Level 3 Certificate/Extended Certificate
APPLIED SCIENCE

Unit 3 Science in the Modern World

January 2019

Pre-release Material

- This pre-release material should be opened and issued to learners on or after **1 November 2018**.
- **A clean copy of the pre-release material will be provided at the start of the examination.**

Information

This pre-release material is to be issued to learners for use during preparation for this examination. The pre-release material consists of four sources (**A–D**) on the subject of **genetic modification of human embryos**.

This material is being given to you in advance of this examination to enable you to study each source in preparation for questions based on the material in **Section A** of the examination.

A wider understanding of the topics and issues raised in the sources would be beneficial for the assessment. You are **not** required to understand any detailed scientific explanations beyond that outlined in **Sources A–D** and that in the Applied Science specification.

You may write notes on this copy of the pre-release material, but you will not be allowed to bring this copy, or any other notes you may have made, into the examination room. You will be provided with a clean copy of this pre-release material at the start of the examination.

It is suggested that a minimum of three hours detailed study is spent on this pre-release material.

Source A: Adapted article from www.sciencealert.com, February 2016.

10 Things You Need to Know About The UK Allowing Genetic Modification of Human Embryos

Keep calm and get the facts.
FIONA MACDONALD
2 FEB 2016

A few hours ago, the UK Human Fertilisation and Embryology Authority (HFEA) made a landmark decision to grant scientists in London permission to genetically edit human embryos.

Thanks to the new licence, scientists at the Francis Crick Institute will be able to use a system called CRISPR-Cas9 (which is like a URL copy-and-paste tool for DNA) to modify the genes of developing embryos, with the goal of improving IVF success rates and reducing miscarriages.

This is the first time a national regulatory body anywhere in the world has given the procedure the green light, and it's a huge day for science. But the move has also sparked a lot of concern about the creation of designer babies.

So what does it really mean for society? We've broken down the facts, so you can share them with your concerned parents and co-workers.

1. Genetically editing humans isn't suddenly 'legal' in the UK

Only one group of scientists, led by molecular biologist Kathy Niakan, has been given permission to use CRISPR-Cas9 on human embryos, for the sole purpose of better understanding human embryo development. No one else has permission to use the technique in the UK (or anywhere else in the world, although some countries are less regulated - see point 8).

2. The embryos used in the experiments will come from donors

The research team will be working on embryos donated by women who have previously undergone IVF and have excess embryos.

3. Don't worry, nothing's happening without ethics approval

"The committee has added a condition to the licence that no research using gene editing may take place until the research has received research ethics approval," explained the HFEA in an emailed statement, as reported by Motherboard. That means the researchers now have to go through a separate ethics approval process before they can start research on human embryos - they don't just automatically have permission to do whatever they like.

4. The embryos won't be brought to term

The researchers only want to examine the effect of different genes on the first seven days of embryonic development, when the embryo goes from having one to around 250 cells.

The new licence also states that the embryos need to be destroyed within 14 days, and can't be implanted into a woman.

5. This work could *finally* reveal how a healthy human embryo develops

This is something that's still poorly understood in the world of molecular biology, and could help scientists to improve IVF and prevent miscarriages. As the BBC reports, out of every 100 fertilised eggs, fewer than 50 reach the early blastocyst stage, 25 implant into the womb and only 13 develop beyond three months.

"The reason why it is so important is because miscarriages and infertility are extremely common, but they're not very well understood," said team leader Kathy Niakan.

6. Experts are calling the decision a "victory for level-headed regulation over moral panic"

While there are still concerns about genetic editing, this first, highly regulated step has been labelled by some scientists as "a triumph for common sense".

"It is a clear example of how the UK leads the world not only in the science behind research into early human development but also the social science used to regulate and monitor it," University of Kent geneticist, Darren Griffin, told French Newspaper AFP.

7. But critics are worried that we're on a path towards designer babies

Let's face it, there are definitely big ethical questions to be answered going forward. At the end of last year, a UNESCO panel of scientists, philosophers and lawyers called for a halt on genetic editing until it's better understood what affect it would have on heritability and the human germline. And today's decision was met with concern by some groups.

But the licence in this case is extremely limited in its scope, and it's still illegal for ANYONE to implant genetically modified babies into women, or bring them to term, so we're a long way off any of these scenarios.

