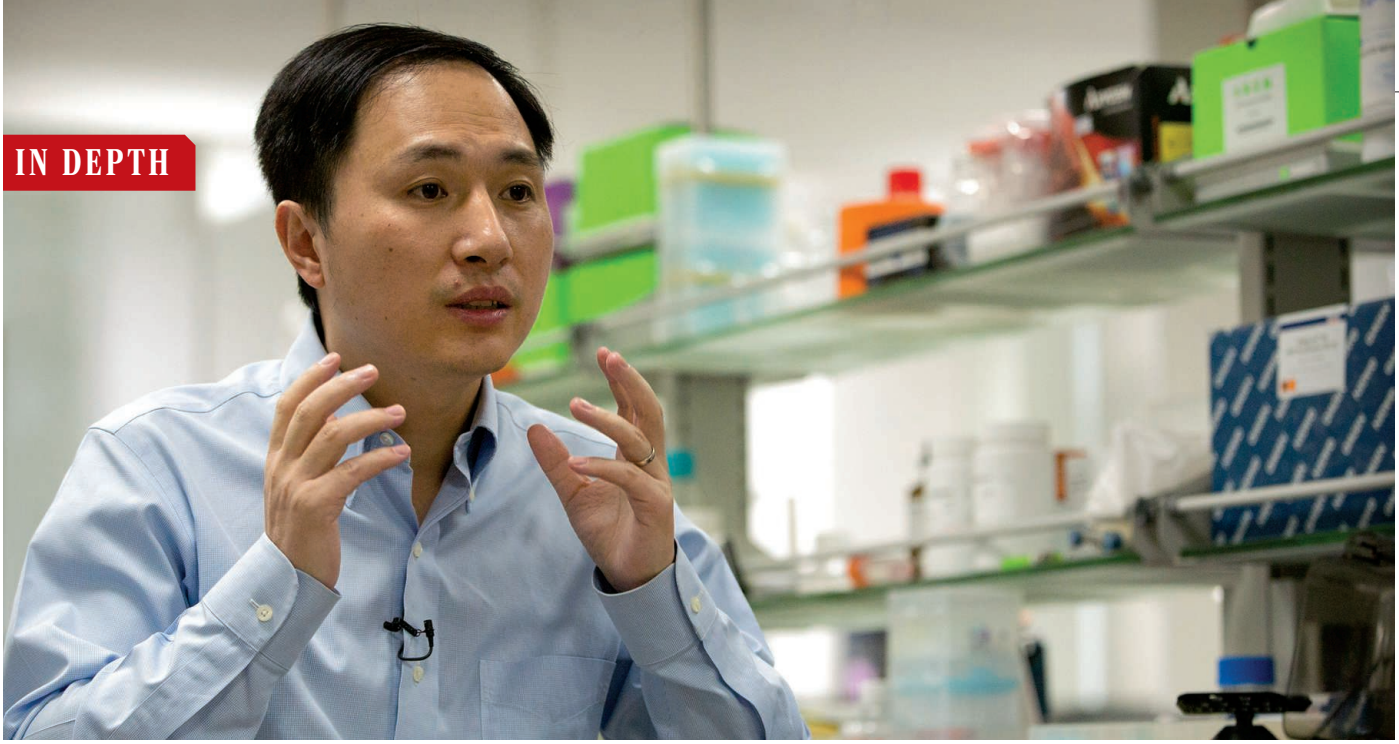


PHOTO: MARK SCHIEFELBEIN/AP IMAGES

BIOETHICS

Shock greets claim of CRISPR-edited babies

Apparent germline engineering by Chinese researcher prompts outrage and investigations

By **Dennis Normile**, *in Hong Kong, China*

The idea that humanity can rewrite its own genetic code long seemed the stuff of a science fiction novel—and a pretty scary one at that. But rapid advances in techniques such as CRISPR have made it possible, at least in principle, to make precise changes to the genome of a human embryo that could help rid families of crippling genetic diseases—or lead to "designer" babies, gene edited to be smarter or more beautiful. A few years ago, at an international summit where scientists, ethicists, and policymakers pondered the consequences of editing human genomes, biologist David Baltimore of the California Institute of Technology in Pasadena declared: "The unthinkable has become conceivable. We're on the cusp of a new era in human history."

