DANA VERKOUTEREN

The 6 December hearing was the first and only time that the two sides will speak to the judges before the court rules on the patent rights. An hour before the hearing began, the line of people waiting to watch the arguments wrapped around the Christmas tree in the lobby of the USPTO and filled two overflow rooms. Each side's lawyer had only 20 minutes to present his case to the three judges.

During the hearing, the Broad's lawyer quoted liberally from news articles and interviews in which Doudna said that her lab had struggled to adapt CRISPR–Cas9 to eukaryotic cells. "This is the antithesis of something that would have been obvious," said the Broad's lawyer, Steven Trybus.

Berkeley's lawyer Todd Walters downplayed these difficulties, saying that Doudna did not immediately publish CRISPR–Cas9 to edit eukaryotic cells because she knew it would work. Once the technology's ability to edit DNA had been proven, he told the judges, "the only thing left was to do it".

A QUESTION OF INTENT

But the judges seemed to disagree, and grilled Walters far harder than they did Trybus, who represented the Broad. "I'm not buying that everyone who does an experiment believes it would work," said Judge Richard Schafer. Rather, he added, a scientist such as Doudna may simply hope that her research will succeed.

This exchange suggests that Berkeley will have a hard time convincing the court that Doudna expected CRISPR–Cas9 to work in eukaryotes, Sherkow says. The university's lawyers "were trying to clarify what a biologist in 2012 would have contemplated", he notes.

But biochemist Dana Carroll of the University of Utah in Salt Lake City, who wrote a declaration to the court on Berkeley's behalf, disagrees. "To embark on a project takes a certain amount of time, effort and money," he says. "I don't think you'd do that unless you had some expectation of success." He points out that several other groups began working on CRISPR–Cas9 in eukaryotes at the same time as Zhang did.

Several experts who watched the proceedings say that the Broad's prospects look brighter now, given the judges' heavy questioning of Berkeley's lawyer. "My impression is both will end up with something," says legal scholar Robert Cook-Deegan of Arizona State University's campus in Washington DC.

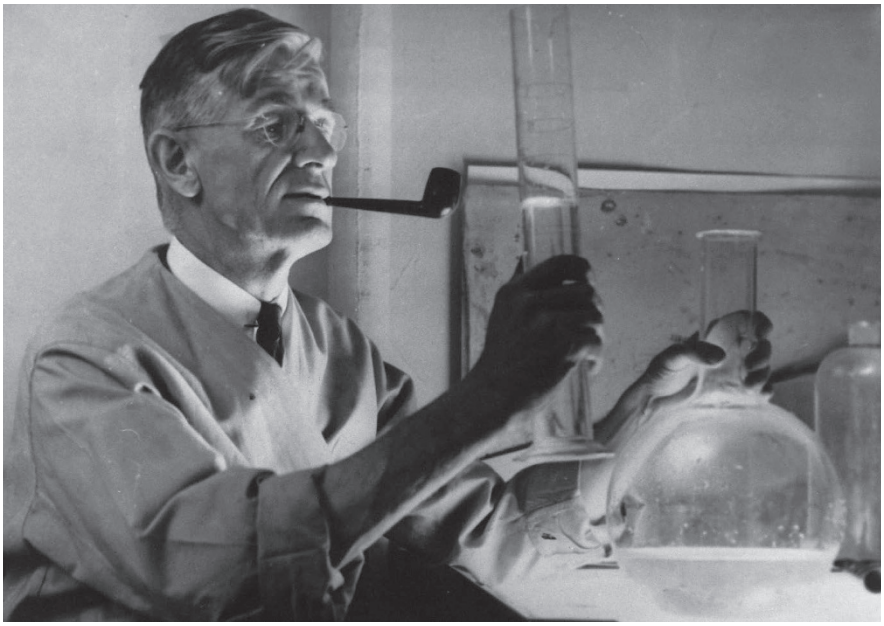
The Broad has hedged its bets by filing 13 patents related to CRISPR. Several of these deal with an alternative CRISPR system in which the DNA-cutting enzyme is taken from a different species of bacteria. Because it was developed independently, Sherkow doubts that Berkeley could claim any rights to it.

He expects that the USPTO will decide the case in the next two months, although there is no deadline by which it must do so. ■

POLICY

Top US science job still in question

President-elect Donald Trump has given no clues as to whether he will appoint a science adviser.



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Electrical engineer Vannevar Bush became the first US presidential science adviser in the 1940s.

BY ALEXANDRA WITZE

US president-elect Donald Trump has chosen people for key jobs overseeing national security, defence and environmental policy. But he has not addressed whether he will fill the most important job in US science: presidential science adviser.

Historically, many incoming presidents — who are elected in November — have designated a science adviser in December, as they move to the White House. But Trump's transition team has not contacted the White House Office of Science and Technology Policy (OSTP), which the science adviser leads, to discuss the changeover. Many researchers worry that if Trump does not pick an adviser soon, science will have a much weaker voice during the next four years.

"I have some questions as to whether Trump is going to want a science adviser at all," says Albert Teich, a science-policy expert at George Washington University in Washington DC. "He doesn't like briefings, he doesn't like to listen to people. I can't imagine that whoever he appoints would have a very influential position."

