

How our cells sense oxygen wins Nobel prize

By James Gallagher Health and science correspondent 7 October 2019

Three scientists who discovered how cells sense and adapt to oxygen levels have won the 2019 Nobel Prize.

Sir Peter Ratcliffe, of the University of Oxford and Francis Crick Institute, William Kaelin, of Harvard, and Gregg Semenza, of Johns Hopkins University share the physiology or medicine prize.

Their work is leading to new treatments for anaemia and even cancer.

The role of oxygen-sensing is also being investigated in diseases from heart failure to chronic lung disease.

Sir Peter said: "I'm honoured and delighted at the news.

"It's a tribute to the lab, to those who helped me set it up and worked with me on the project over the years, to many others in the field, and not least to my family for their forbearance of all the up and downs."

The Swedish Academy, which awards the prize, said: "The fundamental importance of oxygen has been understood for centuries but how cells adapt to changes in levels of oxygen has long been unknown."

Oxygen levels vary in the body, particularly:

- during exercise
- at high altitude
- after a wound disrupts the blood supply

And when they drop, cells rapidly have to adapt their metabolism.

Why does this matter?

The oxygen-sensing ability of the body has a role in the immune system and the earliest stages of development inside the womb.

If oxygen levels are low, it can trigger the production of red blood cells or the construction of blood vessels to remedy this.

More red blood cells mean the body is able to carry more oxygen and is why athletes train at altitude.

So, drugs that mimic it may be an effective treatment for anaemia.

Tumours, meanwhile, can hijack this process to selfishly create new blood vessels and grow.

So, drugs that reverse it may help halt cancer.

"The work of these three scientists and their teams has paved the way to a greater understanding of these common, life-threatening conditions and new strategies to treat them," Dr Andrew Murray, from the University of Cambridge, said.

"Congratulations to the three new Nobel Laureates. This is richly deserved."

How was the discovery made?

Levels of hormone erythropoietin (EPO) were shown to rise as those of oxygen fell.

And the scientists discovered this was because a cluster of proteins called hypoxia-inducible factor (HIF) was changing the behaviour of DNA, the genetic code.

Further work showed when oxygen levels were normal, cells constantly produced HIF only for it to be destroyed by another protein, VHL.

But when oxygen levels fell, VHL could no longer stick to HIF, leading to the build-up sufficient levels to change the behaviour of DNA.

Nobel prize for medicine goes to cancer therapy

By Michelle Roberts Health editor, BBC News online 1 October 2018

Two scientists who discovered how to fight cancer using the body's immune system have won the 2018 Nobel Prize for physiology or medicine.

The work, by Professor James P Allison from the US and Professor Tasuku Honjo from Japan, has led to treatments for advanced, deadly skin cancer.

Immune checkpoint therapy has revolutionised cancer treatment, said the prize-giving Swedish Academy.

Experts say it has proved to be "strikingly effective".

Prof Allison, of the University of Texas, and Prof Honjo, of Kyoto University, will share the Nobel prize sum of nine million Swedish kronor - about \$1.01 million or 870,000 euros.

Accepting the prize, Tasuku Honjo told reporters: "I want to continue my research ... so that this immune therapy will save more cancer patients than ever."

Prof Allison said: "It's a great, emotional privilege to meet cancer patients who've been successfully treated with immune checkpoint blockade. They are living proof of the power of basic science, of following our urge to learn and to understand how things work."

Treating the untreatable

Our immune system protects us from disease, but it has built-in safeguards to stop it from attacking our own tissue.

Some cancers can take advantage of those "brakes" and dodge the attack too.

Allison and Honjo, now both in their 70s, discovered a way to unleash our immune cells to attack tumours by turning off proteins that put the brakes on.

And that led to the development of new drugs which now offer hope to patients with advanced and previously untreatable cancer.

Immune checkpoint therapy is being used by the NHS to treat people with the most serious form of skin cancer, melanoma.

It doesn't work for everyone, but for some patients it appears to have worked **incredibly well**, getting rid of the tumour entirely, even after it had started to spread around the body.

Such remarkable results had never been seen before for patients like these.

Doctors have also been using the treatment to help some people with advanced lung cancer.

Prof Charles Swanton, from Cancer Research UK, congratulated the prize winners, saying: "Thanks to this groundbreaking work, our own immune system's innate power against cancer has been realised and harnessed into treatments that continue to save the lives of patients. For cancers such as advanced melanoma, lung, and kidney, these immune-boosting drugs have transformed the outlook for many patients who had run out of options.

"The booming field of immunotherapy that these discoveries have precipitated is still relatively in its infancy, so it's exciting to consider how this research will progress in the future and what new opportunities will arise."

Medicine is the first of the Nobel Prizes awarded each year. The literature prize will not be handed out this year, after the awarding body was **affected by a sexual misconduct scandal**.

Body clock scientists win Nobel Prize

By James Gallagher Health and science reporter, BBC News website 2 October 2017

Three scientists who unravelled how our bodies tell time have won the 2017 Nobel Prize for physiology or medicine.

The body clock - or circadian rhythm - is the reason we want to sleep at night, but it also drives huge changes in behaviour and body function.

