at the Sapienza University of Rome.

The new particle has also been vouched for by a second experiment, the Beijing Spectrometer III (BESIII) at the Beijing Electron Positron Collider. BESIII found 307 $Z_c(3900)$ particles, sifted from 10 trillion trillion electron-positron collisions².

"This gives credence to all of the other particles that Belle has seen," says Fred Harris, a particle physicist at the University of Hawaii in Manoa and a spokesman for BESIII. In 2008, Belle found another four-quark candidate³, and in 2011, it saw two other particles that may have been made of four 'bottom' quarks⁴ — but no other particle colliders have confirmed those sightings.

No one questions the number of quarks in the latest particle. More controversial is their arrangement, which could have implications for quantum chromodynamics, the theory describing the strong force that connects quarks. Theorists fall primarily into two camps.

One side proposes that the particle is actually a union of two ordinary particles called mesons, which contain one quark and one antiquark. $Z_c(3900)$ particles could be made up of two mesons joined by a loose connection to form a molecule-like structure (see 'Quark soup').

Other theorists have tentatively labelled the new particle a true tetraquark — four quarks stuck together tightly to form a compact ball. Within the ball, two quarks are bound together, as are two antiquarks. Such pairings do not occur in any known particle and would thus introduce new building blocks of matter — with the potential to guide computer simulations aimed at working out all the structures that quarks can form.

Proponents of the tetraquark theory point out that a 'molecule' made of mesons should split easily into two halves, and that such a breakdown has not appeared in the data. "The signature of a molecule is not seen, which favours the tetraquark picture," says Ahmed Ali, a particle physicist at DESY, Germany's high-energy physics laboratory in Hamburg. But the experiments' margin of error is still too great to rule out the possibility of molecular mesons breaking down. Another way to test the two theories would be to look for other particles that each predicts should exist.

Hoping to end the debate, researchers at BESIII are continuing to dig through data collected since their first experimental run in December and January. Depending on what they find, the unmasking of $Z_c(3900)$ may have to wait for the new, more powerful version of the Belle detector planned to come online in 2015. ■

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BIOTECHNOLOGY

Myriad ruling causes confusion

Change to gene patents leaves US biotech in a lather.

BY HEIDI LEDFORD

There was a party waiting for Elizabeth Chao when she arrived for work last week at Ambry Genetics, a medical-diagnostics company in Aliso Viejo, California. On 13 June, the US Supreme Court ended the 30-year-old practice of awarding patents on human genes — an outcome that Chao, a geneticist and chief medical officer of Ambry, had wanted for a long time. "It's such a win for patients," says Chao. "Everyone was crying, jumping up and down and shouting."

In Washington DC at law firm Sughrue Mion, patent lawyer William Simmons was having a rather different day, fielding phone calls from agitated clients in the US biotechnology industry. Although the Supreme Court case was limited to human DNA, the ruling will probably be applied to other molecules such as proteins, as well as to other organisms — including agriculturally important plants. "It's a mess," says Simmons. "We had a lot of clients saying, 'What are we going to do?'"

The Supreme Court decision ended a long-running, emotionally charged legal challenge to gene patents held by Myriad

Genetics, a genetic-testing company in Salt Lake City, Utah, on two cancer-associated genes: *BRCA1* and *BRCA2*. The court's first point rang clear — that naturally occurring human genes cannot be patented — and seems poised to broaden the genetic-testing market (see 'Competitors stake their claims').

Yet the grey area between this ruling and the court's second point — that patents can be claimed on modified DNA — has puzzled observers. Gene patent holders, including Myriad, had long argued that the mere act of isolating a piece of DNA from a genome was enough modification for a patent claim, because isolation requires severing the chemical bonds that tether the gene to its surroundings. The Supreme Court justices — and many scientists — disagreed. But patent lawyers are now tearing their hair out over the issue of how much modification is enough. "They've created this bizarre rheostat about the amount of change that would need to take place chemically in order to justify a patent," says Simmons.

Some of the confusion stems from how the Supreme Court justices defined the term synthetic DNA. The court seemed to use it to refer to DNA that had been modified ►

GENE TESTING

Competitors stake their claims

Despite the US Supreme Court decision, Myriad Genetics still has more than 500 claims covering its tests for breast-cancer genes. This reassured investors, and its stock price soared (see 'Patently unclear').

But the price later slumped as firms including California's Ambry Genetics and Quest Diagnostics in Madison, New Jersey, said that they plan to launch their own tests. Myriad's test costs US\$4,000, but competitors' tests could cost half that.

