

*Neural Circuits*³ disputing Zhang's work on the protein's potential to magnetically control cells.

This has all given rise to serious questions about the role of the molecule at the centre of the dispute. In their 2015 paper¹, Xie and his colleagues reported that a protein called IscA1 forms a complex with another protein, Cry4, that explains how organisms pick up magnetic cues. The study found that this complex incorporates iron atoms, which gives it magnetic properties, and has a rod-like shape that aligns with an applied magnetic field.

Two months earlier, Zhang had described using IscA1 to control neurons and muscle cells in worms². Zhang learned of IscA1's properties and obtained his IscA1 samples from Xie, and so the fact that his team published first was an early source of tension in what quickly became a bitter dispute. Officials from both Tsinghua University and Peking University asked *Science Bulletin* to retract Zhang's paper. And that November, Zhang lost his position at Tsinghua — for reasons that the university did not specify.

Doubts about Xie's research have emerged since then. Michael Winklhofer, a geophysicist at the University of Oldenburg in Germany, examined Xie's data and found that the complex would be too weakly magnetic to sense Earth's field⁴. Markus Meister, a biophysicist at the California Institute of Technology in Pasadena, raised similar concerns: Xie had reported that the complex would contain only 40 iron atoms, but Meister argues that the smallest known naturally occurring iron-based magnet

has 1 million iron atoms packed into a smaller space⁵.

David Keays, a neuroscientist at the Institute of Molecular Pathology in Vienna, has also questioned the study. He says that IscA1 and Cry4 are found throughout many tissues, whereas one would expect them to be sequestered in specific areas if they were functioning as parts of a magnetic-field receptor. "Sensory receptors, whether they be taste, hearing or photoreceptors, tend to have a restricted expression pattern," he says.

Collaborators of Xie say that they have been able to reproduce some of his findings, and Xie told *Nature* that he stands by his results. He disputes the contention that the magnetic properties of IscA1 would be too weak by saying that Cry4 might boost its effect. "The data are what they are," he says. "This may expand our knowledge of molecular magnets."

The challenge to Zhang's paper has been more pointed. Zhang claimed to have transferred IscA1 into worm neurons and then used a magnetic field to induce the cells to take up calcium. The ability to manipulate such a basic cell function could promise neuroscientists a powerful tool that is less invasive than optogenetic techniques, which use light-sensitive proteins to control neurons in living animals.

But last month, Xie, Tsinghua University neuroscientist Lu Bai and Lu's student Pang Kelian reported³ carrying out experiments under various conditions, including some almost identical to those used by Zhang. They

found no change in calcium flowing into cells in any of the cases. The authors conclude that the "findings cast serious doubts" that IscA1 alone could influence the activity of neurons, as Zhang had claimed.

Several scientists outside China also told *Nature* that they could not reproduce Zhang's results. *Nature* tried to reach Zhang through multiple e-mails and phone calls to Shenzhen University in China, where he now has a position, but he did not respond to requests for comment. (Neither *Nature Materials*, which is editorially independent from *Nature's* news team, nor *Science Bulletin* responded to requests for comment about criticism of the papers.)

Meanwhile, even as his critics become increasingly aggressive, Xie says he has convincing data that demonstrate the reaction of an IscA1 complex to a magnetic field, and that he plans to publish them within a year. "We are more and more confident — 100% sure — that we are right about this," he says. ■

1. Qin, S. *et al. Nature Mater.* **15**, 217–226 (2016).
2. Long, X., Ye, J. & Zhang, S.-J. *Sci. Bull.* **60**, 2107–2119 (2015).
3. Pang, K. *et al. Front. Neural Circuits* <http://dx.doi.org/10.3389/fncir.2017.00011> (2017).
4. Winklhofer, M. & Mouritsen, H. Preprint at bioRxiv <http://dx.doi.org/10.1101/094607> (2016).
5. Meister, M. *eLife* **5**, e17210 (2016).

REPRODUCTIVE BIOLOGY

Baby's DNA mix revealed

But parents of boy conceived with DNA from three people plan to forego long-term monitoring.

When a US fertility clinic revealed last year that it had created a baby boy using a controversial technique that mixes DNA from three people, scientists were quick to raise the alarm. Some objected on ethical grounds, and others questioned the scientific claims made by the clinic's leader, physician John Zhang.

