revived the E word in 2007, it didn't mention a deadline. Bill Gates later said it would take "multiple decades" and acknowledged it was "dangerous" to set unattainable goals (*Science*, 7 December 2007, p. 1544). Still, Margaret Chan, then WHO's director, pledged the agency's support, and the eradication goal began to shape policy and research.

But Alonso thought the feasibility of eradication needed a closer look, and in 2016 he convened SAGme and asked Marcel Tanner, a former director of the Swiss Tropical and Public Health Institute in Basel, to lead the panel. Its report, which partly relied on modeling by a team at the University of Oxford in the United Kingdom, says eradication is still a long-term goal worth pursuing, and that time is on humanity's side: Megatrends such as socio-economic development, urbanization, and climate change—which can influence transmission by changing temperature, humidity, and rainfall—will all help drive down malaria incidence. But it concludes that even in the rosiest of scenarios there will still be 11 million cases in 2050.

The *Lancet* panel used models from the same Oxford group and will concur with many of SAGme's findings, Dondorp says. But he and others argue that the Gates Foundation's embrace of eradication reinvigorated malaria research, attracted money, and boosted control efforts. That helped trigger a decadelong decline in cases, from an estimated 247 million in 2006 to 214 million in 2015. (The decline has flattened since then, however, and a WHO plan to reduce incidence by 40% between 2015 and 2020 is badly off track.)

Whether the *Lancet* commission's 2050 target could deliver a similar boost is unclear; 2050 is so distant that "it's not really a target at all," says William Moss, a malaria researcher at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. He notes that other Gates-backed eradication campaigns, such as those for polio and Guinea worm, have repeatedly missed deadlines. "What you end up with," he says, "is donor fatigue, public fatigue, and loss of political will and commitment."

How Bill and Melinda Gates feel about the rift is unclear. Philip Welkhoff, director for malaria at the Gates Foundation in Seattle, says he can't speak for the couple, but he is a member of SAGme and supports its conclusions. "My personal take is that the most effective goals are the ones that are in a 10- to 12-year time frame," he says. "That's where the energy should go." At the same time, he says, "Our leadership and myself are completely committed to carrying through all the way to eradication. We are in it for the long haul." ■

Ancient people apparently followed rivers more than 500 kilometers inland to Cooper's Ferry in western Idaho.

ARCHAEOLOGY

# *Ancient site in Idaho implies first Americans came by sea*

## 16,000-year-old occupation predates possible land route

*By* **Lizzie Wade**

About 16,000 years ago, on the banks of a river in western Idaho, people kindled fires, shaped stone blades and spearpoints, and butchered large mammals. All were routine activities in prehistory, but their legacy today is anything but. The charcoal and bone left at that ancient site, now called Cooper's Ferry, are some 16,000 years old—the oldest radiocarbon-dated record of human presence in North America, according to work reported on p. 891.

The findings do more than add a few centuries to the timeline of people in the Americas. They also shore up a new picture of how humans first arrived, by showing that people lived at Cooper's Ferry more than 1 millennium before melting glaciers opened an ice-free corridor through Canada about 14,800 years ago. That implies the first people in the Americas must have come by sea, moving rapidly down the Pacific coast and up rivers. The dates from Cooper's Ferry "fit really nicely with the [coastal] model that we're increasingly getting a consensus on from genetics and archaeology," says Jennifer Raff, a geneticist at the University of Kansas in Lawrence who studies the peopling of the Americas.

A 6-centimeter blade is among the oldest at an Idaho site.

The Clovis people, big game hunters who made characteristic stone tools dated to about 13,000 years ago, were once thought to have been the first to reach the Americas, presumably through the ice-free corridor. But a handful of earlier sites have persuaded many researchers that the coastal route is more likely. Archaeologists have questioned the signs of occupation at some putative pre-Clovis sites, but the stone tools and dating at Cooper's Ferry pass the test with flying colors, says David Meltzer, an archaeologist at Southern Methodist University in Dallas, Texas. "It's pre-Clovis. I'm convinced."

Over 10 years of excavations, the Cooper's Ferry team uncovered dozens of stone spear points, blades, and multipurpose tools called bifaces, as well as hundreds of pieces of debris from their manufacture. Although the site is near the Salmon River, most of the ancient bones belonged to mammals, including extinct horses. The team also found a hearth and pits dug by the site's ancient residents, containing stone artifacts and animal bones.

Radiocarbon dates on the charcoal and bone are as old as 15,500 years. In North America, few tree ring records can precisely calibrate such early radiocarbon dates, but a state-of-the-art probabilistic model placed the start of the occupation at between 16,560 and 15,280 years. "I may not think it goes back to 16,000 years ago, but I surely can be-

PHOTOS: (TOP TO BOTTOM) LOREN DAVIS; L. DAVIS *ET AL.*, SCIE... (2019)





Corrected 30 August 2019. See full text.

lieve it goes back 15,000 years," says Michael Waters, an archaeologist at Texas A&M University in College Station.

The only rival to Cooper's Ferry as the oldest site in North America is the Gault site in Texas. Researchers dated that site to about 16,000 years ago by optical luminescence, a method with larger error bars than radiocarbon dating.

