

Winner

Akira Wiberg, University of Oxford

Getting on your nerves



“Does this feel sharp?”, I ask my patient, as I use my forceps to pinch the skin of her hand. She says no, so I proceed to make a 2-inch incision in her palm. I dissect through the layers of fatty tissue to expose a greyish-white structure called the transverse carpal ligament. I take the scalpel and proceed to my favourite part of this operation – cutting through this thick, gristly ligament until I see the glistening, white cord running under it. This is the median nerve, and I am seeing it as it’s running through the carpal tunnel – a narrow channel created by the wrist bones underneath and the transverse carpal ligament on top. I have to carefully divide the whole ligament to free the nerve from the confines of this tunnel.

My patient has carpal tunnel syndrome, and her median nerve has become severely compressed within the carpal tunnel. Nerves that get compressed stop working properly, so she wakes up at night with severe pain in her hand and has tingling and numbness in her fingers. Recently, she’s started dropping objects and has struggled to do up her buttons as her thumb has become progressively weaker.

About one in twenty people will develop carpal tunnel syndrome at some point in their life, but we don’t understand why the median nerves gets compressed in certain people. A big part of the answer lies in our DNA, and my research is trying to answer how your genes make you more likely to develop carpal tunnel syndrome.

Your DNA consists of a sequence of 3 billion chemical “letters”. You and I share 99.9% of the sequence of letters in our DNA, and it’s the 0.1% that we don’t share that makes us different in all sorts of ways, from our physical appearance to the likelihood of us developing diseases like carpal tunnel syndrome. During my PhD project, I performed something called a genome-wide association study (GWAS), in which I used a powerful computer to examine the 0.1% of the

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genome that we don't share, to compare the DNA letters between thousands of people who have carpal tunnel syndrome against thousands who don't.

My study found 16 locations in the genome where people with carpal tunnel syndrome are significantly different from those without, and we've used this information to discover several genes that are likely to be important in an individual developing the condition.

This sort of genetic study is important in many ways. After the GWAS, I performed an experiment called RNA-sequencing to show that the genes that we found in the GWAS are overactive in the tissues that surround the median nerve in the carpal tunnel. We can therefore potentially target some of these genes with drugs to stop the changes that take place in these tissues as the median nerve gets compressed in carpal tunnel syndrome. We are several years away from such a drug, but understanding how genes are involved in a disease process is the necessary first step in developing new treatments.

Another application of this research is in disease prediction, and I have developed something called a polygenic risk score for carpal tunnel syndrome. Using a patient's DNA sequence, I can calculate a number that reflects how much "genetic risk" for carpal tunnel syndrome they carry in their genes. I've found that patients who need surgery have, on average, a higher polygenic risk score than patients who don't end up needing an operation.

Ten to twenty years from now, it's likely that all of us will have had our DNA sequenced, and this information will be used by doctors to help treat patients in a way that is tailored to their genetics. In carpal tunnel syndrome, we could use this information to predict things like who is likely to develop a severe form of the disease, or who is likely to have symptoms that come back after surgery. The way we practise medicine will change dramatically in the next couple of decades, and it's important to me that hand surgery patients will also benefit from what's described as "the genomics revolution".

Carpal tunnel syndrome isn't cancer or heart disease, so it will never get the same amount of publicity or funding. But it's an important disease that affects millions of people's lives in very profound ways. We use our hands for so much of our interaction with the world around us, and I think it's easy to take a pair of fully functioning hands for granted.

Back to the operating theatre. After suturing the wound closed, I apply a bandage to the patient's hand, hoping that the operation will improve her symptoms, or at least stop her already advanced disease from progressing any further. It's a long way from DNA to the operating theatre, but as surgeons who study genetics, we are working hard to bridge that gap to improve treatments for our patients.

Runner up

Erin Attrill, Living Systems Institute, University of Exeter

The enemy of my enemy is my friend



The year is 2050, the stench of plague fills the air and 10 million people are dying from cuts and grazes due to an enemy that cannot be seen. You would be forgiven for believing that we had entered a dystopian, parallel future, but alas not. This is the current future of mankind if we do not address the ever-growing threat: antibiotic resistance.

Whether we want to face it or not, our antibiotics are failing. Drugs that we have relied upon to so effectively treat bacterial infections are no longer working due to these crafty bugs becoming resistant to them. Over time, bacteria have evolved to survive antibiotics, with this “survival of the fittest” process resulting in populations of menacing “superbugs”. No matter how many different antibiotics we throw at these resistant microbes, some can no longer be killed and so what were once minor infections become fatal.

So how can we fight back!?

One avenue is to discover and develop new antibiotics. However, this has proven to be extremely costly and difficult, so alternative options are being explored. Mankind’s possible saviour: bacteriophages.

Bacteriophages, or simply phages, are viruses that infect and kill bacteria. Just as humans get viruses like flu, bacteria suffer from their own invaders which hijack the bacterial cell and turn it into a virus making factory, before killing them. With their large bulbous head and spindly legs (think War of the Worlds alien invader fighting ships), they are perfectly adapted for attaching to bacteria. Phages are the optimal killing machines. Currently, phages are not widely used to treat infections in the Western world as not enough is known about them. If we want to be able to harness the power of these microscopic bacteria killers, then we need to know more about how they work.

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Most research studying bacteria and phages use methods that involve growing billions of cells in a test tube, and looking at how fast the population grows and dies on average. But this is not always the most informative. Imagine you want to know how fast humans run 100m. Someone tells you the average time is 15 seconds. Although all humans, not everyone would take 15 seconds. Clearly if Usain Bolt ran the race he would be much quicker, and the man who decided to hop all the way much slower! This also applies to bacteria. Even though they should all be identical, individual bacteria can behave very differently.

