models back then couldn't have predicted how the abrupt warming in the stratosphere might affect the weather, says Harry Hendon, head of climate processes at the Australian Bureau of Meteorology.

Climate models have improved significantly over the past 15 years, partly driven by faster, cheaper computers. They're also much better at combining sources of observational data, such as satellite measurements of stratospheric temperature and atmospheric humidity.

Such advances helped meteorologists to forecast the start of the current stratospheric warming about a week in advance. The events typically start towards the end of winter, when mountains or the contrast between warm ocean temperatures and cold land masses generate continental-scale atmospheric disturbances known as Rossby waves. If these are large enough, they can reach into the stratosphere and break like a wave over a beach, compressing and warming the air in the stratosphere above the pole. This pressure can force the strong stratospheric winds encircling the pole — the polar-night jet stream — to abruptly slow and reverse, changing from being westerly winds to flowing in an easterly direction, says Scaife.

A complete reversal has not yet occurred in the current event, but wind speeds have already plummeted. Scientists at the Bureau of Meteorology don't know exactly what sparked this year's event, but they predict that it will be stronger than in 2002 — and so have a greater effect on the weather.

Lim's model, which teases out how stratospheric conditions bleed down into the troposphere, has helped to predict how this might play out. Apart from bringing warmer weather to eastern Australia, the event will drive colder, wetter conditions to western Tasmania, New Zealand's South Island and the southern tip of South America.

The warming so far has also sent an influx of ozone-rich air to counter the thinning of ozone over Antarctica that usually occurs in spring.

Meteorologists are now waiting to see whether the forecast holds. Hendon hopes that, if it does, the bureau will incorporate Lim's model into its standard operations, to provide short-term climate predictions every spring. ■

MEDICINE PRIZE

Biologists who decoded oxygen sensing win Nobel

Laureates' discovery underpins understanding of diseases such as anaemia and cancer.

BY HEIDI LEDFORD & EWEN CALLAWAY

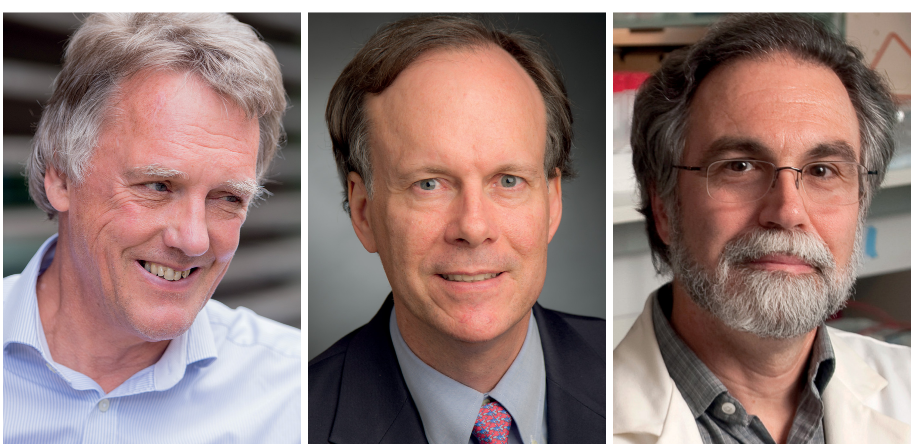
A trio of researchers has won the 2019 Nobel Prize in Physiology or Medicine for describing how cells sense and respond to changing oxygen levels by switching genes on and off — a discovery that has been key in understanding human diseases such as cancer and anaemia.

The three scientists are cancer researcher William Kaelin at the Dana-Farber Cancer Institute in Boston, Massachusetts; physician–scientist Peter Ratcliffe at the University of Oxford, UK, and the Francis Crick Institute in London; and geneticist Gregg Semenza at Johns Hopkins University in Baltimore, Maryland. The team also won the Albert Lasker Basic Medical Research Award in 2016.

Their work has helped researchers to understand how the body adapts to low oxygen levels by, for example, cranking out red blood cells and growing new blood vessels.

