

Pioneer warns of embryo factories

Oliver Moody Science Correspondent

A couple of years ago Jennifer Doudna had a nightmare about a gene-surgery tool called Crispr-Cas9, the revolutionary discovery that made her name. She was asked to explain it to a man sitting in the next room.

When she opened the door, this man turned out to be Adolf Hitler, but with the face of a pig. "I want to understand the uses and implications of this amazing technology you have developed," he said.

He is not the only one. Days after researchers in the UK published the results of the most effective use of Crispr-Cas9 on human embryos yet, Professor Doudna is losing sleep over what their findings might mean for the future of our species.

In an interview with *The Times*, she raised concerns that Britain could allow scientists to set up "factories" churning out embryos for research, or roll back the ban on keeping them alive in the laboratory for longer than two weeks. Professor Doudna, a molecular biologist at the University of Califor-



nia, Berkeley, and one of the pioneers of Crispr gene-editing, praised the latest study but said it gave her troubling visions of science bumping up against the boundaries of what is legal and ethical to do to a clutch of cells that is, in some sense, a human.

The British researchers, headed by Kathy Niakan at the Francis Crick Institute in London, have begun removing individual genes to learn how they make the very earliest human cells tick. The experiment, the world's first of its kind, involved only surplus IVF embryos that

could not survive much longer than a week under any circumstances. This is not about eugenics. It is about reading the prologue to our lives.

Last year Professor Doudna named Dr Niakan as one of *Time* magazine's 100 most influential people in the world, citing the power of her work to "answer previously unanswerable questions about human reproduction".

Yet she also feels that it has opened a Pandora's box of quandaries. "The question I was lying awake asking myself last night was this," she

Jennifer Doudna has nightmares about the possible uses of Crispr

said. "I read the Kathy Niakan paper and it's a very carefully done study. It's clearly a technology that can work efficiently in human embryos. She's doing it to study human development. But the challenge immediately becomes: what's the next experiment? Is it that you need to make many thousands more embryos? Do you need to request that the 14-day limit is extended so that you can see what happens further along in the developmental process? It definitely does raise questions that to me are very uncomfortable."

In the race for scientific firsts, Professor Doudna thinks the UK could end up crossing some difficult lines. "I myself am struggling with this," she said. "I'm trying to get my mind around what's a responsible path forward. I have to admit that I feel personally uncomfortable with the idea that there could eventually be factories pumping out lots of human embryos for the purposes of experimentation. I can't put my finger on why but it feels like it cheapens something about human life."

Robin Lovell-Badge, a senior stem cell biologist at the Crick Institute who has worked closely with Dr Niakan, said that while her experiments had been strictly controlled, others elsewhere in the world might not be. "With all the appropriately strict regulation, we are not going to see embryo 'factories' in the UK. This vision owes more

Potential uses ... and abuses

- Protecting children against inherited diseases
- Designer babies with enhanced traits
- Crops and livestock modified to grow faster and use less food and water
- Fighting illnesses such as cancer
- Bringing back woolly mammoths and other extinct species
- Designing powerful stem cells for use in medicine
- "Frankenpets" with customised body features

to dystopian views in science fiction than to reality. Of course in the UK each project will have to be subject to regulatory approval so it is unlikely that there will be hundreds of scientists doing this. But I can see why Jennifer was concerned by this, especially as work could or will happen in less regulated countries, and with projects of dubious relevance or done badly."

It is only five years since Professor Doudna and the French microbiologist Emmanuelle Charpentier showed that Crispr-Cas9 could be used to cut out any piece of DNA a scientist wants.

Older gene-surgery methods have

been around since the 1980s. The special thing about Crispr-Cas9 is the peerless ease and precision with which it can be rigged up for each new experiment. For some biologists, this god-like editing suite for the book of life is the most important technology since the gene reader.

For the White House, it is an object of deep suspicion. One member of the Trump administration is said to have recently asked a scientist: "What about Crispr? That's dangerous. We need to get rid of it."

For others, the most interesting prospect is the ability to make predictable changes to the human gene pool.

This summer another group of scientists in the US, China and South Korea showed that Crispr-Cas9 could excise the gene for cardiomyopathy, a congenital heart condition, from a few dozen embryos. The results have since been disputed. Nevertheless, Professor Doudna thinks it is almost inevitable that this treatment will be attempted sooner or later in IVF clinics. "There are few cases where this kind of intervention would make sense medically, especially with the level of risk involved," she said. "But the reality is I think this is probably coming in the future. The take-away from [the cardiomyopathy paper] is that it will encourage anyone of those inclined to use gene editing in embryos to proceed."