daring, swooping polar orbit around Jupiter on 4 July, was designed to avoid that problem. It will thread the gap between the radiation belts and the top of the atmosphere.

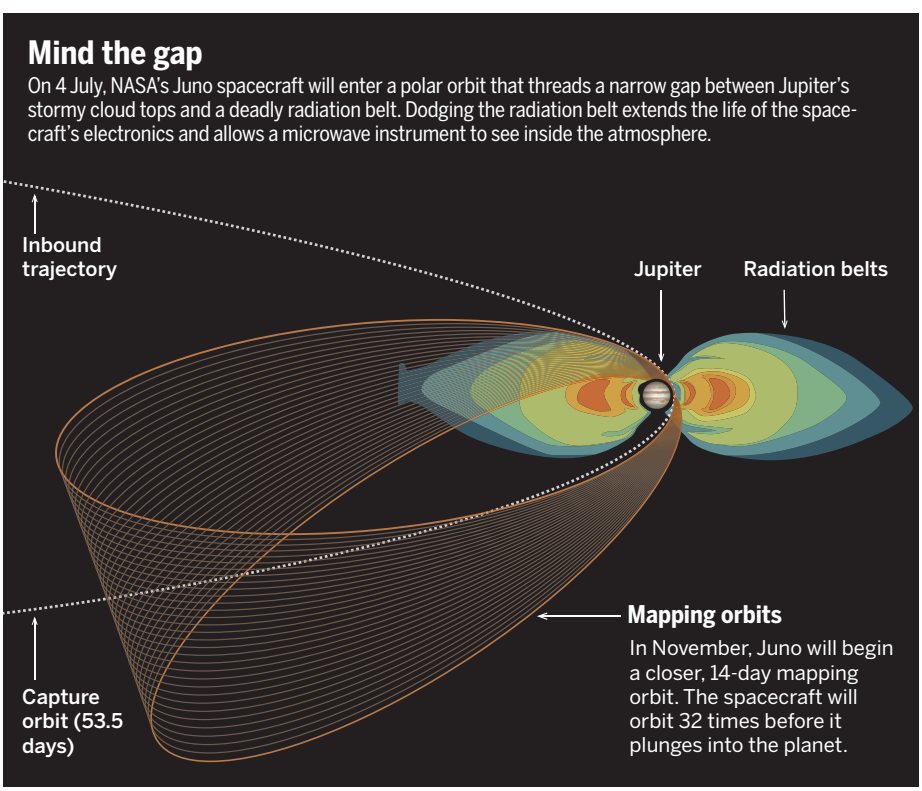
The special orbit will protect the spacecraft's electronics from frying—allowing for 32 14-day mapping orbits beginning in November—while giving the spacecraft's microwave detector an unobstructed view inside the atmosphere. "They're looking through a fog," says Juno principal investigator Scott Bolton of the Southwest Research Institute in San Antonio, Texas, of the VLA team's results. "We'll have a clean view."

Observing in microwave wavelengths, Juno should be able to see several hundred kilometers down, deep enough to spot a water layer that the Galileo probe didn't reach, Bolton says. Mapping that layer should reveal the roots of many structures high in the atmosphere, including the ammonia wave, along with Jupiter's zones, bands, and the famed Great Red Spot. Measuring the overall abundance of water in the atmosphere is also important for understanding the planet's formation. The water originally came from bits of ice that froze out of the protoplanetary disk of gas and dust. If Jupiter has roughly equal amounts of water and elements such as nitrogen and carbon, the planet must have formed farther out in a colder part of the solar system and later migrated inward. In such cold, nitrogen- and carbon-containing ices could freeze out alongside water ice and become part of the planet. But if water abundances are very high relative to nitrogen and carbon, Jupiter probably formed roughly where it is now: in a neighborhood too warm for the nitrogen and carbon to freeze out and stick to the growing planet.

There is another, long-shot possibility: Jupiter might really be as dry as Galileo said it was. If the probe's hot spot measurement holds for the rest of the atmosphere, "then we have a lot of explaining to do," says Amy Simon, a planetary scientist at Goddard Space Flight Center in Greenbelt, Maryland.

Juno will perform much more science. Some of its instruments will map the planet's radiation belts and magnetic fields. And by measuring the way Jupiter tugs on the spacecraft, scientists will make the most precise map ever of the planet's gravitational field—information that can be used to study Jupiter's deepest interior structure and perhaps answer the key question of whether it has a core. Many planet formation models suggest that Jupiter needed a rock-and-ice core of about 10 Earth masses for its gravity to capture hydrogen and helium in the protoplanetary disk before the sun dispersed the gases into space.

