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The former SNP leader, pictured in his Westminster office, said right-wing papers were 'lunatic' – and accused the BBC of being shamelessly unionist TERI PENGILLEY

Britain to genetically modify human embryos

- Research licence allows manipulation of IVF embryos for only the second time
- Scientists aim to discover causes of repeat miscarriages, giving hope to millions

STEVE CONNOR
SCIENCE EDITOR

The genetic manipulation of human IVF embryos is to start in Britain for the first time, following a licence application by scientists who want to understand why some women suffer miscarriages.

If the research licence is granted by the Government's fertility watchdog, it will be only the second known occasion in the world where the chromosomes of human embryos have been genetically manipulated using a revolutionary gene-editing technique called Crispr/Cas9. When Chinese scientists announced earlier this year that they had genetically altered "spare" human IVF embryos using Crispr/Cas9 for research purposes, there was deep concern among many who thought that they had gone too far.

The American government later imposed a moratorium on federally funded research in the United States.

The researchers behind the UK application emphasised that the GM embryos will be destroyed once the study is completed, with no risk of them being transplanted into women – which is illegal in Britain. There will be no "GM babies" because the project is aimed solely at basic research into the genetics of early human development, the researchers insisted.

But critics of the manipulation of human IVF embryos – even when done for research purposes – have argued that it is a slippery slope to genetically enhanced "designer babies". The scientists behind

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Scientists given the go-ahead for the genetic modification of human embryos

← Continued from P.1

the proposed study in the UK said they have no intention of altering the DNA of future generations but accept this may at some point in the future be safe, medically justifiably and ethically acceptable – for instance to avoid inherited disorders or to confer disease resistance on IVF babies.

"We want to understand the genes human embryos need to develop successfully," said Kathy Niakan of the Francis Crick Institute in London, who has applied to the Human Fertilisation and Embryology Authority (HFEA) for a research licence to use Crispr/Cas9 on spare IVF embryos donated by couples undergoing fertility treatment.

"We are not contemplating altering genes for clinical purposes – we are interested in basic mechanisms of embryonic development. If any of our discoveries suggest ways to improve embryo development after IVF, or to improve implantation frequency, or to prevent miscarriage, these would involve conventional approaches, not the manipulation of genes," Dr Niakan said.

"There are suggestions that the methods could be used to correct genetic defects, to provide disease resistance, or even to introduce novel traits that are not found in humans.

"However, it is up to society to decide what is acceptable – science will merely inform what may be possible," she added. Parliament amended the UK's IVF legislation in 2008 to allow genetic manipulation of embryos less than 14 days old, provided it was for research purposes and sanctioned by the HFEA. Under the HFE Act 2008, it remains illegal to create GM embryos for implanting into the womb, or to edit the "germline" DNA of chromosomes passed on to future generations.

"What we are proposing is in keeping with the HFE Act 2008, which is purely for research purposes. We hope to use this technology to improve our understanding of the earliest stages of human development," Dr Niakan said. "The knowledge we acquire will be very important for understanding how a healthy human embryo develops, and this will inform our understanding of the causes of miscarriage. The knowledge may also improve embryo development after IVF and might provide better clinical treatments for infertility," she said.

"If we receive a licence, I would hope to start work as soon as possible. However, it is difficult to know how long it will take to carry out the project. In particular, we need to obtain sufficient embryos," she added.

Professor Robin Lovell-Badge, a senior scientist at the Francis Crick Institute, who took part in a major review of the ethical implications of Crispr/Cas9, the gene-editing technique that allows accurate and efficient engineering of the human genome, said that germ-line gene therapy is not on the agenda, and that Dr Niakan's proposal is purely aimed at understanding why some women suffer repeated miscarriages.

"The ultimate clinical benefits could be improved methods of IVF and better implantation rates in women who have big problems maintaining a pregnancy because there is something wrong with the interaction between the placenta and the uterus," Dr Kathy Niakan of the Francis Crick Institute in London, who has applied for a licence to carry out the research on donated embryos using the Crisp/Cas9 technique

Professor Lovell-Badge said: "There is no intention at all [to do germline gene therapy]. It is purely a tool for the understanding the basic biology of early human development," he said.

However, both scientists emphatically denied that the licence application marks the start of a slippery slope to designer babies.

"Absolutely not. I don't believe in the slippery slope anyway, but within the UK we have very clear regulations. If you do any sort of manipulations on an embryo it is no longer a permitted embryo, it cannot be transferred into a woman. It is illegal to do so," Professor Lovell-Badge said.

Dr Niakan, who moved from the US to the UK to carry out her research, added: "It is not a slippery slope, because the UK has very tight regulation in this area, and it would be illegal to move in that direction... The HFEA has been instrumental in establishing a culture of proper discourse and regulatory oversight. At the moment, I believe the UK is the best place in the world to do this work."

