High levels of these skills in early life have been shown to correspond to better relationships with friends and family, better results at school, and better job prospects in adulthood.

We know that many, but not all, children and adults with autism have difficulties with aspects of executive function. Specifically, autism has been linked with problems with cognitive flexibility – the ability to mentally shift gears in response to new information or changing social demands. But we don't yet know when these problems emerge, or how they relate to other difficulties associated with autism.

My research aims to help answer these questions by observing children as their executive function skills are just developing – at ages two to three – and then checking whether those who show early signs of autism behave differently to those who show no symptoms.

There aren't any well-established tasks to test executive function that are suitable for toddlers with additional difficulties with language, social interactions or muscle

control (all common problems among children with autism). So I've had to create some.

I've learned how to use technology and toys to maximise toddlers' performance, and become an expert on how to motivate children with Peppa Pig cartoons, chocolates and stickers. Along the way, I've found that toddlers solve problems in ways most adults would never expect. I'm currently halfway through the study so it's too soon to tell if I am right in my prediction that toddlers with lower levels of executive function go on to show more severe autism symptoms and general difficulties at age three.

If this does turn out to be the case, the next step will be to see whether we can help children at risk for autism to develop stronger executive function skills, and then to assess whether this builds their resilience to the aspects of autism that make life harder. Not to try to cure them of autism, but to help them be the best 'them' they can be.

Martin Holding, MRC Institute of Hearing Research

The sound of silence

It's easy to forget about sound. It's easy to forget about the sound of birdsong as you walk through the park. It's easy to 'zone out' when you're deep into your work in a bustling office or café, the chatter of the people around you disappearing into a distant hum. However, there is one sound that is not so easy to forget. Tinnitus.

This perpetual and persistent, din permeates every aspect of the lives of those who experience it. They cannot tune it out, nor will their brains get used to it. A lucky few will learn to live with it, to accept it and move on. The less fortunate will be tormented with years of sleepless nights, the inability to concentrate, and even anxiety, depression and suicide.

Too often, people with tinnitus are told by their doctors that nothing can be done, and that they must simply "try not to think about it". Imagine having a constant pain in your stomach, and being told by your doctor to learn to live with it. You wouldn't accept this, and neither should they. More must be done to understand tinnitus and offer a treatment to those who suffer from it.

Tinnitus is not a new condition - it has been recorded as far back as ancient Rome – nor is it a rare one, around 15 per cent of the UK population has it in its permanent form. You yourself will likely have experienced it in its temporary form after going to a loud concert as a ringing, hissing or buzzing in your ears.

And yet, despite this, very little is known about. What causes it? Why is it permanent in some cases but not in others? Why can't we make it go away? In my research I am doing the necessary fundamental science that will help us

understand what we are up against – research that will hopefully lead to future remedies and preventions.

One thing we are almost certain of is that tinnitus is generated within the brain, not the ear. This has led to a host of research on tinnitus using techniques for imaging the brain, such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) to try and determine where in the brain tinnitus is coming from.

EEG analyses what brain cells or neurons are doing in the brain, while fMRI targets where those neurons are. This has led to important discoveries. For example we now know that the perception probably arises in the part of the brain associated with hearing – the auditory cortex – and that the neurons of people with tinnitus are firing differently to those without tinnitus.

My research is a new spin on the traditional style of tinnitus research. Up until now most studies have focused on comparing the brain activity of people with tinnitus to people without tinnitus. Unfortunately, we do not yet know enough about the brain to really determine whether the changes observed in these studies are really due to tinnitus or just due to the way different peoples brains are responding – every person's brain is wired differently.

Instead of doing this, my research is comparing the brain activity of people with tinnitus while they are perceiving their tinnitus versus when their tinnitus is 'off'. But how can we turn off someone's tinnitus? We can't do this for people in everyday life, but in the lab we can. For just a few, short seconds, we can induce a phenomenon known as residual inhibition.