My work lets us identify the Usain Bolts and the Hop-Alongs of the bacteria world, as well as many others in between. I want to know which responses occur when we expose bacteria to phages and how this may affect the killing ability of these viruses.

I use technology called 'microfluidics' that allows me to isolate and experiment on individual bacteria. With 'micro' meaning small, and 'fluidics' relating to the movement of liquids, I perform experiments on bacteria with equipment no larger than a postage stamp. Using networks of thousands of tiny channels, I can trap single bacteria in their own tiny chamber under a microscope and watch what happens when I add phages. Over the course of a day, I can continually monitor and photograph the same cells and record whether they are growing, dividing and even the exact point at which they lyse – that is, when they burst open releasing hundreds more phages.

I have observed that although all identical, some bacteria die instantly, but others grow much faster and divide multiple times before finally lysing hours later. Perhaps most importantly, some bacteria in the experiments are not killed by the phages at all. These bacteria survive the exposure and fill their chambers with more bacteria offspring. What makes these cells special and able to survive is unclear, and one aim of my work is to use microfluidics to try and understand why.

It is important to understand these differences to be able to optimise how many phages would be needed to eradicate the bacteria in a human as a potential treatment. If most bacteria are killed with two hours of phage treatment, a person may begin to look healthy, but if the "Usain Bolt" variants survive, then they could cause the infection to return. A longer dose or a higher concentration of phages may be required to eradicate the entire population so we need to fully understand how the different cells behave.

There is no need to be afraid of the word 'virus' – the good news is that phages cannot infect human cells. These minuscule invaders are the enemy of bacteria and so we should harness their power to defeat our bacterial foes. As stated, the enemy of my enemy is my friend. So let's welcome in the age of the phage.

Commended

Anna Beukenhorst, MRC Doctoral Training Programme, University of Manchester

Smartphones for healthcare research: data at our fingertips



When motorcycle legend Barry Sheene moved to Australia, it was not for another Grand Prix victory. It was for the weather. Sheene had retired from racing because of his arthritis. Like many arthritis patients he believed that the damp British weather worsened his arthritic pains.

Barry Sheene's hypothesis has never been proven, even though many researchers tried to. Ideally, we would like to place arthritis sufferers in a controlled experiment, with rain on one day and sunshine on the next. We would measure their pain, while holding everything else constant. Statistics help us determine what weather conditions (such as temperature, or humidity) aggravate pain. Alas, such an experiment is not possible, though. We have to rely on observing people in their daily lives. Patients have to record their pain and the weather in diaries to pinpoint the association. These observational studies come with challenges. We can't hold everything else constant, so how do you know it is really the weather changing someone's pain? The culprit can also be a third factor, like medication, mood, or physical activity. We can only unpick the link between pain and weather by observing many participants for a long time, and record the potential third factors alongside pain. Previous studies had too few participants, too short time frames or little information on third factors to conclusively underpin Barry Sheene's hypothesis.

We wanted to have another go and started Cloudy with a Chance of Pain. We hoped we could get better daily life data from...people's pockets. Most people carry a smartphone wherever they go. So we made an app: Cloudy with a Chance of Pain. Reporting pain only takes one swipe. In ten seconds participants also record their mood and physical activity. Smartphones know the location of their owners, which allows us to link pain reports to accurate weather data, even for commuters or frequent travellers.

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Our plan worked. Our study, with 13,000 participants, is ten times bigger than the biggest previous study. Our participants reported 5 million symptoms during 15 months, linked to hourly weather reports from the closest Met Office station. My role was analysing this humongous dataset. I investigated where our participants were from (every postcode from Land's End to the Orkneys), on how many days they reported their pain (our most faithful participant for 457 days), how their pain changes during the week (Sundays are least painful) .

Sometimes, smartphone data caused new problems. I discovered that iPhone users had many gaps in their location data. To link their pain reports to the right weather station, I had to find a way to fill those gaps. Luckily, most people have strong habits: depending on the day and time, they are at home, in the office or at the supermarket. If participants had a location gap, I let the computer analyse where they usually were at that day and time, and used the weather from that location.

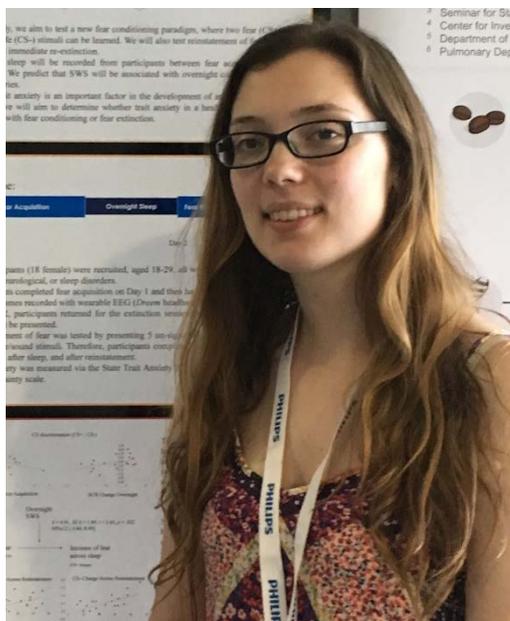
To link the weather and pain, I use the so-called the 'case-crossover design'. It is the statistification of common sense. You may have inadvertently used it in your own life. Have you ever had a headache and wondered what triggered it? Maybe you asked yourself: "What did I do differently, compared to days that I feel fine?" I do the same for each of our participants. I look at days of high pain and quantify what was different in the weather compared to days that they felt fine.