"This is a fundamental discovery that they've contributed to," says Celeste Simon, a cancer biologist at the University of Pennsylvania in Philadelphia. "All organisms need oxygen, so it's really important."

"The field really coalesced around this discovery, which was dependent on each one of their findings," says Randall Johnson, a physiologist at the University of Cambridge, UK, and the Karolinska Institute in Stockholm, and a member of the Nobel Assembly. "This really was a three-legged stool."



L TO R: UNIV. OF OXFORD; HARVARD UNIV.; JOHNS HOPKINS MEDICINE

Nobel prizewinners Peter Ratcliffe (left), William Kaelin (centre) and Gregg Semenza (right).

OXYGEN DEPRIVATION

The body's tissues can be deprived of oxygen during exercise or when blood flow is interrupted, such as during a stroke. Cells' ability to sense oxygen is also crucial for the developing fetus and placenta, as well as for tumour growth, because the mass of rapidly growing cells can deplete oxygen in a tumour's interior.

In work conducted in the 1990s, the scientists discovered the molecular processes that cells go through to respond to oxygen levels in the body. They found that central to this is a mechanism involving proteins called hypoxia-inducible factor (HIF) and VHL.

Semenza and Ratcliffe studied the regulation of a hormone called erythropoietin (EPO), which is crucial for stimulating the production of red blood cells in response to low oxygen levels. Semenza and his team identified a pair of genes that encode the two proteins that form the protein complex HIF, which turns on certain genes and boosts EPO production when oxygen is low.

Meanwhile, Kaelin showed that a gene called *VHL* also seemed to be involved in how cells respond to oxygen. Kaelin was studying a genetic syndrome called von Hippel-Lindau's disease; families with the disease carry mutations in *VHL*, and the condition raises the risk of certain cancers.

Ratcliffe and his team later found that the protein expressed by *VHL* interacts with a component of HIF, turning off responses to low-oxygen conditions by marking the HIF component for destruction once oxygen levels rise.

And in 2001, teams led by Kaelin and Ratcliffe elucidated more details about this process. They discovered that, when oxygen is present, a chemical modification to the VHL protein called prolyl hydroxylation allows VHL to bind HIF, which leads to the latter's breakdown. But this modification is blocked when cells are oxygen-starved, kick-starting the activity of HIF.

As a result, cells can react to low oxygen levels by simply blocking the breakdown of HIF, notes Mark Dewhirst, a cancer biologist at Duke University in Durham, North Carolina. "The cell can respond in minutes."

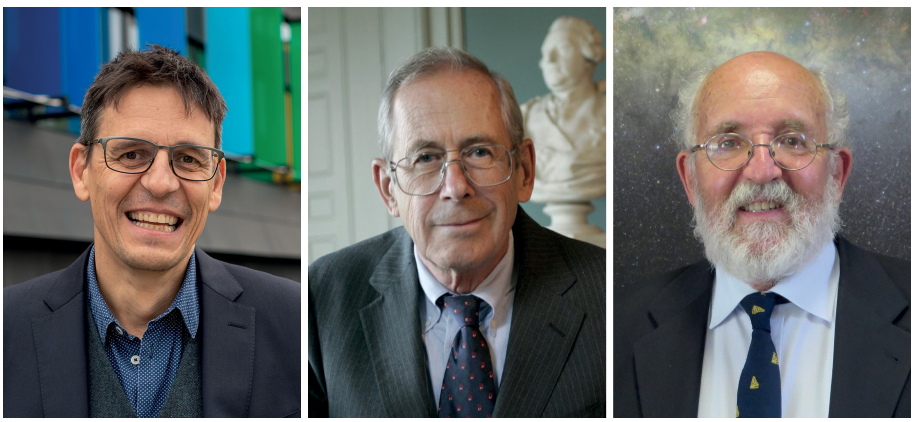
DRUG DEVELOPMENT

The work has led researchers to develop drugs that target oxygen-sensing processes, including those in cancer. Drugs, called prolyl hydroxylase inhibitors, that prevent VHL from binding to HIF and causing its degradation are also being investigated as treatments for anaemia and renal failure. Chinese regulators approved the first of these drugs in 2018.