To supplement Juno's close-up view of its host planet, NASA has asked amateur astronomers to map Jupiter's visible surface throughout the mission. That will help scientists connect what lies beneath to what sits on top. ■



DEVELOPMENT

CRISPR views of embryos and cells

Genome editor helps record development, cell influences

By **Kai Kupferschmidt**

Alexander Schier simply wanted to make sure he destroyed a gene in zebrafish embryos. So, like many biologists these days, he turned to the genome-editing system called CRISPR. But Schier, a developmental biologist at Harvard University, ended up doing much more than knocking out a gene. He and colleagues devised a new way to trace cells in a developing animal. In its first test, described online last week in *Science*, they used CRISPR-induced mutations to reveal a surprise: Many tissues and organs in adult zebrafish form from just a few embryonic cells.

Other researchers are already looking to adapt the method to probe development. "The technique promises to allow the reconstruction of the 'family tree' of the cells that compose an animal's body," says James Briscoe, a developmental biologist at the Francis Crick Institute in London, who calls it "a creative and innovative use of [the] CRISPR technique." Some also intend to exploit the method to trace the evolution of tumors. And several groups are racing to develop similar ways of using CRISPR to record a cell's history—for example, its responses to environmental signals.

Schier and his colleagues took advantage of what Harvard geneticist George Church calls CRISPR's "genome vandalism." In its normal editing, a so-called guide RNA precisely targets the enzyme Cas9 to a particular site in the genome so that it can break the double-stranded DNA there. In one of CRISPR's original uses, a template DNA then tells the cell's machinery how to repair the double-stranded break, allowing edits as precise as the changing of a single nucleotide. But if scientists supply no template, the gene usually ends up with a "scar," where some nucleotides go missing or some are added that don't belong, that knocks out its function.

To make sure the zebrafish gene in his sights was truly obliterated, Schier targeted multiple sites within the gene by introducing several different guide RNAs without any re-

DIAGRAM: A. CUADRA/*SCIENCE*

pair templates. But repeating the experiment led to very different outcomes: The size of the deletions varied, and the scars included both small and large insertions. That destructive diversity could be put to use, Schier and geneticist Jay Shendure of the University of Washington, Seattle, realized.

In the genomes of zebrafish embryos, Schier and Shendure inserted a cassette of extra DNA, consisting of 10 different target sequences for CRISPR. Then they injected the single-celled embryos with the Cas9 enzyme and 10 guide RNAs that matched the target sequences. As the embryo developed, the CRISPR system repeatedly disrupted the target DNA in each cell, marking it with a pattern of deletions and insertions—a distinctive barcode. Whenever a cell divided, the daughter cells would start out with the same barcode and then diverge when Cas9 cleaved it at different places. The first changes in the barcode seem to happen in the two-cell stage, and then the editing machinery runs out of steam after about 4 hours, when the embryo consists of thousands of cells—after that point, the barcodes that remain will populate the adult animal as cells continue to multiply.

Four months later, the scientists collected organs from the adult fish and isolated more than 1000 different barcodes from about 200,000 cells. Cells with more similar barcodes are likely to have diverged later in development, so the scientists were able to use a computer program to calculate a family tree for the 200,000 cells—essentially a lineage map revealing which cells spawned others. "When you sacrifice the zebrafish at the end of the experiment you've actually got a full time readout of all the cells and where they came from," Church says.

One of the most striking findings was how few cells give rise to the bulk of the tissue in any given organ. More than half of the cells in most organs shared fewer than seven barcodes. In every organ except the brain, more than 90% of the cells had one of just 25 different barcodes. "Tissues may be founded by a much smaller group of cells than I would have anticipated," Briscoe says.

For developmental biologists, the new technique could help clarify how animals take shape from a single cell. It could also shed light on important questions in cancer research, such as how many precursor cells give rise to a tumor and how cancer cells that have spread are related to the initial tumor.

The technique has shortcomings, Schier says—for example, it does not reliably mark each new generation of cells. But compared with other ways of tracing cells and their progeny, like dyeing them or relying on natural mutations, a CRISPR-generated barcode is potentially more powerful and easier to use. "I think cancer biologists will start thinking about this because it is a more elegant way of marking cells than we currently use," says Leonard Zon, who directs the stem cell program at Boston Children's Hospital. "We definitely want to try it."