We are doing this by playing a masking noise (that is, a noise that is loud enough to cover, or mask, their tinnitus) through headphones. This has the effect of temporarily quietening their tinnitus after the noise has stopped playing. The few seconds this lasts for are just enough to record changes in brain activity. Using state-of-the-art equipment we are now able to look at the brain in far more detail than ever before. By measuring this detail using EEG we can determine with much greater accuracy what changes in activity are the result of the tinnitus. If we

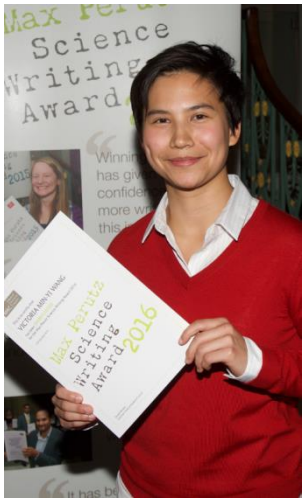
know what activity is the problem then it will help us to develop much more effective, targeted treatments and therapies.

The benefits could also extend beyond tinnitus. If we can find similar phenomenon to residual inhibition in other conditions such as chronic pain, or even hallucinations, we can use methodologies such as ours to further our understanding of a range of conditions.

This research has the potential to have a huge impact on a large portion of society. A portion of society that is only set to get bigger as more and more people are exposed to high levels of work and leisure noise. There are at least 600,000 people in the UK alone living with tinnitus. It’s time they could hear, once again, the sound of silence.

Victoria Min-Yi Wang, The Francis Crick Institute

Not all cancer cells are equal



Look at yourself in the nearest mirror and, if you aren't too squeamish, imagine seeing the inside of your body. It's obvious that not all your cells are the same. We are made of many different tissues that perform different tasks: skin cells protect us from the environment, white blood cells defend us against infections, nerve cells allow us to move and think.

Cancer – the uncontrolled growth of cells – can arise from virtually any type of tissue. We hear about new treatments for skin cancers, about raising money for childhood leukaemias, about inoperable brain tumours, and we know that there are different types of cancer.

But an individual tumour in a tissue is also complex. Researchers realised decades ago that, like our healthy bodies, tumours aren't simply lumps of identical cells; that *within* each tumour there are different cell types. For instance, some tumour cells divide indefinitely to keep the cancer alive, others invade into surrounding tissue and spread to other sites of the body, while yet others stimulate blood vessels to grow. Some cancer cells even combine several of these properties.

In our laboratory we study the pancreas, an organ of the digestive system, which aids digestion and controls metabolism throughout the body by secreting hormones such as insulin. In particular, we investigate variations among cell types in the most common kind of pancreatic cancer called pancreatic ductal adenocarcinoma (PDAC for short).

PDACs are among the most deadly cancers with only about three per cent of patients diagnosed with PDAC in the UK surviving for longer than five years. One of the reasons for this gruelling statistic is that PDACs are often diagnosed late,

when the cancer cells have already spread to and wreaked havoc in other internal organs.

Previously, several labs, including ours, noticed that some PDAC cells are more aggressive than others, more capable of re-growing new tumours from scratch. Now, we aim to understand what makes the more aggressive PDAC cells different from the rest of the cancer cells and how they contribute to the deadliness of this cancer. With that knowledge in hand, the broader aim will be to find anti-cancer drugs to target and kill the most dangerous cells that lie at the heart of PDAC.

A previous PhD student in our lab discovered that the more aggressive PDAC cells make and display large amounts of a certain protein – let's call it protein X – on their cell surfaces. We say that the more aggressive cells are "marked" by protein X. This realisation was my gateway into finding out exactly how these two cell types, the more and less aggressive cells, differ.

First, I wanted to know whether protein X not only marks the more aggressive cells but whether it is directly responsible for making those cells more dangerous. Therefore I experimentally reduced or elevated the levels of protein X in PDAC cells we grow in the lab. Then I assessed whether the PDAC cells grew more or fewer, larger or smaller so-called organoids, miniature replicas of pancreatic tumours. Astonishingly, the cancer cells actually grew less well when I removed most of protein X, or they divided and proliferated much more when they had more of protein X. This is a good indication that, in future, drugs might be delivered directly to protein X to eliminate the aggressive cells or convert them into tamer cells.

In the meantime, I am on the lookout for other characteristics that might distinguish between the more and less aggressive cells. From one of my experiments I have data hinting that the two cell types might in fact have different *physical* properties. However, until I've repeated these experiments I can't be certain that this difference in appearance contributes to the more aggressive cells' behaviour.