It's easy to see how seafaring people might have reached Cooper's Ferry, says Loren Davis, an archaeologist at Oregon State University in Corvallis who led the excavations. Although the site is more than 500 kilometers from the coast, the Salmon, Snake, and Columbia rivers link it to the sea. "As people come down the coast, the first left-hand turn to get south of the ice comes up the Columbia River Basin," Davis says. "It's the first off-ramp."

The area is now federal land but was long occupied by the Nez Perce Tribe, or the Niimíipuu. They know Cooper's Ferry as Nipéhe, an ancient village founded by a young couple after a flood destroyed their previous home, says Nakia Williamson, the tribe's director of cultural resources. "Our stories already tell us how long we've been here. … This [study] only reaffirms that," Williamson says. He hopes the excavations—in which Nez Perce archaeologists and interns participated—will help others recognize the deep ties the Nez Perce have to their ancestral lands. "This is not just something that happened 16,000 years ago. It's something that is still important to us today," he says.

Cooper's Ferry may also offer a glimpse of the tools carried by the first arrivals to the Americas. Many of the spearpoints found there belong to the western stemmed point tradition, smaller—about the size of a pinkie—and lighter than the hefty Clovis points. Such tools have been found at early sites from British Columbia to Peru, and as far inland as Texas. Similar points are known from Japan from about 16,000 to 13,000 years ago, Davis says. He and others argue that western stemmed points are emerging as the best markers of the first people to arrive in the Americas, and that they carried the tradition with them from Asia.

But Meltzer isn't convinced the western stemmed tradition conclusively predates Clovis or represents a coastal connection around the Pacific Rim. There are plenty of sites in Siberia in Russia without the technology, he says, and the complete points at Cooper's Ferry are almost the same age as Clovis. (The site's oldest tools are blades, bifaces, and fragments of points, fashioned with the same methods used to make western stemmed points.) Just as archaeology puts one debate about stone tools in the Americas to rest, it could be gearing up for the next one. ■

SYNTHETIC BIOLOGY

# *Modified CRISPR cuts and splices whole genomes*

## New tools bring editing to synthetic biology

*By* **Robert F. Service**

Imagine a word processor that allowed you to change letters or words but balked when you tried to cut or rearrange whole paragraphs. Biologists have faced such constraints for decades. They could add or disable genes in a cell or even—with the genome-editing technology CRISPR—make precise changes within genes. Those capabilities have led to recombinant DNA technology, genetically modified organisms, and gene therapies. But a long-sought goal remained out of reach: manipulating much larger chunks of chromosomes in *Escherichia coli*, the workhorse bacterium. Now, researchers report they've adapted CRISPR and combined it with other tools to cut and splice large genome fragments with ease.

"This new paper is incredibly exciting and a huge step forward for synthetic biology," says Anne Meyer, a synthetic biologist at the University of Rochester in New York who was not involved in the paper on p. 922. The technique will enable synthetic biologists to take on "grand challenges," she says, such as "writing of information to DNA and storing it in a bacterial genome or creating new hybrid bacterial species that can carry out novel [metabolic reactions] for biochemistry or materials production."

*"This new paper is incredibly exciting and a huge step forward for synthetic biology."*
**Anne Meyer**, University of Rochester

The tried and true tools of genetic engineering simply can't handle long stretches of DNA. Restriction enzymes, the standard tool for cutting DNA, can snip chunks of genetic material and join the ends to form small circular segments that can be moved out of one cell and into another. (Stretches of linear DNA don't survive long before other enzymes, called endonucleases, destroy them.) But the circles can accommodate at most a couple of hundred thousand bases, and synthetic biologists often want to move large segments of chromosomes containing multiple genes, which can be millions of bases long or more. "You can't get very large pieces of DNA in and out of cells," says Jason Chin, a synthetic biologist at the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, U.K.

What's more, those cutting and pasting tools can't be targeted precisely, and they leave unwanted DNA at the splicing sites—the equivalent of genetic scars. The errors build up as more changes are made. Another problem is that traditional editing tools can't faithfully glue large segments together. These issues can be a deal-breaker when biologists want to make hundreds or thousands of changes to an organism's genome, says Chang Liu, a synthetic biologist at the University of California, Irvine.

Now, Chin and his MRC colleagues report they have solved these problems. First, the team adapted CRISPR to precisely excise long stretches of DNA without leaving scars. They then altered another well-known tool, an enzyme called lambda red recombinase, so it could glue the ends of the original chromosome—minus the removed portion—back together, as well as fuse the ends of the removed portion. Both circular strands of DNA are protected from endonucleases. The technique can create different circular chromosome pairs in other cells, and researchers can then swap chromosomes at will, eventually inserting whatever chunk they choose into the original genome. "Now, I can make a series of changes in one segment and then another and combine them together. That's a big deal," Liu says.

The new tools will bolster industrial biotechnology by making it easier to vary the levels of proteins that microbes make, Liu and others say. They also promise an easy way to rewrite bacterial genomes wholesale, Meyer adds. One such project aims to alter genomes so they can code not just for proteins' normal 20 amino acids, but also for large numbers of nonnatural amino acids throughout the genome. That could lead to synthetic life forms capable of producing molecules far beyond the reach of natural organisms. ■





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Science

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