8. This isn't the first time that human embryos will be genetically modified

Last April, Chinese scientists admitted to tweaking the genes of 28 embryos to try to prevent a deadly blood disorder. They encountered serious challenges in their research, and said the technology has a long way to go before it can be used to treat disease in humans.

9. Still, CRISPR-Cas9 is a really big deal

CRISPR-Cas9 has been heralded as the biggest biotech discovery of the century.
The system works by using the Cas9 enzyme to cut human DNA, which means scientists can either snip out damaged genes, or insert new ones. Although it's not perfect, the technique is incredibly simple and adaptable compared to gene editing tools that have been trialled in the past.

Since its development in 2012, it's shown great promise in being able to treat conditions such as vision loss, muscular dystrophy, and even drug-resistant superbugs. If it works in humans, the technique could quite literally change everything.

10. There's no sign of gene editing being allowed in human embryos in the US any time soon

Last year, the US National Institutes of Health made it clear that it wouldn't be allowing scientists to edit human embryos any time soon, stating that it "will not fund any use of gene-editing technologies in human embryos".

END OF SOURCE A

Source B: Adapted article from *inews*, July 2017.

One giant step for designer babies

By Steve Connor Thursday 27th July 2017 inews.co.uk

- Revealed: Era of genetically modified babies moves closer, as scientists prove they can safely alter human embryos
- Inherited diseases caused by defective genes can be corrected in the earliest stage of life, revolutionary technique shows
- Same technology could be used to select stronger muscles or better eyesight, prompting fierce ethical debate
- 'They've done it. The quality of the work is high', top scientist tells *inews*
- Religious organisations likely to oppose ground-breaking research

This technology may open the door to 'pick-and-choose' designer babies

Altering the genes of a one-day old human embryo – a single-cell "zygote" formed by the fusion of sperm and egg – is one of the momentous operations that any medical scientist can perform. It means an inherited disease mutation can be eliminated from all subsequent generations of any child born by the procedure, known as germline genetic engineering. It means none of their own children or grandchildren needs to suffer from the genetic disorder that plagued their ancestors. But it also means that the same technology could be used to enhance the genes that children inherit from their parents; stronger muscles, perhaps, or keener eyesight. It opens the door to the "pick and choose" future of designer babies genetically engineered with desirable traits, fictionalised by Aldous Huxley in his 1932 novel Brave New World.

Exploding the myth

What Shoukhrat Mitalipov of the Oregon Health and Science University in Portland, Oregon, has achieved marks an important milestone in this direction. He has effectively and convincingly modified the genes of scores of one-day old human IVF embryos with a powerful gene-editing tool known as CRISPR-Cas9. None of the embryos, which were created specifically for research purposes, was allowed to live beyond a few days in the laboratory and there was never any intention of implanting any of them into a woman's womb, which is illegal both in the United States and Britain.

However, if what we have reported today is confirmed when Mitalipov's full study is published in a leading scientific journal in the coming weeks, it will finally explode the myth that human germline genetic engineering will never be technically possible or safe enough for use in IVF clinics.

One of the important goals of Mitalipov's work was to see how effective CRISPR-Cas9 can be when editing out a harmful disease mutation. We understand that he created many tens of embryos using the sperm of men carrying inherited disease genes, such as sickle-cell anaemia or cystic fibrosis. What was important was to get the CRISPR-Cas9 molecules inside the fertilised egg early enough for it to do its editing work on the mutated disease gene before the single-cell zygote had chance to divide. This was critical to avoid something called mosaicism, when only some of the cells of an embryo are genetically repaired, leaving the embryo with a mixture or mosaic of repaired and unrepaired cells.

"If they have come up with a solution to mosaicism, then it could be a game changer," said one senior scientist familiar with Mitalipov's work.

Another scientist who knows of the work said that Mitalipov seems to have overcome mosaicism with a clever trick pioneered by a British scientist called Tony Perry at Bath University.

Proof of principle

Mitalipov injected the CRISPR-Cas9 molecules into the unfertilised egg alongside a sperm cell. This was done during a routine IVF procedure known as intra-cytoplasmic sperm injection (ICSI), when the unfertilised egg is fertilised artificially with a single sperm.

We understand that the CRISPR-Cas9 editing tool successfully repaired the mutation of each sperm donor's defective gene. What is more, the repair was found to have worked on all the cells in almost all the IVF embryos created for the study – only "one or two" suffered from mosaicism, we have been told.

