

News in focus

That need not delay the progress of the therapies, says analyst Geulah Livshits at Chardan, a health-care investment bank in New York City. Two companies have claimed patent rights to the lipid nanoparticle that Moderna Therapeutics in Cambridge used to encase its mRNA-based COVID-19 vaccine. But that ongoing dispute did not keep the vaccine from reaching the market, Livshits notes.

The CRISPR–Cas9 patent landscape remains unclear, she adds. CVC might appeal against the USPTO's decision in a federal patent court, but the case is unlikely to go all the way to the US Supreme Court, says Kevin Noonan, chair of the biotechnology and pharmaceuticals group at the law firm McDonnell Boehnen Hulbert & Berghoff in Chicago, Illinois. "There's no big policy question here for the court to address," he says.

It's also possible that neither CVC nor the Broad will reap the rewards of the foundational CRISPR–Cas9 patents. Both are facing challenges on these patents from two other companies: ToolGen in Seoul and Sigma-Aldrich, now owned by Merck in Darmstadt, Germany.

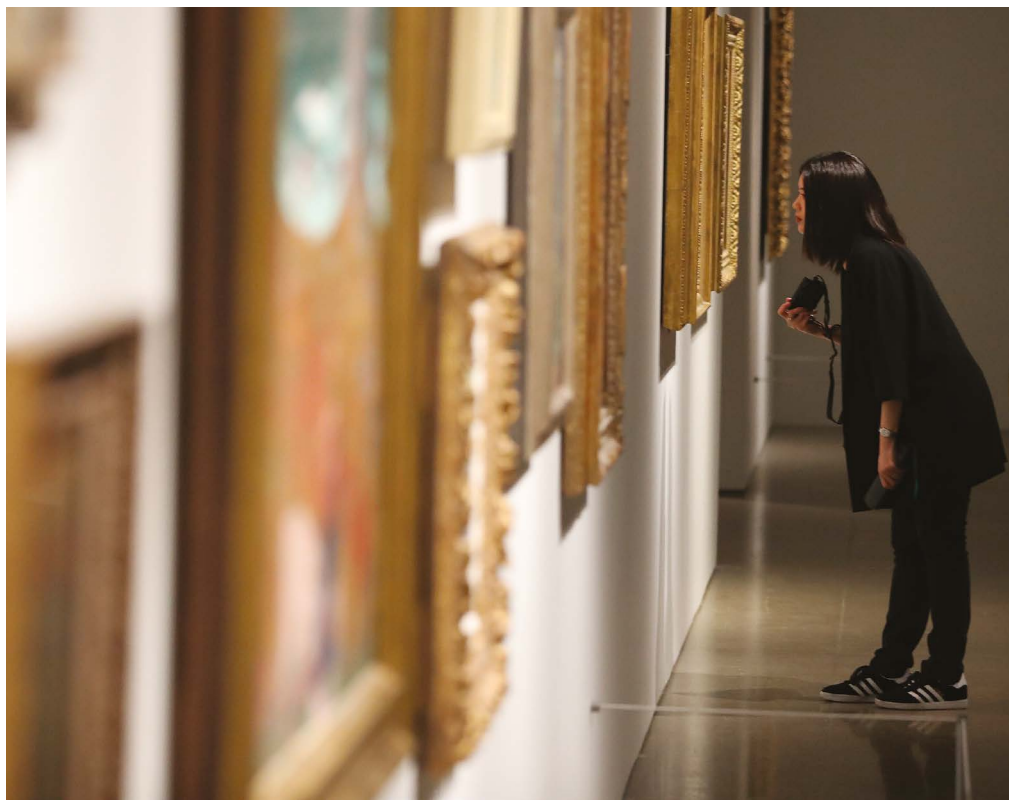
And in the European Union, the key CRISPR–Cas9 patents in the Broad's portfolio have been tossed out altogether owing to missing paperwork. In the course of finalizing its patents, the Broad team decided to drop one of its inventors from the filings – but neglected to get written approval from him, a requirement in the EU system. As a result, CVC has the upper hand in Europe. "Europe's gone in a completely different direction to the US," says Coombes, "which makes things interesting from a licensing perspective."

Gene-editing alternatives

Companies now also have the option of avoiding these patents altogether by using different CRISPR systems. Such systems occur naturally in many bacteria and archaea, and can have various properties. Over the past two years, says Fabien Palazzoli, a senior patent analyst at Centredoc, there has been a dramatic increase in the number of patent applications claiming new diagnostic tests for viruses and bacteria, possibly spurred by the COVID-19 pandemic.

Relatively few of these use CRISPR–Cas9, he says; instead, they use alternative enzymes such as Cas13, or Cas14, which is remarkably small and easy to transport into human cells. Labs have also engineered new CRISPR-associated enzymes, such as base editors, that are better able to make specific edits. Patent filings on base editors are doubling every year, Palazzoli says, and now exceed 730.

Against the backdrop of so much activity, it will be years until it becomes clear how much the original CVC and Broad patents are worth, says Coombes. "I don't think CRISPR–Cas9 is the be all and end all," she says. "There's still a lot up for grabs."



Forged artwork could pollute humanity's understanding of history, researchers say.

RADIOCARBON DATING HELPS POLICE IDENTIFY FORGED PAINTINGS

Advances in the technique have bolstered its reputation as a tool for investigating faked artwork.

By Carolyn Wilke

Radiocarbon dating has unmasked two forged paintings in France – probably the first time the technique has been used in a police investigation. The paintings were supposedly impressionist and pointillist works from around the early twentieth century. But a team led by heritage scientist Lucile Beck at the University of Paris-Saclay used radiocarbon levels in the fibres of their canvases to date them to sometime within the past 70 years. The researchers concluded that the paintings are modern forgeries in a 4 February report published in *Forensic Science International*¹.