Now, that era may have started—suddenly, and in almost surreal fashion. On 26 November, just before Baltimore opened a new summit on genome editing here, a little-known Chinese researcher named He Jiankui announced in an Associated Press (AP) interview and a series of YouTube videos that his team had engineered the DNA of twin baby girls born earlier this month to cripple a key receptor, CCR5, on white blood cells, a modification they may pass on to their descendants. The revelation shocked many scientists—one called the work "monstrous"—because He appears to have skipped the profound ethical debate that participants at the 2015 summit, and many meetings since, agreed should take place before such experiments began. (He did not responds to requests for an interview.)

Fueling the outcry was the fact that He didn't produce any data, let alone a paper, to back up his claim. The biologist was scheduled to speak at the International Summit on Human Genome Editing here this week, but whether he would show up was unclear as *Science* went to press. Meanwhile, the purported justification for He's study—to protect the two girls, named Lulu and Nana, from the AIDS virus, which uses CCR5 to infect cells—was almost immediately dismissed as flawed by HIV experts.

Although He reportedly consulted with bioethicists, condemnation was swift and widespread, even in China, where restrictions on such work are less clear-cut than in other countries. He's academic home, the Southern University of Science and Technology (SUST) in Shenzhen, China, has launched a probe into the research, which it said may "seriously violate academic ethics and academic norms." National authorities have promised investigations as well; the Chinese Society for Cell Biology called the research "a serious violation of the Chinese government's laws and regulations and the consensus of the Chinese scientific community."

Scientists are exploring the use of CRISPR and other gene-editing techniques as treatments for genetic diseases, such as muscular dystrophy and sickle cell anemia. So far, clinical trials have only modified somatic cells—not sperm or eggs, the germ line. But He altered the genome in early stage embryos, creating edits that may be heritable. Many scientists and ethicists don't rule out making such changes to the germ line, but recent reports from the United States's National Academies of Sciences, Engineering, and Medicine and the United Kingdom's Nuffield Council on Bioethics agreed they should only be undertaken under "stringent conditions" and to address a serious unmet medical need.

He's effort had no such justification, critics say. The team worked with embryos created by in vitro fertilization (IVF) with sperm and eggs from seven couples, He said. In each couple the man was infected with HIV, but the woman was not. The small percentage of people who have a natural mutation in the *CCR5* gene are resistant to HIV infection; by disabling the gene in the embryos, He's team aimed to endow children with the same resistance. (Researchers have already used gene-editing techniques to cripple the gene for CCR5 in immune cells from HIV-positive adults and then infused the cells back into the patients, as an experimental treatment.)

Preventing father-to-child transmission of HIV was not the stated purpose of He's work; there is little risk of that, especially with IVF.

He Jiankui says he genetically edited an immune gene in embryos, leading to the birth of healthy twin girls.

He, noting pervasive discrimination against HIV-positive people in China, told AP his goal was instead to protect the babies from possible infection later in life. (An informed consent document for potential study volunteers describes the work as "an AIDS vaccine development project.")

Many HIV scientists say He's goal is a poor reason to subject embryos to the potential risks of CRISPR, which include "off-target" mutations that might lead to cancer. "There are so many ways to adequately, efficiently, and definitively protect yourself against HIV that the thought of editing the genes of an embryo … in my mind is unethical," says Anthony Fauci, who heads the U.S. National Institute of Allergy and Infectious Diseases in Bethesda, Maryland.

He received his Ph.D. at Rice University in Houston, Texas, where he published a paper with his adviser, Michael Deem—who is under investigation by Rice for any role in the human embryo work—about CRISPR's evolution as a bacterial defense mechanism. He later won a generous grant under the Thousand Talents Program to return to China, where he obtained an associate professorship at SUST—although the university says he has been on unpaid leave since February. In various talks, He has described his in vitro work on editing human genetic material.

But Robin Lovell-Badge of The Francis Crick Institute in London, a member of the current summit's organizing committee, says few if any were aware He was trying to implant modified embryos. Where the studies were conducted is unclear; SUST said it wasn't at a university lab. Lovell-Badge says He is not disclosing the hospital involved to protect the family's privacy.

"We believe ethics are on our side of history," He says in one video. Yet some scientists say He has ignored the ethical concerns he and co-authors laid out in a paper this week in *The CRISPR Journal*, in which they wrote: "Performing gene surgery is only permissible when the risks of the procedure are outweighed by a serious medical need."