"It is proof of principle that it can work. They significantly reduced mosaicism. I don't think it's the start of clinical trials yet, but it does take it further than anyone has done before," one scientist said.

The only previous study involving viable human IVF embryos and CRISPR-Cas9 was carried out by Jianqiao Liu and colleagues at the Third Affiliated Hospital in Guangzhou Medical University in China, published in June. It involved just six experimental embryos carrying mutations in the genes for the blood disease beta-thalassaemia and an inherited eating disorder known as favism.

More substantial

The team injected the CRISPR-Cas9 components into the one-cell zygotes. Only three of the six embryos were genetically altered by CRISPR and two of them suffered from mosaicism, suggesting the gene editing did not take place fast enough before the cell divided into two.

"[Mitalipov's study] is a lot more substantial than the Chinese work and it was different in that they got CRISPR in earlier. They injected the CRISPR components alongside the sperm during ICSI [intra-cytoplasmic sperm injection] before fertilisation took place," the scientist said.

Only two other groups in Europe are known to be working actively on the use of CRISPR gene editing for modifying the genes of human IVF embryos.

But both Fredrik Lanner of the Karolinska Institute in Sweden and Kathy Niakan of the Francis Crick Institute in London only want to investigate the genes involved in early embryonic development to understand the causes of miscarriage.

They are both searching for new insights into pregnancy loss, rather than Mitalipov's aim of altering the defective genes behind the many thousands of inherited single-gene diseases, such as sickle-cell anaemia and cystic fibrosis.

A more meaningful use

"Kathy Niakan is focussing more on how she can use CRISPR to understand embryo development. This time, [Mitalipov's study] seems to be a more meaningful use of this technology," said one scientist.

The next stage for Mitalipov's research will be to carry out further experiments testing the safety and efficiency of CRISPR-Cas9. Ultimately there will be a desire to carry out a clinical trial, in other words to create a genetically modified embryo that is implanted into a woman's womb and allowed to develop into a full-term "GM baby".

As things stand, laws will have to be changed in both the United States and Britain to allow this. But if scientists can show it to be safe, effective and the only route to allowing a couple to have a healthy IVF baby of their own, the clamour to change the law and permit its use will undoubtedly grow.

But then comes the next question. If CRISPR-Cas9 is permitted to repair inherited diseases, could it also be used for genetic enhancements? Yet, what is seen as a genetic enhancement for one person may actually be viewed as a medical treatment by another.

Cosmetic surgery was developed initially to treat people disfigured by accidents. Now it is used as beauty aid. Could germline genetic engineering go the same way?

END OF SOURCE B

Source C: Adapted article from *National Geographic*, 2016.

Pro and Con: Should Gene Editing Be Performed on Human Embryos?

The most potent use of the new gene editing technique CRISPR is also the most controversial: tweaking the genomes of human embryos to eliminate genes that cause disease. We don't allow it now. Should we ever?

PRO: RESEARCH ON GENE EDITING IN HUMANS MUST CONTINUE

By John Harris

John Harris is professor emeritus in science ethics at University of Manchester, UK, and the author of *How to be Good,* Oxford University Press 2016.

In February of this year, the Human Fertilisation and Embryology Authority in the United Kingdom approved a request by the Francis Crick Institute in London to modify human embryos using the new gene editing technique CRISPR-Cas9. This is the second time human embryos have been employed in such research, and the first time their use has been sanctioned by a national regulatory authority. The scientists at the Institute hope to cast light on early embryo development—work which may eventually lead to safer and more successful fertility treatments. The embryos, provided by patients undergoing in vitro fertilisation, will not be allowed to develop beyond seven days. But in theory—and eventually in practice—CRISPR could be used to modify disease-causing genes in embryos brought to term, removing the faulty script from the genetic code of that person's future descendants as well. Proponents of such "human germline editing" argue that it could potentially decrease, or even eliminate, the incidence of many serious genetic diseases, reducing human suffering worldwide. Opponents say that modifying human embryos is dangerous and unnatural, and does not take into account the consent of future generations. Who is right?