Still, some of Trump's earliest moves as president may involve scientific topics. He has said that on his first day in office, 20 January, he will repeal many of the executive orders that Barack Obama has used to set policy — including those on energy and climate.

Getting a science adviser in place early would help Trump to understand the scientific implications of such issues, says Neal Lane, a physicist at Rice University in Houston, Texas, who advised President Bill Clinton from 1998 to 2001. "The president could make really good use of advice from someone he has chosen who's knowledgeable about science and technology," Lane says.

"I can't imagine that whoever he appoints would have a very influential position."

Given Trump's lack of ties to the academic or scientific communities, some speculate that he will seek technical advice from business or high-tech leaders. His transition team includes Silicon Valley billionaire Peter Thiel, who — among other things ▶

— funds a fellowship for young adults to bypass college and develop business ventures. "We're going to have a whole new set of people in Washington," says Deborah Stine, a science-policy expert at Carnegie Mellon University in Pittsburgh, Pennsylvania, who served in the Obama White House for three years.

Trump may also prove open to arguments about how research can strengthen US competitiveness. Stine points to an influential report released in 2005, during George W. Bush's administration, that described the importance of research to the national economy. Put together by a committee led by aerospace chief executive Norman Augustine, the analysis helped shape bipartisan legislation to support innovation — with strong backing from the White House.

Being named early in a president's administration increases the chance that a science adviser can influence who will lead science agencies, and other key decisions. Presidents Clinton and Obama both chose their advisers the month after they were elected. But George W. Bush took seven months to pick physicist John Marburger. (Every presidential science adviser has been male, and most have been physicists.) By the time Marburger started the job, the Bush administration had made several crucial science-related announcements, such as restricting funding for research with human embryonic stem cells.

Many scientists criticized Marburger for serving in what some called an anti-science administration. But the adviser's job is to provide technical input into policy decisions, not to make them, says Roger Pielke Jr, a science-policy expert at the University of Colorado Boulder. "The science adviser is not a philosopher-king," he says.

Although the OSTP is codified in law, the president does not have to make use of it. Several members of Trump's transition team came from the Heritage Foundation, a conservative think tank in Washington DC that issued a policy paper in June suggesting that the office be eliminated to reduce bureaucracy.

Only Congress could shrink or eliminate the OSTP. Doing so would hurt US science, says Rosina Bierbaum, an environmental scientist who headed the office for eight months in 2001 until Marburger took over. That's because it coordinates funding for science across government agencies, and is the main entity looking for redundancies and gaps in those portfolios.

Wherever it comes from, science advice in the Trump administration will be crucial, says Lewis Branscomb, a physicist who has served in various presidential advisory groups stretching back to 1964. "The new president is going to need all the help he can get — that he will take." ■

DRUG DEVELOPMENT

Programs face off in cancer contest

Predictive algorithms may help to whittle down the possible candidates for personalized cancer vaccines.

BY HEIDI LEDFORD

Could predictive algorithms be the key to creating a successful cancer vaccine? Two US nonprofit organizations plan to find out by pitting a range of computer programs against each other to see which can best predict a candidate for a personalized vaccine from a patient's tumour DNA.

The Parker Institute for Cancer Immunotherapy in San Francisco, California, and the Cancer Research Institute of New York City announced the algorithmic battle on 1 December. It is part of a multimillion-dollar joint project to solve a major puzzle in the nascent field of cancer immunotherapy: which of a patient's sometimes hundreds of cancer mutations could serve as a call-to-arms for their immune system to attack their tumours.

If the effort succeeds, it could spur the development of personalized cancer vaccines that use fragments of these mutated proteins to fire up the body's natural immune responses to them. Because these mutations are found in cancer cells and not healthy ones, the hope is that this would provide a non-toxic way to battle tumours.

The idea is gaining traction. In 2014, news that vaccines containing such mutated proteins had vanquished tumours in mice set off a mad dash to find out whether the approach would work in people. A generation of biotechnology companies has been founded around the concept, and clinical trials run by academic labs are under way.

Still, a challenge remains. To be a good candidate for a vaccine, a mutated cancer protein must be visible to T cells, the soldiers of the immune system. And for that to happen, tumour cells must chew up the protein into fragments. Those fragments then must bind to specialized proteins, which are shipped to the cell's surface to be displayed to passing T cells.

The trick that vaccine researchers must master is using a tumour's DNA to predict which mutations to home in on. "We can do the sequencing and find out the mutations, but it's very hard to know which of these tens or hundreds or thousands of mutations are actually going to protect people from the growth of their cancers," says Pramod Srivastava, an immunologist at the University of Connecticut School of Medicine in Farmington.

One approach is to use algorithms to predict which bits of a mutated protein might be seen by a T cell. These work by analysing where the proteins could be cleaved, for example, and which of the resulting fragments will bind tightly to the molecules that put them on display.

"It's very hard to know which of these tens or hundreds or thousands of mutations are actually going to protect people."

But each laboratory has a different "secret sauce", says Robert Schreiber, a cancer immunologist at Washington University in St. Louis, Missouri. And most are not very predictive: Robert Petit, chief scientific officer of biotechnology company Advaxis in Princeton, New Jersey, estimates that the algorithms are typically less than 40% accurate.

To solve the problem, the Parker Institute and the Cancer Research Institute launched their challenge. They have arranged for

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