But it is plausible, for example, that the more aggressive cells can attach to other cells or blood vessels more easily, aiding their movement to the lungs or liver. These secondary tumours, also known as metastases, are the tumours that PDAC patients usually die from. Next, I need to determine whether there is a direct connection between protein X and the variations among the physical properties of the PDAC cells.

We really want to pin down the differences between the more and less aggressive cells so that hopefully researchers and pharmaceutical companies will be able to design and develop more effective drugs to tackle PDAC. In a few years, once we know more precisely what protein X is doing in the more aggressive cells, our findings might matter a great deal to patients.

For the moment I am simply trying to find out more about how PDAC cells work and I know that can sound theoretical. However, I am certain that knowing why and how some cancer cells, clearly, are more equal than others will – help patients in the future.

Katie Walwyn-Brown, University of Manchester

Emergency service

It's late at night and you are safe in bed. Suddenly you hear a crash from downstairs. Something is wrong. You climb out of bed and move closer to the sound. That's when you hear voices: a burglary. What would you do? Perhaps stay quiet and call the police? What if, instead of hearing voices, you had smelled smoke from a fire? You would get out of the house and call the fire brigade.

The way we react to danger depends on the source of the threat. Your immune system works the same way. It is responsible for defending your body from hundreds of different sources of disease, from tiny viruses hiding inside your cells to large parasites in your gut. To do this your immune system has developed specialised reactions, like the different emergency services. White blood cells detect danger and call for the right response, but in some diseases the message doesn't get through. The goal of my research is to understand these messages better, so that we can make sure people's bodies produce the right immune response at the right time.

How does your immune system know what kind of danger it faces? The first clues come from white blood cells called dendritic cells. They patrol your body looking for signs of different infections. Just as you heard voices or smelled smoke, they look for patterns that tell them the nature of the threat. Once they find these clues, it's time to call in teams of other white blood cells to fight the infection.

A cold virus demands one emergency service while a parasitic worm needs another. For you making the call is simple, you pick up the phone and ask for police or fire brigade. Cells don't have it so easy. They need something more obvious than a phone call to communicate with other cells. Instead they change their appearance with tiny structures called proteins. Proteins are a bit like road signs on the surface of the cell, being put up or taken down depending on the

situation. Scientists haven't decoded which signs are important for raising the alarm in every kind of danger, nor how cells read them. Especially when it comes to parasitic worm infections, we have a lot to learn.

Parasitic worms, or helminths, affect more than 24 per cent of the global population[1]. They are deeply linked to poverty, and slow down the physical and mental development of children. When the immune system fails to control these infections they can cause serious health issues like anaemia, organ damage and cancer.

If we can understand the cell's alarm signs for helminth infections we might be able to find medicines to copy them and make a stronger response. Sometimes, for reasons we don't yet understand, the same team of white blood cells which fights helminths gets over excited without parasites. Picture the chaos if the fire brigade showed up and started hosing down your house with no invitation. This leads to auto-immune problems like allergic asthma. Understanding the messages inviting white blood cells to the scene could help us to cut them off, stopping this unwanted response.

Your body is full of different immune cells doing their jobs, with millions of messages going back and forth. In all this noise how can we study one alarm? I am starting by isolating the source. I take dendritic cells out of human blood to study them in simple situations. Mixing them with different sources of infection, like playing you voices or turning on a smoke machine, I can see how they react.

But a dendritic cell is small – you could line up over 100 of them on the head of a pin – so I need some special tools to see what it is doing. To tell which signs the cell is putting up I use detectors called antibodies. These are proteins made in thousands of shapes to stick to different signs. They are also labelled with colours so I can tell them apart.

Using a machine called a flow cytometer, I can quickly look at millions of cells to see if an antibody has stuck to them, telling me whether they are showing a

[1] http://www.who.int/mediacentre/factsheets/fs366/en/

particular sign. But what if I want more detail? That's where microscopes come in. Under a microscope I can see exactly where on a cell the signs sit. I can also tell how they are being read by looking at how quickly cells move and how long they touch each other for.

I hope to use all this information to understand which signs are important for fighting helminth infection. This knowledge could help other researchers to develop better medicines for both parasites and asthma in the future. Fire brigade or police, we want to get everyone the emergency service they need.

Congratulations!