Let's start with the objection that embryo modification is unnatural, or amounts to playing God. This argument rests on the premise that natural is inherently good. But diseases are natural, and humans by the millions fall ill and die prematurely—all perfectly naturally. If we protected natural creatures and natural phenomena simply because they are natural, we would not be able to use antibiotics to kill bacteria or otherwise practise medicine, or combat drought, famine, or pestilence. The health care systems maintained by every developed nation can aptly be characterised as a part of what I have previously called "a comprehensive attempt to frustrate the course of nature." What's natural is neither good nor bad. Natural substances or natural therapies are only better than unnatural ones if the evidence supports such a conclusion.

Finally, there's the argument that modifying genomes is inherently dangerous because we can't know all the ways it will affect the individual. But those who fear the risks of gene editing don't take into account the inherent dangers in the "natural" way we reproduce. Two-thirds of human embryos fail to develop successfully, most of them within the first month of pregnancy. And every year, 7.9 million children—6 percent of total births worldwide—are born with a serious defect of genetic or partially genetic origin.

Turn over ►

Certainly we need to know as much as possible about the risks of gene-editing human embryos before such research can proceed. But when the suffering and death caused by such terrible single-gene disorders as cystic fibrosis and Huntington's disease might be averted, the decision to delay such research should not be made lightly. Just as justice delayed is justice denied, so, too, therapy delayed is therapy denied. That denial costs human lives, day after day.

CON: DO NOT OPEN THE DOOR TO EDITING GENES IN FUTURE HUMANS

By Marcy Darnovsky

Marcy Darnovsky, Ph.D., is executive director of the Center for Genetics and Society. She speaks and writes on the politics of human biotechnology.

The gene editing tool known as CRISPR catapulted into scientific laboratories and headlines a few short years ago. Fast on its heels came the re-emergence of a profoundly consequential controversy: Should these new techniques be used to engineer the traits of future children, who would pass their altered genes to all the generations that follow? This is not an entirely new question. The prospect of creating genetically modified humans was openly debated back in the late 1990s, more than a decade and a half before CRISPR came on the scene and several years before the human genome had been fully mapped. It wasn't long before we saw provocative headlines about designer babies. Princeton mouse biologist Lee Silver, writing in *Time* magazine in 1999, imagined a fertility clinic of the near future that offered "Organic Enhancement" for everyone, including people with "no fertility problems at all." He even wrote the ad copy: "Keep in mind, you must act before you get pregnant. Don't be sorry after she's born. This really is a once-in-a-lifetime opportunity for your child-to-be." During the same millennial shift, policymakers in dozens of countries came to a very different conclusion about the genetic possibilities on the horizon. They wholeheartedly supported gene therapies that scientists hoped (and are still hoping) can safely, effectively, and affordably target a wide a range of diseases. But they rejected human germline modification—using genetically altered embryos or gametes to produce a child—and in some 40 countries, passed laws against it.

The issue of human germline modification stayed on a slow simmer during the first decade of the 21st century. But it roared to a boil in April 2015, when researchers at Sun Yat-sen University announced they had used CRISPR to edit the genomes of nonviable human embryos. Their experiment was not very successful in technical terms, but it did focus the world's attention. In December 2015, controversy about using CRISPR to produce children was a key agenda item at the International Summit on Human Gene Editing organized by the national science academies of the United States, the United Kingdom, and China. Nearly every speaker agreed that at present, making irreversible changes to every cell in the bodies of future children and all their descendants would constitute extraordinarily risky human experimentation. By all accounts, far too much is unknown about issues including off-target mutations (unintentional edits to the genome), persistent editing effects, genetic mechanisms in embryonic and fetal development, and longer-term health and safety consequences.

Beyond technical issues are profound social and political questions. Would germline gene editing be justifiable, in spite of the risks, for parents who might transmit an inherited disease? It's certainly not necessary. Parents can have children unaffected by the disease they have or carry by using third-party eggs or sperm, an increasingly common way to form families. Some heterosexual couples may hesitate to use this option because they want a child who is not just spared a deleterious gene in their lineage, but is also genetically related to both of them. They can do that too, with the embryo screening technique called pre-implantation genetic diagnosis (PGD), a widely available procedure used in conjunction with in vitro fertilisation.

It is true that a few couples—a very small number—would not be able to produce unaffected embryos, and so could not use PGD to prevent disease inheritance. Should we permit germline gene editing for their sake? If we did, could we limit its use to cases of serious disease risk?