The first results look promising. It would be fantastic to unravel the age-old question of the weather and pain. Our participants tell me it would help them manage their pain better. On days with high pain, they often can't drive their car, go to work or even walk. Even if patients cannot move to Australia, they can anticipate 'being under the weather'. They can take medication, avoid activities that are heavy on their joints or plan in extra physiotherapy. Some participants suggested that, the NHS could cover holidays to places with very un-British weather based on our results, but with 18 million arthritis sufferers that may not be feasible....

Cloudy with a Chance of Pain has a second result. We have shown the potential of smartphones for research: better data from the daily lives of thousands of patients. Even though mobile health has been in newspapers for years, our study is the first that succeeded in getting symptom and location data from so many participants on so many days. Hopefully, this will inspire other researchers, doctors and patients to build their own apps. The methods I showcased will help them make the most of their big datasets. Smartphones will help us answer many more healthcare questions, now we finally have daily life data at our fingertips.

Imogen Birch, The Cardiff University Brain Research Imaging Centre (CUBRIC)

Get some sleep, you'll feel better in the morning



You're in a burning building. There's fire everywhere, the flames are dancing up the walls and the heat is radiating from every direction. Acrid smoke fills your throat. Your eyes are stinging, and you can barely breathe. Fear overwhelms you, and yet you know you must get out. There's no time to consider the options, you just run for the door.

Fear is universal, inescapable, terrible. It also alerts you to danger, enables the classic 'fight or flight' release of adrenaline, and can save your life.

But how long should this fear last?

A few hours? A few weeks? A few years?

Normally, with time, we process fearful memories and move on. However, in Post-Traumatic Stress Disorder, or PTSD, the fear of a dangerous situation stays with the person long after they are safe.

This is difficult to put right, because although our brains are amazing, they can't always be told consciously what to do.

DO NOT think about a red car.

...

What just appeared in your mind's eye?

You cannot tell yourself to stop thinking about something, it usually has the opposite effect. Just like this, people with PTSD cannot help but relive the emotion of their traumatic event. That's why I am looking for a more unconscious way to steer the brain away from that fear. I'm looking to do it during sleep.

You probably know that sleep is important, but do you know why? When researchers first started looking at the sleeping brain, they were amazed to discover that it did not just 'shut down' as previously thought, it was hard at work. In particular, when we go into the deepest stage of sleep,

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our brain cells synchronise, forming long slow waves of activity that wash across the brain. More than 100 years after this discovery, we now know that this stage of sleep – called slow wave sleep – is really important for processing memories.

My research aims to reactivate the fear memory during slow-wave sleep, encouraging additional processing, and fast-tracking the natural process where fear fades normally over time.

Reactivate memories during sleep? That sounds like science fiction.

Well, yes, to some extent, but you'll be surprised to hear how simple it is. Because this is a new idea, I'm testing it on healthy volunteers first, like this...

First, I create a very simple fear memory. I do this by presenting a picture and a spoken word together, for example you see a lamppost and hear the German word for lamppost Laternenmast. I use a word you're less familiar with, so this creates a unique memory.

This doesn't sound scary at all. But wait... every time you see and hear this lamppost, I give you a small electric shock.

This might sound quite medieval, but the shock isn't harmful. It feels a lot like a static shock you might get from a door handle. Despite this, it's enough to create a small fear response – I measure this by looking at the sweatiness of the palm and heart rate changes.

This is a model of fear learning. It's like being bitten by a dog, and then having a fear of dogs. Or having a car accident and feeling anxious when you start to approach the road where it happened. You don't need too many of those experiences to develop a fear of something.

So now people are fearful of the lamppost. I want to see how I can use sleep to reduce this fear unconsciously. This is deceptively simple. I just play the sound to you when you're asleep – in this case the word Laternenmast. The next morning, your fear response to the lamppost should be reduced, because your brain has been given a small nudge to devote some extra processing to this memory.

If we really can reduce fear responses during sleep, as easily as playing a sound related to the fear memory, this could really aid treatment of PTSD, and perhaps other anxiety disorders too. PTSD is, put simply, an exaggerated fear response, causing flashbacks, nightmares, and general anxiety in everyday life. Reducing the fear then, could really help sufferers return to a better quality of life.

It's not a one-stop cure. However, such a simple technique could be incorporated into existing treatments. For example, playing gentle background music while talking about the traumatic event during therapy, and then playing the music again when asleep.

In a world of increasing mental health problems and a reliance on medication, there is a real need for a new approach. So maybe not too far in the future, we really can, with a few background sounds, get some sleep, and feel better in the morning.

Alice Waitt, University of Nottingham

How to RECOGNeyes your attention



Have you ever found your eyes wandering? Do they float towards the window during a meeting, or flicker to the background when talking to someone? We can all relate to moments where our attention drifts and we become distracted.

But what if you can't concentrate enough to complete a task you only started ten minutes ago?

This can be a difficult reality for people with attention deficit/hyperactivity disorder (ADHD) or specific learning difficulties (SpLDs) such as dyslexia. You may know someone with ADHD or a SpLD and possibly notice they have a shorter attention span and are prone to distractions. I would often catch a university friend of mine with dyslexia on her iPad after only fifteen minutes into a lecture. She managed to read the entirety of the Game of Thrones series after the first semester in this way!

Having attentional problems doesn't mean you can't achieve your goals or succeed in life. It just means you may have an inability to focus for too long and benefit from different and adapted approaches to learning. My same friend used different techniques to regain focus. For example, she would take regular, short breaks whilst working, record lectures and make her notes colourful and visually interesting. Thanks to these personally-tailored learning methods, she achieved a first for her degree.

However, for some people with ADHD and SpLD-related attentional problems, distractions can negatively interfere with academic, social and emotional development. Sometimes this leads to poorer education performance, reduced self-esteem and increased chance of being involved in criminal activities.