Now, after months of intense debate and speculation, Zhang's team has provided more details about the child's conception, in a paper published on 3 April in *Reproductive Biomedicine Online*¹. But major questions remain about the boy's long-term health and the scientific value of the experiment.

Techniques to create 'three-parent babies' seek to offer mothers a way to have a child without passing on metabolic diseases caused by faulty mitochondria, the structures that provide energy to cells. Researchers do this

by exchanging the diseased mitochondria of a prospective mother with those of a healthy, unrelated donor: the 'third parent'.

In this case, a team led by Zhang, who works at the New Hope Fertility Center in New York City, removed the nucleus from a healthy donor egg and replaced it with a nucleus taken from the egg cell of a woman who carries a rare neurological disease called Leigh syndrome, leaving the donor's healthy mitochondria intact. The scientists then fertilized the modified egg with the father's sperm before implanting it into the mother's uterus. The resulting baby was born in April 2016.

The paper reports new details about the procedure, such as the method used to transfer the mitochondria. The study also reveals that some diseased DNA from the mother was carried over inadvertently into the donor egg, which could have long-term

repercussions for the child's health.

Other scientists welcomed the information. "Certainly, this is a landmark study," says Dietrich Egli, a stem-cell scientist at the New York Stem Cell Foundation.

But no one knows whether the child's health will be affected by the traces of the mother's mitochondrial DNA, which could prompt some of his mitochondria to function improperly. The percentage of affected mitochondria can differ between tissues. Zhang's paper reveals that just 2% of the mitochondrial DNA of cells in the boy's urine came from the mother, as compared to 9% in cells from the circumcised foreskin.

Scientists don't know what amount of diseased mitochondria would cause noticeable symptoms in a child created with genetic material from two women. But studies in mice have shown that mixtures of mitochondria can result in neurological disorders ▶

▶ or metabolic conditions².

It is not clear how these results will compare to the outcome of mitochondrial replacement in human babies. “Whatever we learn in a person will be completely new,” Egli says.

ADVISE AND CONSENT

The answers are not likely to come from the child born in Zhang’s clinic. The study says that the baby’s parents have refused any further mitochondrial testing of their child unless there is a medical need. It is not clear whether the family was ever asked to consent to long-term medical monitoring; Zhang and New Hope did not respond to *Nature*’s request for comment on the issue.

The value of the experiment will be limited if scientists cannot track the boy as he grows, Egli says. “It looks like a rush to use this as a treatment and telling patients that this is the treatment, during a time when we still know very little about what the outcomes are.”

Guidelines for human research generally require that people be allowed to withdraw from experiments. When this happens, it can make it hard to determine whether a treatment is safe, says Alta Charo, a bioethicist at the University of Wisconsin–Madison. In this case, she says, it is unclear whether the parents received enough information to appreciate how long-term follow-up could



John Zhang holds the baby boy in his clinic.

benefit their child as well as science.

A three-page editorial³ accompanying the study notes that the researchers asked the baby’s parents to sign a consent form acknowledging that their egg was undergoing an experimental technique. But the form only described the procedure superficially, and did not inform the couple of the potential risks of using this

method to create a child.

Because the boy could not give consent, “the duties were even higher for clinicians and participants to protect the best interest of the future child”, says Rosario Isasi, a legal scholar at the University of Miami in Florida. In his paper, Zhang says that the parents received “cautious counselling for mitochondrial replacement therapy”.

He told *Nature* last week that his team will continue to test the technique, using eggs from prospective mothers who are between 42 and 47 years of age. They want to explore whether mitochondria from younger donors’ cells may stimulate the older eggs’ ability to be fertilized and develop normally. ■

1. Zhang, J. *et al. Reprod. Biomed. Online* **34**, 361–368 (2017).
2. Wallace, D. C. *et al. Cold Spring Harb. Perspect. Biol.* **5**, a021220 (2013).
3. Alikani, M., Fauser, B. C. J., Garcia-Valesco, J. A., Simpson, J. L. & Johnson, M. H. *Reprod. Biomed. Online* **34**, 333–368 (2017).

CORRECTION

The News Feature ‘How to hunt for a black hole’ (*Nature* **543**, 478–480; 2017) erred in saying that Heino Falcke led a team that made one of the first VLBI observations. He was one of the team’s investigators.