POLITICS

Anti-vaping bill goes up in smoke

Demise of California legislation highlights rise of lobbying.

BY DANIEL CRESSEY

The failure last week of an attempt to extend California's smoking ban to electronic cigarettes has disappointed researchers who worry that a boom in vaping will re-normalize smoking in places where it now carries social stigma, and lead to a new generation of people addicted to nicotine. Although several other US states have already passed e-cigarette legislation, the California bill had special resonance because the state has a reputation for pioneering anti-tobacco legislation.

The bill's demise, says Vaughan Rees, director of the Center for Global Tobacco Control at the Harvard T. H. Chan School of Public Health in Boston, Massachusetts, also highlights the rise of intensive political lobbying in this arena. "The e-cigarette industry is acquiring the kind of influence that the conventional tobacco industry has used for many years to prevent the implementation of sensible measures to protect the health of the public," he says.

Since the modern e-cigarette emerged a decade ago, the United States has taken to the technology in a big way (see *Nature* **513,** 24–26; 2014). In 2013, around 2.5% of people across the country reported having used the devices in the past month; among adolescents, e-cigarettes are now used more than conventional cigarettes, said the US Centers for Disease Control and Prevention in April this year.

But regulation has not kept up. The Food and Drug Administration (FDA) proposed a rule for regulating the devices in April 2014, but the rule has been mired in political controversy ever since, leaving an absence of country-wide laws. Even if the FDA does regulate e-cigarettes, it will still be up to local law-makers to decide where the devices can be used, and how much they will be taxed. North Dakota, New Jersey, Utah and Hawaii prohibit use of e-cigarettes in public spaces, and nearly 400 municipalities have similar laws, says the American Cancer Society Cancer Action Network in Washington DC, which campaigns for cancer-fighting legislation.

In January, the California Department of Public Health asked physicians to urge e-cigarette users to quit, and released a report warning that without more regulation, "it is likely that California's more than two decades of progress to prevent and reduce traditional tobacco use will erode".

The California bill, pushed by state senator Mark Leno (Democrat), would have regulated e-cigarettes in the same way as conventional tobacco products, making it illegal to use them in restaurants, bars, hospitals and workplaces. Leno withdrew the bill on 8 July, after a committee in the state assembly amended it to such an extent that he said it had become pointless.

Whether to tax e-cigarettes at the same rate as tobacco is also a contentious issue. Advocates of e-cigarettes say that vaping is less dangerous than smoking, and that taxing e-cigarettes at below the rate for tobacco makes it more attractive. "Any time they are vaping, they're not smoking a cigarette. That's a win," says Cynthia Cabrera, executive director of the Smoke-Free Alternatives Trade Association in Washington DC. Critics contend that lower taxation encourages people to maintain their nicotine addictions, and to start using the drug in the first place, perhaps as a gateway to tobacco. Washington DC will put a 70% mark-up on the devices in October.

Researchers are broadly split into those who think that the products undermine attempts to free society from nicotine addiction entirely, and thus should be subject to the same restrictions and taxes as tobacco, and those who think that e-cigarettes deserve lighter regulation than normal cigarettes because they could help smokers to quit. Still, even proponents of the harm-reduction strategy would support reasonable efforts to limit marketing and sale of e-cigarettes to minors, says Rees. ■

PARTICLE PHYSICS

Forsaken pentaquark particle spotted at CERN

Exotic subatomic species confirmed at Large Hadron Collider after earlier false sightings.

BY MATTHEW CHALMERS

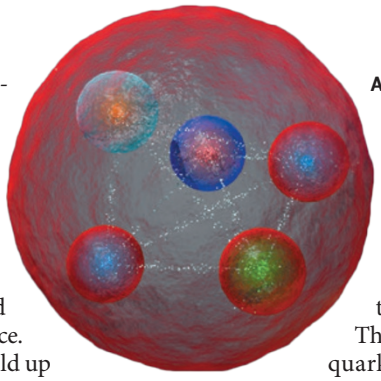
An exotic particle made up of five quarks has been found a decade after experiments seemed to rule out its existence.

The short-lived 'pentaquark' was spotted by researchers analysing data on the decay of unstable particles in the LHCb experiment at the Large Hadron Collider (LHC) at CERN, Europe's particle-physics laboratory near Geneva. The finding, says LHCb spokesperson Guy Wilkinson, opens a new era in physicists' understanding of the strong nuclear force that holds atomic nuclei together.

"The pentaquark is not just any new particle — it represents a way to aggregate quarks, namely the fundamental constituents of ordinary protons and neutrons, in a pattern that has never been observed before," he says. "Studying its properties may allow us to understand better how ordinary matter, the protons and neutrons from which we're all made, is constituted."

Protons and neutrons are made up of three kinds of quarks bound together, but theorists calculate that, in principle, particles could be made of up to five quarks. Such particles would be rich testing grounds for quantum chromodynamics (QCD) — the theory that describes the forces that hold quarks together.

In 2002, researchers at the SPring-8 synchrotron in Harima, Japan, caused a stir when they announced that they had discovered a pentaquark, roughly 1.5 times heavier than a proton, inferring its existence from the debris of collisions between high-energy photons and neutrons. Within a year, more than ten other labs had reported finding evidence for the particle by reanalysing data. But many others saw no evidence for such a state and, in 2005, ▶



Artist's impression of a pentaquark.