Creating new strategies and techniques to improve attention could increase positive life outcomes for these individuals, such as going into further education and improved interpersonal skills. Currently, prescription medication is the main treatment for ADHD symptoms. However, these

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drugs can lead to a range of side-effects and can be abused as a 'study aid' for non-ADHD individuals. This has created a demand for alternative treatment options.

Our team at the University of Nottingham developed a unique computer game called RECOGNeyes to train attention. However, this is a video game with a twist. Using an eye-tracker, the player must use only their eyes for the controller in a range of mini-games.

RECOGNeyes trains gaze-control, which describes learning to control voluntary eye movements. This is a part of attention known as inhibitory control where you have to actively stop yourself looking at something – in other words, preventing distraction. Some of the mini-games are based on the 'antisaccade task', where you deliberately look in the opposite direction to a target that appears on screen – a challenging task if you have attentional problems.

In our study, a group of university students with ADHD and/or SpLDs were asked to complete RECOGNeyes training for two weeks. We wanted to see if their attention improved and whether training causes changes in brain activity patterns.

We recorded brain activity before and after training using magnetoencephalography (affectionately known as MEG), which as the 'magnet' part suggests, measures changes in magnetic fields around the head. Without going into too much detail about the complex physics behind it all (which even I am still getting to grips with!), MEG measures brainwaves that tell us about activity in different parts of the brain.

During the MEG scanning session, each participant had their brainwaves recorded whilst doing the antisaccade task (similar to the RECOGNeyes mini-games), where you look towards or away from a red box appearing on the left or right of the screen.

After RECOGNeyes training, on average people completed the task in the MEG scanner quicker and made fewer mistakes. Currently, we are looking at brainwave patterns and so far we have also detected changes after training.

This suggests as little as two weeks of training eye movements may improve attention. Since this is the first 'pilot' study using RECOGNeyes, it would be interesting to establish long-term implications after training. We also aim to introduce the game to younger children to see if it helps their attention and ability to focus during school – plans for which are already underway.

RECOGNeyes, and similar types of games, could pave the way for an easily accessible and engaging tool for a child to use at home or school to ease attentional problems. These interventions introduced at a young age could optimise life outcomes for a child diagnosed with ADHD or SpLDs.

Even those without a formal diagnosis may be interested in improving attention and focus using games like RECOGNeyes. Eye-tracking games are already available, but who knows – in the future these games may become more commonplace as technology develops. With smartphones becoming an essential part of day-to-day life and our world becoming a more distracting and stimulating place, we may all benefit from improving our attention with these pioneering technologies.

Katrina Wesencraft, The EPSRC and MRC Centre for Doctoral Training in Optical Medical Imaging (OPTIMA CDT), Centre for Biophotonics, University of Strathclyde

Could a cell invisibility cloak help cure diabetes?



Do you know where your pancreas is? I didn't until I started to study anatomy. It's a squishy, pear-shaped organ that sits just behind your stomach. The pancreas has two important jobs: it helps us to digest our food and it produces a hormone called insulin. After we eat a meal, insulin helps our cells to use the sugar in our food as fuel for energy.

Diabetes is a condition that affects the pancreas. There are over 4 million people in the UK living with diabetes, but only 10% of these people have the kind known as type 1. In type 1 diabetes, the cells in the pancreas that produce insulin (the 'beta' cells) are completely destroyed. Scientists still don't know exactly how this starts, but the immune system attacks these cells by accident.

As type 1 diabetes develops, insulin production stops. The amount of sugar in the bloodstream begins to rise. Without insulin, this sugar has nowhere to go - it can't be used as fuel and your body can't flush it out of your system fast enough.

After meals, people with type 1 diabetes take injections of insulin to manage their blood sugar levels. Most people who are strict with their insulin treatment can still be relatively healthy. But this treatment isn't perfect.

Even if they are very careful (by eating a healthy diet and calculating the exact amount of insulin to inject), people with diabetes will always have higher blood sugar. The sugar damages blood vessels, especially small ones called capillaries. After years of living with the condition, many people have problems with their eyesight and kidneys and have a higher risk of heart attack and stroke.

Researchers have different ideas about how to cure type 1 diabetes. Some are trying to stop or reverse the damage to beta cells, but I'm interested in transplant surgery. Surgeons and researchers are working together to replace the damaged beta cells. This would mean people with type 1 diabetes could start making their own insulin again. It sounds simple, so why does it fail? There are two main problems:

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1) Surgeons must prescribe antirejection drugs. Without drugs to dampen the immune system's response, the transplant would be rejected straight away.

2) Even a successful transplant of beta cells seems to fail over time. When the new insulin-producing cells die, the patient's diabetes comes back.

We still don't know exactly how the transplant stops working. We think that despite the drug treatment, the patient's immune system can still see that the donor's cells are 'foreign' and attacks them. It might even be happening because of the drug treatment. Beta cells are very sensitive and antirejection drugs can be toxic. It's a Catch-22 situation.

So how can we sneak donor beta cells into the body undetected? 'With a tiny invisibility cloak' might sound like I've spent too much time re-reading the Harry Potter books, but this suggestion might not be as ridiculous as it seems. Some materials can be implanted in the body without being rejected. Effectively, these materials are 'invisible' to our immune systems. Some of these materials are naturally occurring, like alginate – a chemical found in seaweed.

In our lab, we have a machine that lets us trap clusters of beta cells in miniscule alginate bubbles. Alginate could be the perfect 'invisibility cloak' for beta cells. The bubbles are porous, letting insulin out and nutrients in. Most importantly, alginate stops immune cells from entering the bubble and damaging the cells within.