A spokesman for the HFEA said: "Genome editing of embryos for use in treatment is illegal. It has been permissible in research since 2009, as long as the research project meets the criteria in the legislation and it is done under an HFEA licence. We have recently received an application to use Crispr-Cas9 in one of our licensed research projects, and it will be considered in due course."

How 'The Independent' revealed the breakthrough in genetics in November 2013

PROFILE DR KATHY NIAKAN

Kathy Niakan, an American, has two first degrees from the University of Washington in Seattle: one in cell and molecular biology, the other in English literature. However, she chose to pursue science – in particular biology and genetics – when, as an undergraduate, she had her first experience of a top-level research laboratory.

After obtaining a PhD at the University of California, she did postdoctoral research at Harvard where she worked on mouse and human "pluripotent" stem cells.

She later moved to the UK and now works at the National Institute for Medical Research at Mill Hill, which has merged with the new Francis Crick Institute in London.

CHINESE TRIAL FIRST HUMAN TESTS

The only known occasion when the gene-editing technique Crispr/Cas9 was used on human embryos was in China, in a study published last April. Researchers in Sun Yat-sen University in Guangzhou used Crispr on 86 "non-viable" fertility treatment embryos to modify the gene responsible for beta-thalassaemia, a potentially fatal blood disorder.

The researchers wanted to see whether it would be feasible to eradicate the disease by altering the diseased gene at an early point in embryonic development – although the non-viability of the embryos demonstrated there was never any intention of using them to produce GM babies.

However, only a fraction of the embryos contained the replacement DNA – suggesting the technique is still too immature for clinical use.

ON OTHER PAGES
Editorial P.2

HOW GENE EDITING WILL BE USED ON HUMAN EMBRYOS

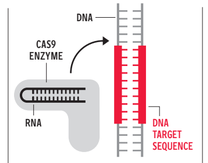
WHERE CRISPR WILL BE USED

The gene editing will take place in the **outer cells of the embryo called trophectoderm,** which form the placenta

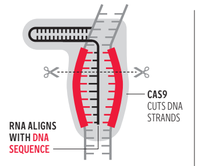
HOW CRISPR WORKS

Crispr system derived from bacteria works on human cells to edit genes

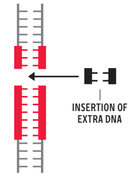
1 An RNA "guide" molecule can be **programmed to match any unique DNA sequence found in the trophectoderm**



2 A special enzyme, called **CAS9, can be attached to the RNA guide.** Its job is to find the target sequence of DNA in the genome



3 The RNA aligns with the target DNA sequence and the **CAS9 attaches and cuts both strands of the DNA double helix**



4 The DNA cuts can be **amended with an extra DNA insertion** (above), **or a deletion** to eliminate the gene

SOURCE: UC BERKELEY

Q&A GENE EDITING – THE HOPES AND THE RISKS

Q | What is being proposed?
A | Scientists want to use a new and incredibly efficient method of "gene editing", known as Crispr/Cas9, to alter the genes of IVF embryos. They specifically want to change or delete certain genes in the outer cells or "trophectoderm" of the early human embryo. These are the cells that go on to form the placenta which attaches to the uterus when the embryo becomes implanted in the womb during pregnancy.

Q | Why are they doing this?
A | The researchers want to understand the genetic mechanism that underpins the development of the placenta. By doing this, they hope to be able to find out what goes wrong in women who suffer repeated miscarriages, which may be the result of irregularities in the way the placenta forms during the crucial early stages of embryonic development. They also want to use it for generating embryonic stem cells.

Q | Will this lead to GM babies?
A | No. This licence application is for research purposes only. It will be carried out on spare IVF embryos donated by couples undergoing fertility treatment. The embryos are less than 14 days old and will be destroyed once the project is finished – it will be illegal to transfer them into the womb.

Q | Can't this be done in some other way?
A | A lot of work in this area is done on mice, but scientists know that the early development of the trophectoderm in mice embryos is significantly different to the development of human embryos. Because of these differences, the scientists would like to work directly on human IVF embryos by, for instance, deleting certain genes using Crispr/Cas9 to see how this affects the development of the tissue that gives rise to the placenta.

Q | Why is this controversial?
A | Crispr/Cas9 is so powerful some see it as a neat way of safely engineering the human genome. Doing it in eggs, sperm or human embryos used in fertility treatment will alter the "germline" DNA passed on to future generations. If ever it were to be allowed, it raises the prospect of ridding inherited disorders or conferring disease resistance to future generations, but could also usher in an era of genetically-enhanced "designer babies".