The US scientists Jeffrey Hall, Michael Rosbash and Michael Young will share the prize.

The Nobel prize committee said their findings had "vast implications for our health and wellbeing".

A clock ticks in nearly every cell of the human body, as well as in plants, animals and fungi.

Our mood, hormone levels, body temperature and metabolism all fluctuate in a daily rhythm.

Even our risk of a heart attack soars every morning as our body gets the engine running to start a new day.

The body clock so precisely controls our body to match day and night that disrupting it can have profound implications.

The ghastly experience of jet lag is caused by the body being out of sync with the world around it.

In the short term, body clock disruption affects memory formation, but in the long term it increases the risk of diseases, including type 2 diabetes, cancer and heart disease.

"If we screw that system up we have a big impact on our metabolism," said Prof Russell Foster, a body clock scientist at the University of Oxford.

He told the BBC he was "very delighted" that the US trio had won, saying they deserved the prize for being the first to explain how the system worked.

He added: "They have shown us how molecular clocks are built across all the animal kingdom."

The trio's breakthroughs were on fruit flies, but their findings explain how "molecular feedback loops" keep time in all animals.

Jeffrey Hall and Michael Rosbash isolated a section of DNA called the *period* gene, which had been implicated in the circadian rhythm.

The *period* gene contained instructions for making a protein called PER. As levels of PER increased, it turned off its own genetic instructions.

As a result, levels of the PER protein oscillate over a 24-hour cycle - rising during the night and falling during the day.

Michael Young discovered a gene called *timeless* and another one called *doubletime*. They both affect the stability of PER.

If PER is more stable then the clock ticks more slowly, if it is less stable then it runs too fast. The stability of PER is one reason some of us are morning larks and others are night owls.

Together, they had uncovered the workings of the molecular clock inside the fly's cells.

Dr Michael Hastings, who researches circadian timing at the MRC Laboratory of Molecular Biology, told the BBC: "Before this work in fruit flies we really didn't have any ideas of the genetic mechanism - body clocks were viewed as a black box on a par with astrology."

He said the award was a "fantastic" decision.

He added: "We encounter the body clock when we experience jet lag and we appreciate it's debilitating for a short time, but the real public health issue is rotational shift work - it's a constant state of jet lag."

Medicine Nobel for cell recycling work

By Michelle Roberts Health editor, BBC News online 3 October 2016

The 2016 Nobel Prize in physiology or medicine goes to Yoshinori Ohsumi of Japan for discoveries about the secrets of how cells can remain healthy by recycling waste.

He located genes that regulate the cellular "self eating" process known as autophagy.

Dr Ohsumi's work is important because it helps explain what goes wrong in a range of illnesses, from cancer to Parkinson's.

Errors in these genes cause disease.

Last year's prize was shared by three scientists who developed treatments for malaria and other tropical diseases.

"Self-eating"

The body destroying its own cells may not sound like a good thing. But autophagy is a natural defence that our bodies use to survive.

It allows the body to cope with starvation and fight off invading bacteria and viruses, for example.

And it clears away old junk to make way for new cells.

Failure of autophagy is linked with many diseases of old age, including dementia.

Research is now ongoing to develop drugs that can target autophagy in various diseases, including cancer.

The concept of autophagy has been known for over 50 years, but it wasn't until Dr Ohsumi began studying and experimenting with baker's yeast in the 80s and 90s that the breakthrough in understanding was made.

Dr Ohsumi is reported to be surprised about receiving his Nobel Prize, but "extremely honoured".

Speaking with the Japanese broadcaster NHK he said that the human body "is always repeating the auto-decomposition process, or cannibalism, and there is a fine balance between formation and decomposition. That's what life is about."

Prof David Rubinsztein, an expert in autophagy at the University of Cambridge, said he was delighted that Dr Ohsumi's vital work had been recognised and rewarded.

"His pioneering work in yeast led to the discovery of the key genes and fundamental biochemical processes that are required for autophagy.

"As autophagy is well conserved from yeast to man, his laboratory's discoveries have also provided the critical tools to many labs to enable the appreciation of the important roles of autophagy in diverse physiological and disease processes.

"These include infectious diseases, cancers, and various neurodegenerative diseases such as Huntington's disease and forms of Parkinson's disease. Indeed, autophagy manipulation may provide a key strategy for treating some of these conditions."

More than 270 scientists were nominated for the prize, which was awarded at Sweden's Karolinska Institute and comes with eight million Swedish kronor (around £728,000 or \$936,000 or 834,000 euros) for the winner.

The winners of the physics, chemistry and peace prizes are to be announced later this week.

Nobel Prize for anti-parasite drug discoveries

By Michelle Roberts Health editor, BBC News online 5 October 2015

The Nobel Prize for physiology or medicine has been split two ways for groundbreaking work on parasitic diseases.

William C Campbell and Satoshi Ōmura found a new way of tackling infections caused by roundworm parasites.

Youyou Tu shares the prize for her discovery of a therapy against malaria.

The Nobel committee said the work had changed the lives of hundreds of millions of people affected by these diseases.