Producing these tiny bubbles of beta cells is quite slow and inefficient. We need to improve this if they're going to become a realistic treatment for people with type 1 diabetes. At the moment, the machine creates a lot of bubbles that are empty or incomplete.

Beta cells cluster together in varying shapes and sizes - I think this affects how well the bubbles are formed. Separating the clusters into individual cells then rebuilding them will hopefully help us to generate more consistent bubbles. I'm using a template to make uniformly shaped beta cell clusters. The template is covered in tiny pits about the width of a human hair. Once the cell cluster touches the sides of the pit, it can't grow any bigger.

This process might take a long time to perfect, but hopefully once someone gets a transplant of beta cell bubbles, their diabetes will be cured for life. It could also lead to cell transplants without antirejection drugs. Many more people with diabetes, especially young people, could then get a transplant. This would prevent them from developing any of the complications that come with having years of high blood sugar. Maybe in the future, young people can get an 'invisible' beta cell transplant as soon as they're diagnosed with type 1 diabetes.

Magda Mareckova, University of Oxford

One in ten women suffers from endometriosis – can studying the endometrium cell by cell help us diagnose it?



Imagine you would suffer from pain that feels like razor blades inside your abdomen. It feels like being cut and burnt from within. You cannot go to school or work for 3-4 days. Each month. The pain really drains you, both physically and mentally. Painkillers do not help. You slowly stop being able to carry out your daily activities and interact with your family and friends. On top of it all, your periods are so heavy, that it becomes challenging to be away from home.

The pain and suffering goes on for years. You think your symptoms are normal. Everybody says that periods can be painful, so you just deal with it. However, the pain keeps getting worse. Roughly 7.5 years after the onset of your symptoms, you finally see a specialist. They mention 'ENDOMETRIOSIS' for the first time and you wonder what it is.

Endometriosis is a gynaecological disease. It affects around 10% of women in their reproductive years. Having endometriosis means, having tissue that resembles the one of the lining of the womb, the endometrium, outside of the womb. The endometriosis tissue attaches to the lining of the abdomen and any organs inside your belly, where it forms the so called lesions. The lesions respond to hormonal changes across the menstrual cycle. The lesions grow, shed and bleed, just like the endometrium does. However, the shed lesion tissue cannot get out of the abdomen, it stays trapped there. The presence of this tissue causes inflammation that irritates the nerves, generating excruciating pain.

Even though endometriosis affects around 190 million women worldwide, the disease is poorly understood. We do not understand what causes endometriosis, the only way to confidently diagnose it is by performing an invasive surgery, and currently there is no cure for endometriosis either. This is when my research project comes in. The overall goal is to reduce the suffering of women with endometriosis, by reducing the time it takes to be diagnosed. More specifically, my work aims to find cues for developing a non-invasive way of diagnosing endometriosis.

To achieve my aims, I study the endometrium one cell at a time. For me, each cell is unique and important and plays a crucial role in the normal functioning of the endometrium. Why do I care so much about the endometrium and not the lesion tissue?

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It is about how the endometrium-like tissue gets into the abdomen. The most accepted theory is the one of retrograde menstruation. Simply speaking, the endometrium shed during menstruation does not leave the body through the vagina. Rather it goes up the fallopian tubes into the abdominal cavity, where the tissue attaches to the lining and organs. Surprisingly, retrograde menstruation occurs in 90% of women. Yet, only 10% of women develop endometriosis. Therefore, I think there is something about the properties of the endometrium that make it more likely to attach and make lesions inside the abdomen.

Unfortunately, not much is known about the endometrium. We know it consists of many different cell types, but we do not understand their function. To understand the endometrium better, I study endometrial 'Pipelle' biopsies donated by patients undergoing surgery. Pipelle biopsies are non-invasive, require no anaesthesia and cause only minimal discomfort. After receiving the biopsy, I digest the endometrium with enzymes into single cells. Then I look at which genes are active in each individual cell, using a new and powerful method called single-cell RNA-sequencing.

So far, scientists have only studied the endometrium using 'bulk' RNA-sequencing. It can be best compared to tasting a smoothie. For example, a blueberry, banana & passion fruit one. When we mash all fruits together, we cannot tell what kind of fruits are in the smoothie. However, in order to be a blueberry, banana, or passion fruit, each of the fruits have a different set of genes activated!

In single-cell RNA-sequencing we look at each individual cell separately. It is more like tasting a fruit salad! We can tell exactly what kind of cells (fruits) there are in the endometrium, what they do and how they behave. Moreover, we might even discover that in the 'endometrial smoothie' there are also papayas (new cell type) that we had no idea about.

Studying the endometrium cell by cell in both healthy women and those with endometriosis, I hope to uncover an endometriosis specific signature, which would allow us to develop a non-invasive way of diagnosing endometriosis early on. Early treatment means improved quality of life for millions of women!

I believe no one deserves to suffer from pain that can sometimes be worse than giving birth for many years! Therefore, I keep working on my DPhil, hoping to find cues to aid endometriosis diagnosis.

Lauren Terry, University of Birmingham

Senolytics – the anti-aging product you've never heard of



As we grow older, our skin gets wrinkly, gravity takes its toll and anti-aging creams become our new best friend. These so-called 'anti-aging' products have become a popular fashion trend over the past few years with our society and social media becoming obsessed with our image and the desire to look 10 years younger. In order to achieve this, the latest beauty products, the trendiest SPF and green smoothies have become part of our everyday routine.

So, what about our internal organs? Do they age like our skin? Should we care for our internal organs in the same way we obsess over our external appearance?

The answer is yes.