Tracking cell lineages

By repeatedly editing a genetic "barcode" in an embryo's cells, the CRISPR system can label tissue in a developing organ with a record of its ancestry.

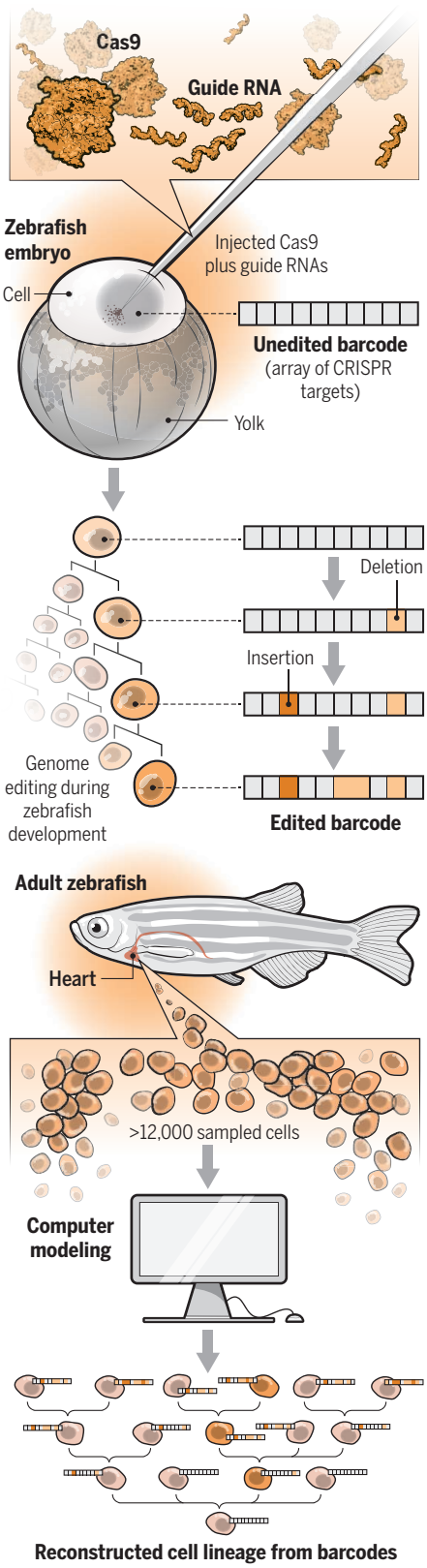


DIAGRAM: C. BICKEL/*SCIENCE*

Researchers are already proposing other ways to turn CRISPR into a kind of cellular memory. "I think conceptually that is the most exciting thing, that you can basically record history in the DNA," Schier says. In a preprint posted online last week, a team from the Massachusetts Institute of Technology in Cambridge may already have demonstrated that. Instead of adding a barcode consisting of 10 CRISPR targets, Timothy Lu and colleagues inserted into cells a single CRISPR target and engineered the site so that it also encodes the guide RNA. As a result, the system targets itself: The guide RNA leads Cas9 to its own source DNA. Cas9 breaks the DNA, leading to a mutation in the sequence, which in turn leads to the production of a mutated guide RNA. That altered guide RNA then leads Cas9 back to the altered target sequence, and the cycle continues, with the DNA sequence and the guide RNA changing in tandem.

By observing how the CRISPR target sequence changed in thousands of single cells endowed with this complicated setup, the researchers estimated how many rounds of Cas9 activity it took to produce certain sequences. (A rough analogy would be estimating how many rounds of the so-called telephone game it takes to scramble the phrase "lobster boil" into "losing team.") In a follow-up experiment, they coupled the activity of Cas9's gene with the activity of an inflammatory pathway.

In cells exposed to more of the inflammatory factor TNF, the target sequence was subjected to more rounds of Cas9 alterations. Then they tested the CRISPR recorder by implanting mice with the engineered cells and injecting some with an inflammation-provoking molecule. In those mice, the CRISPR target sequences had more changes than ones from mice not receiving the molecule. This method can "record physiologically relevant biological signals in an analog fashion," the authors write.

It could also record stimuli that cancer cells are exposed to in the microenvironment of a tumor or track the activity of specific pathways in cells during disease development, Lu and colleagues suggest. Church notes that such methods may also prove valuable in brain studies, for example by recording the activity of pathways involved in memory foundation. "You can take a transient process like the learning of a new task and turn it into a permanent record that's present in the cell body of every neuron in the brain," he says. ■

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