The use of radiocarbon dating is gaining steam in the forensic analysis of artwork, thanks to advances that require smaller samples than ever before. Removing tinier samples from artwork is more palatable to auction houses, museums and owners of paintings. If there is a chance a painting is genuine

– and therefore valuable – they don't want the collection of larger samples to damage it, says art historian Anna Tummers at Leiden University in the Netherlands, who was not part of the new research.

The technique's success might persuade more of the art world to seek radiocarbon dates, which can more definitively pinpoint when a painting was made, Tummers says. Researchers typically use imaging and chemical analysis to sniff out art forgeries. These methods can peer beneath brushstrokes to see how a painting's materials have aged, but they cannot conclusively nail down a painting's date.

The consequences of faked artwork extend beyond forgers lining their pockets in the global art market, which moves tens of billions of dollars every year. Forgeries pollute people's understanding of artworks' meaning, Tummers says. "If we don't weed them out carefully, it might really distort our understanding of our own heritage and our

STEVE RUSSELL/TORONTO STAR/GETTY

own history.”

The two paintings were part of a trove of artwork that French investigators uncovered in a restorer’s workshop in 2019. Of some 600 paintings, dozens appeared to be mid-level masterpieces from the late nineteenth and early twentieth century. But experts questioned the works’ authenticity because the paint seemed relatively fresh.

To investigate the potential forgeries, the French government’s Central Office for the Fight against Illicit Trafficking in Cultural Property (OCBC) called on Beck. Her team selected a few works, including an impressionist garden scene and a pointillist port landscape, to test. At the OCBC office, the researchers used scalpels to remove samples, including a small bit of fibre from the canvases.

Advances in the field

All living things take in carbon, including radioactive carbon-14, from the atmosphere and from food. When a plant – such as linen or hemp, commonly used to make canvas – dies, the carbon-14 that it incorporated continues to decay. Radiocarbon dating measures what’s left to estimate the time that’s passed, says Mariaelena Fedi, a physicist at the National Institute for Nuclear Physics in Florence, Italy. The technique gives an absolute earliest date of an artwork, because there could be years between harvesting linen for a canvas and making the painting.

Atomic-bomb testing, which began in the 1940s and took off in the 1950s, bumped up the amount of carbon-14 in the atmosphere beyond naturally produced levels. Carbon-14 peaked around 1964 and tailed off after a partial ban on nuclear tests. Researchers can easily identify materials containing modern bomb-derived radiocarbon because their carbon-14 concentrations are higher than pre-1950s levels.

Beck’s team tested its samples to see whether they bore the signature of that bomb-derived radioactive carbon-14. In the laboratory, the researchers cleaned and dried the material, whittling down several milligrams into around one milligram of carbon that was pressed into a graphite puck to be measured with accelerator mass spectrometry.

The canvas fibres from both the impressionist and pointillist paintings clearly contained carbon from either the mid-1950s or after the year 2000, the researchers reported. (This is because the carbon-14 concentrations they measured could correspond to either side of the atomic bomb peak.) Another fibre, plucked from the varnish of the pointillist painting and perhaps coming from a brush, also dated to after 1950. Beck acknowledges that, ideally, the team would do further chemical analysis to support its findings, but the researchers were limited by the tight time frame of the investigation.



Beck’s team removed a fibre from the canvas to test the painting’s authenticity.

L. BECK

Although this seems to be the first report of using radiocarbon dating to identify faked artwork in a police investigation, researchers have been laying the groundwork for the past decade.

Fedi and her colleagues made the first report of radiocarbon dating to detect a forged painting in the Peggy Guggenheim Collection in Venice, Italy, in 2014. The team collected snippets of the canvas and dated them to after the presumed artist’s death – concluding that the painting had been forged².

In 2019, Laura Hendriks and colleagues used a known forgery of a village scene to test a radiocarbon dating method that used a much smaller sample size than previous techniques. Hendriks, a chemist at the University of Applied Sciences and Arts of Western

Switzerland in Fribourg, converted a sample of the scene’s oil paint to carbon-dioxide gas before introducing it to the mass spectrometer. The team was able to date the forgery using only micrograms collected from the painting³. The tiny sample was “just a few crumbs of dust, basically”, Hendriks says.

Such advances are good news for the field. There’s a huge need for objective tools to suss out fakes, Fedi says, and radiocarbon dating is excellent when combined with other methods and the expertise of art scholars who can help to interpret the history of these complex objects.

1. Beck, L. et al. *Forensic Sci. Int.* **333**, 112124 (2022).
2. Caforio, L. et al. *Europ. Phys. J. Plus* **129**, 6 (2014).
3. Hendriks, L. et al. *Proc. Natl Acad. Sci. USA* **116**, 27 (2019).

RESEARCHGATE DEALT A BLOW IN COPYRIGHT LAWSUIT

Court ruling says that the academic-networking website is responsible for uploaded papers.

By Diana Kwon

A landmark court case in which two major academic publishers sued the popular website ResearchGate for hosting 50 of their copyrighted papers has come to a close – although both sides say that they will appeal. The court in Munich, Germany, has not only

prohibited ResearchGate from hosting the papers, but also ruled that it is responsible for copyright-infringing content uploaded on its platform. The decision has the potential to set a precedent for further restrictions on the site, which has 20 million users worldwide.

Neither side emerged a clear winner in this case, says Nancy Sims, a librarian at the University of Minnesota in Minneapolis who