Yet, obesity and binge drinking are on the rise and is leading to a decline in our internal health. It is public knowledge that these problems trigger heart attacks, strokes and cancer; the damage they cause to the liver is often overlooked. For example, I'm sure you've said 'I'm never drinking again' after a heavy weekend, or that you need a detox, or that the greasy pizza you've ordered, won't hurt just this once. Comments such as these may seem like a light-hearted joke, but the rate of liver disease is escalating rapidly, and is now the 5th most common cause of death in the United Kingdom – certainly not a joke.

The liver is the largest internal organ in the body and performs over 500 functions, such as the removal of toxins and the breakdown of fat. This is impressive yet its unique feature is that it is the only organ in the human body with the ability to regenerate when it is damaged – like a lizard that can regrow its tail after an attack – by external and internal stress, such as alcohol, viruses and fatty food. However, when one or more of these stresses persistently occurs, such as binge drinking, the liver cannot regenerate efficiently, resulting in liver disease.

Liver disease is often called the silent killer, due to the lack of obvious symptoms, and by the time the symptoms do occur, the damage is already done. If it is left untreated, it can progress and become severe, leaving an individual with other complications, such as high blood pressure, infections and cancer. As it reaches this later stage, the individual most likely has cirrhosis, which

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means the liver is majorly scarred and damaged. At this point, the disease is irreversible, the liver cannot regenerate and a liver transplant is the only option as there is no cure.

So this is where my PhD project comes in.

My research simply involves cutting up and adding drugs to cirrhotic livers that have been removed during a transplant and seeing what happens. Even though every liver is very different in shape and size, they all have one thing in common – a large quantity of senescent cells. Senescence is when a cell stops growing and is protected from dying, so there is a build-up of these cells and limited space for new, healthy cells to grow, regenerate and keep the liver functioning correctly. Does this process sound similar? Well, yes, this is what happens when we age. It is thought that there is a build-up of senescent skin cells, which lead to a loss of elasticity and structure so wrinkles appear.

But can we reverse senescence and make space for young, healthy cells?

Possibly.

In my research, I use a class of drugs called Senolytics, which have become popular in science. Interestingly, many of these drugs are originally from natural products such as fruits and vegetables and have been shown to have anti-aging and anti-cancer benefits alongside improving general health and longevity. So, tell me this isn't another reason to have a healthy, balanced diet!

Firstly, I give the liver tissue its own make-shift circulatory system, like we have, and subsequently add Senolytic drugs. I study what Senolytics do to healthy and cirrhotic liver tissue and look to see if there is a change in the number of senescent cells present. However this is easier said than done, as there is no single test for this so far, so my methods consist of perseverance and motivation, and a bit of trial and error. But, over the course of my PhD, I want to identify a way to remove these senescent cells, regenerate youthful, healthy cells and hopefully improve liver function.

If these drugs have the ability to improve liver disease in any possible way, it will be a step closer to finding a treatment to restore youthful cell function and improve the health of individuals with liver disease.

So, will Senolytics be the future of anti-aging products?

**Peter Gawne, School of Biomedical Engineering & Imaging
Science, Kings College London**

**An optimist's guide to radioactivity: using medical imaging to develop
and improve new treatments**



At 01:23 on the morning of 26th April 1986, one of the reactors at the Vladimir Ilyich Lenin Nuclear Power Plant in Ukraine exploded. In the moments that followed trillions of radioactive atoms were unleashed into the atmosphere. Two days later, fallout from the explosion would be detected, in the form of the radioactive atom iodine-131, at a power station in Sweden, and shortly afterwards the full scale of the disaster would be revealed worldwide.

You will of course recognise the power plant's unofficial name: Chernobyl. It is hard to know how many lives were lost because of the eponymous catastrophe, but estimates range from several thousands up to 200,000. The story of Chernobyl is a cautionary tale known by most and is synonymous worldwide with both man-made disaster and the dangers of radioactive materials. But, when we call something radioactive, what do we actually mean?

Radioactivity refers to the release of energy from unstable atoms. Atoms are made up of electrons, neutrons and protons. A radioactive atom (or radioisotope) has too many neutrons or protons, and so is heavy and 'uncomfortable'. To overcome this, the radioactive atom sheds its extra weight by releasing the excess sub-atomic particles and emitting energy in the process. It's analogous to a wet (and grumpy) dog, dripping with water. It will shake its fur to get rid of the water, spraying it everywhere to make itself happy again. However, unlike Winston ruining the walls and carpet, not all radioactivity is bad.

Consider the radioisotope iodine-131. Whilst its presence shocked Swedish scientists in 1986, today it is used all over the UK to treat patients with thyroid cancer. After its administration, the isotope naturally homes in on a patient's thyroid, and the energy iodine-131 releases is enough to damage and kill the cancerous cells in that area.

Another example of how radiation is used to help people with diseases is the use of radioactive sugar by doctors to detect tumours in patients. Every cell in your body needs sugar for energy. But tumours are made up of much more active cells, so require more sugar. If you inject a patient who has a suspected cancer with radioisotope-doped sugar, then you can keep an eye out for it using

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a medical scanner. These scanners are capable of detecting and visualising the energy emitted by the radioactive sugar. Because cancers are more active, they will take up more of the radioisotope and will light up like a Christmas tree in the image.

In my research I use this principle – of using radioisotopes to image inside of the body – to help develop and test new medicines for treating diseases. In particular, I am using tiny, spherical materials known as nanoparticles. These nanoparticles contain chemotherapy or anti-inflammatory drugs within them, which reduces the nasty side effects of these drugs. Additionally, incorporating these drugs into nanoparticles means they travel differently inside the body. The shape and size of nanoparticles allows them to selectively accumulate at tumours or sites of inflammation. This means you can get more targeted delivery of your drug.