From a policy perspective, how would we draw the distinction between a medical and enhancement purpose for germline modification? In which category would we put short stature, for example? We know that taller people tend to earn more money. So do people with paler skins. Should arranging for children with financially or socially "efficient" varieties of height and complexion be considered medical intervention?

Think back to the hypothetical fertility clinic offering "Organic Enhancement" as a "once-in-a-lifetime opportunity for your child-to-be." Think back to the 1997 movie *Gattaca,* about a society in which the genetically enhanced—merely *perceived* to be biologically superior—are born into the physical reality of those whom we might now call the one percent. These are fictional accounts, but they are also warnings of a possible human (or not so human) future. The kinds of social changes they foresee, once set in motion, could be as difficult to reverse as the genetic changes we're talking about.

In opening the door to one kind of germline modification, we are likely opening it to all kinds. Permitting human germline gene editing for any reason would likely lead to its escape from regulatory limits, to its adoption for enhancement purposes, and to the emergence of a market-based eugenics that would exacerbate already existing discrimination, inequality, and conflict. We need not and should not risk these outcomes.

END OF SOURCE C

Source D: Adapted article from *Guardian* online, September 2016

Gene editing isn't about designer babies, it's about hope for people like me

Alex Lee

What gives someone without an incurable condition such as blindness the right to stand in the way of potentially life-saving treatments?

Thursday 3 August 2017 16.51 BST Last modified on Wednesday 20 September 2017 19.01 BST

A landmark US study by scientists at Oregon Health and Science University in Portland has for the first time successfully edited out a genetic mutation that could cause heart disease, but the fearmongering over designer babies rages on. Where would research into cures for genetic diseases be without a good old debate around the scary future of eugenics?

For once, let's not allow that rhetoric to take over the headlines, in the way that it did two years ago, when research into mitochondrial replacement therapy, so-called three-parent babies, made strides. This is a good and promising breakthrough, not something to fear.

It's easy for those unaffected by genetic diseases to dismiss scientific progress as a step towards a future in which we start selecting a criterion of eye or hair colour from a design-your-own-baby catalogue. But for people like me, affected by an incurable genetic disease that caused me to go blind, scientific advancements into gene editing and mitochondrial replacement therapy offer nothing but hope. If there is any chance of potentially saving yourself or your baby from illness, don't tell me you wouldn't take the opportunity.

Don't get me wrong, being blind has made me who I am today, and I'm grateful for that. I'll continue fighting for equality and for the rights of disabled people, but my eyesight stops me from doing so many things that I could do otherwise. If we stop all progress into scientific research now because of the assumption that we are heading towards a society of designer babies, all that will happen is that some of us will continue to inherit often life-threatening diseases. If the only resistance to the continued research into curing genetic diseases is due to fears over a slide towards producing superhuman babies, I think people need to take a look at things from my perspective.

I am affected by Leber's hereditary optic neuropathy, a rare mitochondrial disease that affects an estimated 35,000 people worldwide. Diseases like mine are rare, and so the chances of this going beyond the ability to cure inherited diseases is unlikely to happen. Scientists are interested in curing us, not trying to change the colour of our eyes. Sometimes the opposition to techniques such as editing is so alarmist that it feels as if people are trying to keep those suffering from inherited diseases from being able to fully participate in society.

The creation of a class of designer babies is on the other side of the spectrum to what is being discussed right now. It's making someone who is disabled by genetics healthy – not making someone as perfect as they can be. Maybe it's near-sighted of me to think only of the current benefits of gene editing, but if the slippery slope from cutting out faulty DNA and genetic mutations helps save lives and gives someone a better quality of life, I'm all for it.

When people see devastating cases such as that of Charlie Gard, they're willing to offer support. But when the situation becomes hypothetical, views change. Mitochondrial replacement therapy could remove life-threatening mutations from family lines, stopping them being passed down. Mitochondrial disease kills an estimated 150 children every year, and if advancements like this can stop children dying, there is no need for mass panic about opening the door to bespoke babies.

I know the dangers. I have read Aldous Huxley's fiction and it's not pretty. But come on, if designer babies is the only argument against trying potentially life-saving treatments, what gives someone without an incurably debilitating disease the right to debate the future of our health? If we're going to debate anything, let's debate the science. Let's debate the risks. Not could-bes or scaremongering predictions. And then we can get on with saving lives.

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