Some lawyers say that firms are risking lawsuits by infringing Myriad's patents, but others think that the competitors could design genetic tests that avoid the remaining narrow claims. Any lawsuits could last for years — by which time many of Myriad's patents will have expired. **H.L.**

PATENTLY UNCLEAR

The stock price for Myriad Genetics initially rose after the US Supreme Court ruled against five of its human gene patents, but has since fallen.

► by the inventor. It also gave explicit patent protection to a modified form of DNA called complementary DNA (cDNA), which is made in the lab with an enzyme that creates DNA using an RNA template. Patents on cDNA are deemed more commercially valuable than patents on naturally occurring genes, in part because cDNA tends to be shorter and easier to work with in the lab than genes in their natural state. It can also be used for diagnostic tests if the mutations of interest are contained within the RNA template, as is often the case. But patents on cDNAs, at least for known genes, are largely a dying breed because making cDNA is a common practice that would be considered too obvious for a robust patent.

Increasingly, scientists define synthetic DNA as that which has been made from scratch by assembling the individual bases of DNA into a given sequence, often using machines. And the justices did not say whether synthetic DNA of this sort could be patentable if it exactly copied a naturally occurring sequence.

Lawyer Patrick Waller, of Boston firm Wolf Greenfield in Massachusetts, says that the decision could jeopardize patents on short stretches of synthetic DNA that are used to check whether the genome contains certain sequences, or to create multiple copies of particular DNA regions.

These issues now fall to the lower courts and to patent examiners who must interpret the Supreme Court opinion. Shortly after the decision was issued, Andrew Hirshfeld, a deputy commissioner at the US Patent and Trademark Office in Alexandria, Virginia, issued a memo suggesting that such patents would no longer be granted. That memo, intended to serve as interim guidance until the office updates its policies to incorporate the new ruling, is a sign that the patent office will be interpreting the Myriad decision strictly, says David Berry, a professor of intellectual-property law at the Thomas M. Cooley Law School in Lansing, Michigan. “Companies are just going to have to think up different approaches to claiming their inventions,” he says.

Biotech companies might already be changing their approach. Simmons now tells clients to protect certain inventions as trade secrets, which are not publicly disclosed, rather than as patents. After the Myriad decision, he says, he may also instruct clients to introduce many modifications to the DNA or proteins they intend to patent, to make them as different as possible from naturally occurring forms.

“There’s no guidance here as to what is a sufficient amount of change to warrant a patent,” says Simmons. “It’s insane.” ■
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LES HIRONDELLES/FLICKR/GETTY

The issue of when or where canines were domesticated has geneticists in a tug of war.

EVOLUTION

Dog genetics spur scientific spat

Researchers disagree over canine domestication.

BY EWEN CALLAWAY

Scientists investigating the transformation of wolves into dogs are behaving a bit like the animals they study, as disputes roil among those using genetics to understand dog domestication.

In recent months, three international teams have published papers comparing the genomes of dogs and wolves. On some matters — such as the types of genetic changes that make the two differ — the researchers are more or less in agreement. Yet the teams have all arrived at wildly different conclusions about the timing, location and basis for the reinvention of ferocious wolves as placid pooches. “It’s a sexy field,” says Greger Larson, an archaeogeneticist at the University of Durham, UK. He has won a £950,000 (US\$1.5-million) grant to study dog domestication starting in October. “You’ve got a lot of big personalities, a lot of money, and people who want to get their *Nature* paper first.”

In January, Erik Axelsson and Kerstin Lindblad-Toh, geneticists at Uppsala University in Sweden, and their colleagues reported in *Nature*¹ that genes involved in the breaking down of starch seemed to set domestic dogs apart from wild wolves. In the paper and in media interviews, the researchers argued that dog domestication was catalysed by the dawn

of agriculture around 10,000 years ago in the Middle East, as wolves began to loiter around human settlements and rubbish heaps (see *Nature* <http://doi.org/mv4>; 2013).

But Larson, who has worked with Lindblad-Toh on other projects, says that their claim is dubious. He notes that bones that look similar to those of domestic dogs predate the Neolithic revolution by at least several thousand years, so domestication must have occurred before then. “Why waste space [in a paper] saying something that is patently untrue?” he says.

Axelsson concedes that the changes in starch digestion in dogs could have occurred after they were domesticated. But he also counters that the Neolithic era lasted for thousands of years, and that dogs may have been domesticated during the earliest steps towards agrarian life — when human hunter-gatherers settled down and began eating more starch-rich wild plants.

A second study, published last month in *Nature Communications*², argues that dogs were domesticated 32,000 years ago when they began scavenging with Palaeolithic humans in southern China. A team led by Ya-ping Zhang at the Kunming Institute of Zoology in China drew that conclusion from studying the whole genomes of several grey wolves, modern European dog breeds and indigenous Chinese dogs.

But Larson says that there is no evidence to