However, these nanoparticles are far from perfect: inject them into a patient you can't know for sure that they'll go where they're needed and treat the disease site. This results in patients potentially being given ineffective treatment; wasting precious time and money, which could have been spent treating the patient more effectively.

This is where my work comes in. I take certain radioisotopes and incorporate them into these nanoparticles – without changing the structure of the particles – and make them radioactive. I do this with lots of different nanoparticles designed to treat various diseases including: cancer, arthritis and heart disease. The radioactive tag I place on the particles means they are now visible with medical imaging equipment – the same doctors use for detecting radioactive sugar. So, when I inject these radioactive nanoparticles into a living subject and then take a scan of their bodies, I can see whether or not the nanoparticles are making their way to the target area.

This information is invaluable for scientists and companies who are designing new nanoparticles, as they can use our technique to know early on in development if their new drug is effective or not. Furthermore, my colleagues and I hope that eventually we will use this method to directly help patients by tracking nanoparticles inside their bodies using medical imaging. Therefore, predicting if they will benefit from treatment with those certain nanoparticles or not.

As Chernobyl tragically showed, radioactivity can undeniably be dangerous. But when used in the correct way, it is a powerful tool for treating and detecting disease, whilst aiding the creation of new and improved disease treatments.

Nora Schmit, Imperial College London

Back to the future: how reconstructing the past hepatitis B epidemic can help prevent liver cancer in the future



What's the first thing that comes to your mind when you think of cancer prevention? Maybe you're thinking of not smoking or maintaining a healthy weight - great strategies to reduce your chance of getting cancer.

But did you know that the hepatitis B vaccine, introduced in the 1980s, has long protected children in many parts of the world from developing one of the most common and deadliest cancers later in life?

Although most people have no symptoms when they first become infected, the hepatitis B virus is the leading cause of liver cancer worldwide. Large-scale efforts to tackle the virus using vaccination have been hugely successful in preventing infections in children. Despite this remarkable achievement, hepatitis B infections are still very common and nearly a million people die from its consequences every year. With around 6% of all people living in Africa currently infected, the death toll there is expected to rise even further.

But while a liver cancer diagnosis is nearly always fatal, treating the infection is possible with the same drugs that work against HIV. So why do so few people receive these drugs, when over half of all liver cancer deaths globally are preventable?

For one, there's the social aspect. Hepatitis B has received far less attention and financial support from the international community than HIV. The lack of awareness means that 9 out of 10 people don't know they are infected, and lifelong treatment remains inaccessible for most.

Then, there's the biology. If you get infected with hepatitis B, you might be completely fine and never realise - or you could develop a chronic infection that progresses to liver cancer 40 years later. The virus can stay silent in the body for decades, slowly damaging the liver, but not everyone goes on to develop life-threatening liver disease. This means that only a small proportion of infected people actually need treatment. The hard, and costly part is identifying who that is.

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This is where my research comes in. While predicting your individual risk of getting sick and prescribing treatment is your doctor's job, my role as an epidemiologist is to predict the risk of liver cancer of entire populations and suggest ways to reduce it.

Think about it like a weather forecast: with measurements on the current weather and knowledge of its local patterns, computer simulations can predict the most likely forecast for tomorrow. Similarly, epidemiologists develop mathematical models to calculate how many people could become infected and fall ill in the future, using our understanding of transmission and disease patterns as the backbone of the model.

In my research, I try to predict the future number of liver cancer cases in The Gambia. This small West African country has been at the forefront of hepatitis B research and prevention for more than 30 years, leading landmark collaborative studies on vaccination and treatment. And since the people who will develop liver cancer in the decades to come are those that are already living with hepatitis B today, I first had to look back into the past to reconstruct the spread of hepatitis B in this region.

So how do I know how Gambian people became infected and developed liver disease in the past? I travel back in time through the scientific literature. By sifting through thousands of publications, I have found valuable pieces of information that tell us a little bit about the history of hepatitis B in West Africa. My model, then, allows me to recycle this previously collected data by assembling the disjointed pieces of evidence in a meaningful way.

Drawing on decades of research and bringing together experience from the field, the lab and clinical observation, I can go beyond any individual study's original purpose, fill in gaps in the data, and paint a picture of the hepatitis B epidemic and liver cancer in The Gambia in the past, as well as in the future. Further down the line, this helps me predict how many liver cancer cases could be prevented by diagnosing and treating people.

Good news though: things are already changing. Mine is one among a growing number of research projects seeking to address this silent epidemic. The World Health Organization has set the aim of eliminating viral hepatitis, marking the beginning of a new era in hepatitis B control. My hope is that combining the success of vaccination with better access to treatment could make this a reality, radically changing the future of liver cancer and saving millions of lives.

Elisabeth Trinh, University of Manchester

Mixed up messages in the gut



There are trillions of non-harmful bacteria that live in the gut. I'm sure you've seen lots of adverts on TV for yoghurts, drinks and probiotics that you can take to help your gut. Scientists call all these microbes that live in the body the "microbiome". And whilst the entire human body has microbes living peacefully with it, the majority of the microbiome is in the gut (weighing up to 2kg!).

Humans depend on these good bacteria in the gut to help digest our food, regulate the immune system and protect us from bacteria that cause disease, as well as helping to produce certain vitamins. All of these important tasks by the microbiome help us stay healthy.

Why don't the immune cells attack the good bacteria? How do the immune cells know which bacteria are "good" and which ones will make the body ill?

There are many types of cells in the human body which are involved in the immune system. I particularly look at cells in the gut called macrophages. These cells are important within the gut for deciding which bacteria and fungi are "good" and which ones are "bad". If macrophages find a disease-causing bacteria, they can send other immune cells to attack them. When macrophages come across a helpful bacteria in the microbiome, they send a message that tells the other immune cells that this bacteria is not harmful. We call this "tolerance."