The mosquito-borne disease malaria kills more than 450,000 people each year around the world, with billions more at risk of catching the infection.

Parasitic worms affect a third of the world's population and cause a number of illnesses, including river blindness and lymphatic filariasis.

Deadly parasites

After decades of limited progress, the discovery of the two new drugs - ivermectin for river blindness and lymphatic filariasis, and artemisinin for malaria - was a game-changer.

Efforts to eradicate malaria had been failing - older drugs were losing their potency - and the disease was on the rise.

Prof Youyou Tu, who in the 1960s had recently graduated from the Pharmacy Department at Beijing Medical University, looked to traditional herbal medicine to find a potential therapy.

She took an extract from the plant called *Artemisia annua*, or sweet wormwood, and began testing it on malaria parasites.

The component, later called artemisinin, was highly effective at killing them.

Today, the drug is used around the world in combination with other malaria medicines. In Africa alone, this is saving more than 100,000 lives every year.

Tu is the 13th woman to win this Nobel Prize.

She shares the award with two men who found a treatment for another parasite - roundworm.

Their research led to the development of a drug called ivermectin, which is so successful that roundworm diseases are on the verge of eradication.

Satoshi Ōmura, a Japanese microbiologist, focused on studying microbes in soil samples. He selected a number of promising candidates that he thought might work as a weapon against diseases.

Irish-born William C Campbell, an expert in parasite biology working in the US, then explored these further and found one was remarkably efficient against parasites.

The active ingredient, avermectin, went on to become a drug known as ivermectin which is now used to treat river blindness and lymphatic filariasis.

River blindness is an eye and skin disease that ultimately leads to blindness. Lymphatic filariasis, also known as elephantiasis, causes painful swelling of the limbs. Both affect people living in some of the poorest countries in the world.

'Out of the blue'

Dr Colin Sutherland, of the London School of Hygiene and Tropical Medicine, said it was immensely gratifying that the achievements in tackling these important diseases had been recognised.

"It's come out of the blue but we are very excited that the committee recognised the importance of parasitic diseases."

The Nobel committee said: "The two discoveries have provided humankind with powerful new means to combat these debilitating diseases that affect hundreds of millions of people annually.

"The consequences in terms of improved human health and reduced suffering are immeasurable."

Omura told Japanese broadcaster NHK: "I have learned so much from microorganisms and I have depended on them, so I would much rather give the prize to microorganisms.

"This is kind of a low-profile research area, but microorganisms are extremely important for humans. They can be our partners. I hope the area gets more attention because of the prize so that it can further contribute to human beings."

Nobel Prize for the brain's GPS discovery

By James Gallagher Health editor, BBC News website 6 October 2014

The Nobel Prize for physiology or medicine has been awarded to three scientists who discovered the brain's "GPS system".

UK-based researcher Prof John O'Keefe as well as May-Britt Moser and Edvard Moser share the award.

They discovered how the brain knows where we are and is able to navigate from one place to another.

Their findings may help explain why Alzheimer's disease patients cannot recognise their surroundings.

"The discoveries have solved a problem that has occupied philosophers and scientists for centuries," the Nobel Assembly said.

Inner GPS

Prof O'Keefe, from University College London, discovered the first part of the brain's internal positioning system in 1971.

On hearing about winning the prize, he said: "I'm totally delighted and thrilled, I'm still in a state of shock, it's the highest accolade you can get."

His work showed that a set of nerve cells became activated whenever a rat was in one location in a room.

A different set of cells were active when the rat was in a different area.

Prof O'Keefe argued these "place cells" - located in the hippocampus - formed a map within the brain.

He will be having a "quiet celebration" this evening and says the prize money "should be used for the common good".

Mapping

In 2005, husband and wife team, May-Britt and Edvard, discovered a different part of the brain which acts more like a nautical chart.

These "grid cells" are akin to lines of longitude and latitude, helping the brain to judge distance and navigate.

They work at the Norwegian University of Science and Technology in Trondheim.

Prof May-Britt Moser said: "This is crazy, this is such a great honour for all of us and all the people who have worked with us and supported us."

The Nobel committee said the combination of grid and place cells "constitutes a comprehensive positioning system, an inner GPS, in the brain".

They added: "[This system is] affected in several brain disorders, including dementia and Alzheimer's disease.

"A better understanding of neural mechanisms underlying spatial memory is therefore important and the discoveries of place and grid cells have been a major leap forward to advance this endeavour."

'Cognitive revolution'

Dr Colin Lever, from the University of Durham, worked in Prof O'Keefe's laboratory for ten years and has already dreamt on two occasions that his former mentor had won the award.

He told the BBC: "He absolutely deserves the Nobel Prize, he created a cognitive revolution, his research was really forward thinking in suggesting animals create representations of the external world inside their brains."

"Place cells help us map our way around the world, but in humans at least they form part of the spatiotemporal scaffold in our brains that supports our autobiographical memory.

"The world was not ready for his original report of place cells in 1971, people didn't believe that 'place' was what best characterised these cells, so there was no great fanfare at that time.

"But his work on hippocampal spatial mapping created the background for discovering grid cells and with grid cells, the world was prepared and we all thought wow this is big news."