CERN

▶ the discovery was pronounced a mirage. The final straw came with an experiment at the Thomas Jefferson National Accelerator Facility in Newport News, Virginia, that repeated the SPring-8 measurement with more data and ruled out the pentaquark's existence.

The episode has been held up as an example of how scientists can be tricked by data into seeing more than is there. In 2008, the annual *Review of Particle Physics*[1] described the pentaquark as "a curious episode in the history of science", and its recent listings have no dedicated entry for the particle.

But the LHCb result leaves little doubt that pentaquarks are real, researchers say. Physicists saw a signal showing the unexpected appearance of two short-lived objects weighing 4.38 and 4.45 gigaelectronvolts (4.67 and 4.74 times heavier than a proton) during the decay of trillions of subatomic particles known as 'Lambda B' baryons, by analysing data from 2009–12.

After exhausting other known particles as candidates, the team concluded that the new objects correspond to a pentaquark in two different configurations. The particle contains two 'up' quarks, a 'down' quark, and a 'charm' quark–antiquark pair, making it a 'charmonium' pentaquark. A preprint on the find was posted on the arXiv server on 14 July[2], and has been submitted for publication in *Physics Review Letters*. "It's about the most exciting discovery in QCD I could imagine," says Frank Wilczek, one of the original architects of QCD, at the Massachusetts Institute of Technology.

The result, which first caught the attention of physicists on LHCb in 2012 as a bump in their data, was a total surprise, says LHCb's Sheldon Stone, at Syracuse University in New York. "In the old days we searched for new particles by bump-hunting, but in this case the bump found us!" he says. "For historical reasons we were quite haunted by the word pentaquark, so we did every conceivable check we could," he says. The LHCb team says that there is a vanishingly small chance of the signal appearing if no new particles existed. Their statistical bar — known as 9-sigma — is higher than the 5-sigma usually required for a discovery in particle physics.

"If I have an immediate feeling of worry it is that they claim two states: is this because they have found a process that favours production of pentaquarks, or because they have not really found the best interpretation of the data?" says theorist Frank Close, of the University of Oxford, UK.

The new pentaquark is not the one, known as the theta+, seen back in 2002: it is almost three times heavier, and contains different kinds of quarks. "I think our result will energize the search for many different pentaquark states, including the debunked theta+," says Stone. ■

1. Particle Data Group. *Phys. Lett. B* **667,** 1061–1206 (2008).
2. LHCb collaboration. Preprint at http://arxiv.org/abs/1507.03414 (2015).

PSYCHIATRY

First robust genetic links to depression emerge

Discoveries energize hunt for genes connected to mental illness.

BY HEIDI LEDFORD

No one was more surprised than Jonathan Flint when his project — an effort to find genetic sequences linked to depression — showed the first hint of success 18 months ago. He knew the odds were slim: a study of 9,000 people with major depressive disorder had come up empty[1], and Flint had heard rumours that a follow-up analysis of 17,000 people had also met with disappointment. "I thought, 'There's no way,'" says the geneticist from the University of Oxford, UK, whose study had by that point analysed only 5,303 people with depression.

Flint has proved himself wrong. In *Nature* this week, his team reports[2] the first two genetic markers reproducibly linked to major depressive disorder, one of the leading causes of disability globally. The findings could guide biologists to new drugs, and could one day be used to aid diagnosis. But many in the field are excited that the markers have been unearthed at all. The results look set to end years of debate over whether sequences for such a complex disorder could be found — and Flint's study may serve as a framework for future attempts to collect data from tens of thousands of people.

More than 350 million people have depression. The disorder's symptoms and severity can vary widely from one person to the next, and particularly between men and women. This suggests that different conditions have been lumped together into one diagnosis, complicating genetic analyses (see *Nature* **515,** 182–184; 2014).

The few hits from early studies attempting to find genetic sequences linked to depression had disappeared on closer scrutiny, so Flint knew that he would need samples from thousands of people, and a way to reduce the variability in their illness. Flint and Kenneth Kindler, a psychiatrist at Virginia Commonwealth University in Richmond who is renowned for his diagnostic prowess, decided to do the study in China, because of its large population and because depression is believed to be under-diagnosed there. In that climate, Flint reasoned, those who are diagnosed are likely to share a severe form of the disorder. To reduce the variability further, his team also limited the study to women of Han Chinese ethnicity.

By early 2014, Flint, Kindler and a team of collaborators had analysed DNA sequences from 5,303 Chinese women with depression, and another 5,337 controls. As Flint expected, 85% of the depressed women had a severe form of the disorder called melancholia, which robs people of the ability to feel joy. "You can be a doting grandparent and your favourite grandchildren can show up at your door," says Douglas Levinson, a psychiatrist at Stanford University in California, "and you can't feel anything."

The analysis yielded two genetic sequences that seemed to be linked to depression: one in a stretch of DNA that codes for an enzyme whose function is not fully understood, and the other next to the gene *SIRT1*, which is important for energy-producing cell structures called mitochondria. The correlations were confirmed in another set of more than 3,000 depressed men and women and over 3,000 controls.

The mitochondrial connection chimes with previous work, including some from Flint's lab[3], that has linked mitochondrial abnormalities to