"You could argue that some aspect of this is going to be germane to all diseases you can think of," says Simon.

Colleagues hailed the trio as role models for other scientists. "They are extremely humble people," says Dewhirst. "All three of them hold scientific rigour and reproducibility to the absolute highest standard," adds Simon.

Kaelin, in particular, has taken his field to task for pursuing possible cancer treatments that aren't backed up by strong evidence. "The most dangerous result in science is the one you were hoping for, because you declare victory and get lazy," he told scientists at a 2018 talk at the US National Institutes of Health in Bethesda, Maryland. ■



Didier Queloz (left), James Peebles (centre) and Michel Mayor.

LEFT TO RIGHT: UNIV. CAMBRIDGE; TORBJÖRN ZADIG; INAMORI FOUNDATION

PHYSICS PRIZE

Planet pioneers win physics Nobel

Exoplanet astronomers share award with cosmologist whose theories describe Universe's evolution.

BY ELIZABETH GIBNEY & DAVIDE CASTELVECCHI

Cosmologist James Peebles and astronomers Michel Mayor and Didier Queloz have won the 2019 Nobel Prize in Physics for discoveries about the evolution of the Universe and Earth's place in it.

In 1995, Mayor, at the University of Geneva, Switzerland, and his then-student Queloz made the first discovery of a planet orbiting a Sun-like star (M. Mayor and D. Queloz *Nature* **378**, 355–359; 1995). Their work launched a field that has become one of astronomy's hottest. They detected the exoplanet through its tiny gravitational pull on its star, 51 Pegasi, a technique that is now used to study some of the more than 4,000 exoplanets now known to exist.

Peebles, who is at Princeton University in New Jersey, developed a theoretical framework that underpins modern understanding of the Universe's history (P. J. E. Peebles and J. T. Yu *Astrophys. J.* **162**, 815; 1970). In particular, he helped to lay the theoretical foundations for the cosmic microwave background (CMB), the 'afterglow' of the Big Bang, and to establish the current 'standard model' of the Universe's evolution. In this model, the mysterious substance known as dark matter plays a central part in assembling large-scale structures of the cosmos, such as galaxies and clusters of galaxies.

Mayor and Queloz share one half of the prize, worth 9 million Swedish kronor (US$910,000), and Peebles will receive the other half.

Mayor and Queloz's discovery "started modern exoplanet science", says Guillem Anglada-Escudé, an astronomer at the Institute for Space Sciences-CSIC in Barcelona, Spain.

Researchers had discovered exoplanets orbiting spinning cores of dead stars known as pulsars, but not around stars similar to our own, which could host habitable planets. The pair's discovery came as a surprise. The planet they detected, called 51 Pegasi b, is a gas giant, a type that astronomers had expected would orbit the outer reaches of a solar system. But it was orbiting much closer to its star than Mercury is to the Sun — an early sign that other planetary systems might not be like our own.

The finding was remarkable for being almost completely unambiguous and quickly confirmed, says Anglada-Escudé.

PROBING FIRST LIGHT

Meanwhile, Peebles' theories have allowed cosmologists to understand much more about the CMB and the Universe's beginnings.

"Were it not for the theoretical discoveries of James Peebles, the wonderful high-precision measurements of this radiation over the last 20 years would have told us almost nothing," said Mats Larsson, a molecular physicist at Stockholm University and chair of the 2019 Nobel physics committee, when he revealed the prize.

Peebles developed a model of the Universe's evolution known as the 'cold dark matter' theory, which describes how cosmological structures formed as the Universe expanded and cooled from its hot, dense beginnings. Together with the later addition of ideas about dark energy, this has become the standard framework of modern cosmology.

Although the precise nature of dark matter has yet to be understood, several high-precision surveys of the Universe have lent support to this theory; these include studies of the CMB and the mapping of galaxies across large swathes of the sky. "This is such a long-deserved recognition," says François Bouchet, an astronomer at the Institute of Astrophysics in Paris.

It is unusual for exoplanets and cosmology to be paired up in the same prize, but both lines of work "give a fresh perspective of the place humans have in the cosmos", says Bouchet. ■