China has not yet developed guidelines specifically applicable to human gene editing. But bioethicist Qiu Renzong, of the Chinese Academy of Social Sciences in Beijing, told the summit on 27 November that He likely violated health and science ministry regulations prohibiting implanting genetically modified human embryos into human reproductive tracts. The ministry's dilemma, Qiu added, "is that there is no penalty if you violate the regulations." ■

With reporting by Jon Cohen.

PLANETARY SCIENCE

Safely settled, InSight gets ready to look inside Mars

Lander will deploy seismometer and heat probe to listen for marsquakes and study the planet's interior

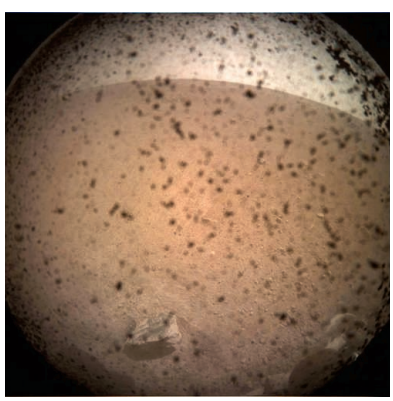
By **Paul Voosen**, *in Pasadena, California*

Ever since Bruce Banerdt saw images of Mars's surface as an intern here at NASA's Jet Propulsion Laboratory (JPL) during the Viking landings of the 1970s, he has wanted to know what lies beneath. Now, his goal is within reach, with this week's arrival of NASA's newest martian robot, the InSight lander, which carries instruments designed to probe the planet's interior. "On some level, I've been planning this for 30 years," says Banerdt, a planetary scientist at JPL and InSight's principal investigator.

On 26 November, the lander's fall from space to the surface made for a tense 6 minutes at JPL's mission control room. But the $814 million lander followed its script to the letter. As it plunged through the atmosphere behind a heat shield, a hush fell over the room during a brief, planned loss of contact. Then came bursts of applause, as communications resumed and the lander relayed signs that it was slowing—first as its parachute deployed and then when its landing thrusters fired. "Thirty meters. Twenty meters," said Christine Szalai, the JPL engineer narrating its descent. "Touchdown confirmed." The ensuing celebrations remained somewhat tempered until confirmation came 6 hours later that the lander had unfurled the solar panels that will power it through its 2-year mission. It was NASA's eighth successful Mars landing in nine tries, and a feat that other space agencies have yet to match, aside from the Soviets with their Mars 3 mission, which failed within a minute of its soft landing in 1971.

That engineers could even monitor the landing so closely was itself a leap. NASA's Mars orbiters were not set up or positioned to relay live signals from InSight's descent. Instead, the signals were shuttled to Earth in near–real time by Mars Cube One, a pair of briefcase-size spacecraft with experimental radio antennas that rode to Mars along with InSight. During InSight's 6-minute descent, the duo worked flawlessly before coasting past the planet. "We were all pulling for them," says Lori Glaze, NASA's acting director of planetary science in Washington, D.C. "They performed absolutely beautifully."

The spacecraft hit its landing site, a vast lava plain near the equator called Elysium Planitia, close to its bull's-eye, says Tom Hoffman, the project manager at JPL. NASA chose the tropical site for its abundant sunlight and apparent lack of rocks, which could have upset the landing and made it hard to deploy the instruments. InSight's first image, speckled by dust on the lens's transparent cap, showed a rusty plain, featureless aside from a rock near the lander's body. "It does look like a parking lot," Hoffman says. A second photo showed the team may just have been lucky: The terrain is rockier beyond InSight's immediate vicinity.



InSight's first view, speckled by dust on a lens cap, showed a mostly featureless plain.

PHOTO: NASA/JPL-CALTECH

The lander is designed to reveal the dimensions and composition of the planet's crust, mantle, and core, details that could help scientists understand how planets lose their magnetic fields or develop plate tectonics. It also marks NASA's return to planetary seismology after 4 decades. The two Viking landers both carried seismometers, but one failed and the other was bedeviled by noise.

Over the next couple of weeks, scientists will plan InSight's next two feats: wielding its robotic arm to place its seismometer and heat probe. The arm will first pluck the volleyball-size seismometer from the lander's deck and set it on the ground, with its power provided by a tether; an encircling wind and heat shield, like a bell jar, will follow. The seismometer, developed with French partners, will be placed as far out as possible—

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