Geneticist warns against intervention in the human germline made possible by the CRISPR/Cas 'gene scissors'

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CRISPR/Cas9 opens up many possibilities in medicine presenting opportunities and risks. It is hoped that the new method can be used for the genetic treatment of serious diseases, such as AIDS. Scientists could simply cut out a gene modified by disease in the body cells and replace it with a healthy one. Scientists in China and the UK are taking this a step further by conducting research in the laboratory using human embryonic stem cells. This has broken a taboo sparking outrage and debate worldwide. How far should research go? Stefan Mundlos, Director of the Institute for Medical Genetics and Human Genetics at the Charité and Research Group Leader at the Max Planck Institute for Molecular Genetics in Berlin, holds a very critical view of interventions in the human germline.

The genetic make-up of human embryos can be modified using CRISPR/Cas. What benefits do scientists hope this research will bring?

In my view, there is no medical indication for such research. Correcting genetic diseases at the embryo's stem cell stage is a purely theoretical possibility. Establishing this procedure would certainly not only involve huge costs but would also be superfluous, as embryos can already be tested for mutations as part of pre-implantation diagnostics. Only the healthy ones would then be placed in the womb.

The manipulation of embryonic stem cells also has far-reaching implications, as all of the organism's cells will then subsequently carry this change. In addition, it involves intervening in the germline, which means the modified gene is passed onto future generations through ovum and sperm cells.

Such research is prohibited in Germany by the Embryo Protection Act. Do you envisage this law being softened as in the United Kingdom?

First of all, while human embryos are indeed being manipulated in the UK, they are not used for implantation. That would also be illegal there.

The experiments currently being performed involve pure basic research. Scientists are seeking to discover which genes play a key role in the early development of the human embryo. Whether such research produces significant gains in scientific knowledge is highly contentious.

And there are of course risks too, as the technology being developed essentially paves the way for medical application. I can't imagine such research being carried out in Germany. There is clearly no medical indication for manipulating embryonic stem cells, and such research should not therefore be authorized in my view.

So where do you believe the benefits of CRISPR/Cas lie?

It provides incredible potential for basic research. By recreating modifications in the genome, the influence of individual genes on the organism can be tested, for example. This is also where I believe the greatest potential for application lies.

The major advancement achieved by this technology is the capability to change the genome with a high degree of precision. CRISPR/Cas enables targeted mutations and modifications to be made to a cell or organism and even allows new parts to be inserted.

CRISPR/Cas also opens up new opportunities in gene therapy in humans. How does that work exactly?

Gene therapy always concerns diseases caused by mutated or altered genes. Diseased cells are removed from the patient, for example from the blood. These are genetically modified in the test tube so that pathogenic mutation is corrected and then put back into the patient's blood. Such modification cannot be inherited, as no other cells – in particular ovum and semen cells – are affected.

What benefits does CRISPR/Cas offer for gene therapy?

Virus systems have thus far been used to make genomic modifications. An artificial virus infects the cells and implants the DNA fragments. The gene encoded in the fragments is precisely the one changing in the patient and which therefore no longer works properly. The healthy gene is then incorporated into the patient's genetic make-up.

Virus systems nevertheless have a major disadvantage: they insert the healthy gene into the genome randomly. This often causes problems, because if the gene ends up in the wrong place it can result in cell degeneration and the onset of cancer. Genetic treatment is therefore not used routinely at the moment.

Being able to insert the healthy gene with great precision – as is possible with CRISPR/Cas technology – would represent major progress. Even

though CRISPR/Cas is still in its infancy, this treatment is expected to be available in the not too distant future.

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