When this process goes wrong, this can result in diseases called Inflammatory Bowel Disease- including Crohn's disease and Ulcerative Colitis. In these diseases, the macrophages call for reinforcements in the form of other immune cells to attack the bacteria, even if they come across good bacteria in the microbiome. Diarrhoea, pain, fever- even blood in the stool- all result from these over-eager immune cells. Inflammatory bowel diseases can't be cured, and treating them involves lots of long term medicines. Treatment of these debilitating conditions can even involve surgery where part of the gut is removed. These illnesses affect thousands of people worldwide, with an estimated 300,000 people just in the UK. People of all ages can also be affected, including children.

Why are the immune cells suddenly attacking the bacteria that they used to think were good?

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There isn't a simple answer. There are lots of factors that contribute to the development of bowel diseases, including genetics, diet and use of antibiotics. One factor that I'm particularly interested in is fungi. As well as the bacteria in the gut, a significant amount of fungi can be found within the gut. Over the past few years, scientists have observed that many people with these specific types of bowel diseases have big changes in their fungal microbiome. By looking at these changes, I investigate how fungi in the gut are involved in telling these immune cells not to attack the helpful bacteria.

So, it's important to find out what messages the cells are sending to each other. Macrophages can be grown in the laboratory and, by giving them extracts of fungi, I aim to find out what signals they produce that make immune cells 'tolerant' to the microbiome in the gut. I also look at how getting rid of all the fungi within the gut, using medicines called anti-fungals, could potentially cause macrophages to respond badly to gut bacteria, leading to diarrhoea and the other symptoms of Inflammatory Bowel Disease. Once I've found out what signals the fungi send to the immune cells, then what messages the immune cells send to each other, I look at various ways to stop these series of messages going wrong.

Finding out how fungi can help the immune cells regulate the response to the gut microbiome would have a huge impact on the prevention of Inflammatory Bowel Disease. If we can find out exactly what is going wrong- why couldn't we stop that happening in the first place? Bowel diseases can be embarrassing- a large number of patients are unable to use the toilet normally, instead having to use a bag called a stoma. Discovering why macrophages respond the way they do may even lead to new treatments- avoiding surgery, long term medications, and most importantly of all, improving the quality of life of thousands of people worldwide. Next time you're watching TV and see those yoghurt adverts, remember all the helpful messages those good bacteria may be sending to your immune cells in your gut!

Amy Southern, MRC Harwell and University of Oxford

Making sense of a sticky situation: finding the 'glue ear gene' in Down syndrome



Down syndrome is a common occurrence in society, but we do not fully understand the genetic changes that occur during development to cause the syndrome. Normally, each newly conceived baby receives a set of 23 chromosomes from their mother and a set of 23 from their father. The genes on these chromosomes determine which characteristics the baby will develop, such as eye and hair colour. But genes also provide the instructions for how the rest of the body is built, including the organs and immune system. If a baby mistakenly ends up with a full or partial 3rd copy of a chromosome (usually chromosome 21), this will have an effect on how those genes operate as they will have 3 copies rather than 2. We aren't quite sure how or why trisomy happens, but the result of this extra chromosome 21 is known as Down syndrome.

People with Down syndrome have many physical and mental differences due to having 3 copies of the genes on chromosome 21, such as congenital heart defects (also known as a 'hole in the heart'), an increased susceptibility to infection, learning difficulties, and reduced hearing due to fluid accumulation behind the ear drum (known as otitis media, or glue ear). Glue ear can affect any child, but either clears up on its own or is treated by the insertion of grommets (a small tube inserted into the ear drum to allow the fluid to escape). Amongst the Down syndrome community, glue ear affects up to 96% of children but they shouldn't undergo the surgery to insert grommets due to their increased susceptibility to infection. The surgery is also more difficult as people with Down syndrome have altered ear anatomy (e.g. small ear canals). Unfortunately, this means that they can only hope that the fluid clears up on its own, and in the meantime suffer the associated hearing loss which can leave them feeling isolated and further compounds their learning difficulties.

It is very difficult to study the effects of Down syndrome in humans, but mice have been found to be a very good model organism. Not only are they easy to breed, but mice are also a lot more genetically similar to us than you might first expect - the genes on the extra human chromosome in Down syndrome are also found in the same order on a mouse chromosome. We can genetically alter mouse embryos to contain this 3rd chromosome copy and, after specific breeding, the resulting mice have heart defects and glue ear, just like people with Down syndrome. The mice also have a slightly different head shape to their 'healthy' littermates, which further correlates with human Down syndrome.

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My research is trying to discover which gene (in 3 copies) causes glue ear in Down syndrome. The mice are bred with a 3rd chromosome of a specific length, meaning they only have 3 copies of certain genes. If the mice have glue ear, then we know that one of these genes is responsible for causing the problem. By systematically testing each set of genes on the extra chromosome, we can work out which gene (in 3 copies) leads to glue ear.

We have currently found a set of mice who all have glue ear, but their 3rd chromosome only consists of 12 genes. This gives us a fantastic starting point in the search for the 'glue ear gene' as it is highly likely to be one or more of these 12. I am currently investigating the expression of these genes. Gene expression is when the DNA in your genes is translated into proteins. These are used to maintain your organs and bodily processes. The gene responsible for glue ear will likely be producing a protein that causes the condition. The way this protein works is not yet known, but once we find out its role in glue ear we can develop treatment to prevent it occurring.

Curing glue ear would allow children with Down syndrome to interact more easily with the world around them. This would hopefully enhance their ability to socialise and give them a better chance at succeeding in school, offering them a brighter future.