Concerns About CRISPR

A technique as powerful as CRISPR needs to be used with some caution. There are several concerns that have been expressed about the rapid development of this technology. For example, a virus has been adapted to be a vector for a CRISPR/Cas9 package designed to target genes a f ecting lung cancer in mice, and is delivered to the mice as an aerosol, which they inhale. Such an air-borne viral package is at risk of escaping the lab environment and being inhaled by a human who will also have the same target sequence as the mouse. CRISPR/Cas9 could then edit genes in their lung cells, with unknown consequences.

There are also serious concerns about the e f ects of 'o f -site' mutations caused by the CRISPR/Cas9 system attacking areas of the genome that it is not aimed at. The older ZFN and TALEN techniques use longer recognition sequences and so target areas of the genome more speci f cally. Shorter sequences mean that CRISPR/Cas9 may occasionally cut the genome in the wrong places. When this happens, mutations may lead to the development of cancer, and this is a real stumbling block to the application of CRISPR in human medicine.

Researches are developing ways to minimise the incidence of o f -target mutations by adapting the structure of the CRISPR/Cas9 system to make it even more speci f c. They are also developing ways of detecting o f -target mutations quickly and e f ciently using whole-genome sequencing.

There are wider ethical concerns about the potential use of CRISPR/Cas9 as a tool for editing germ-line cells (in embryos or gametes) in humans, which could lead to the production of 'designer babies'. In 2015 a group of Chinese scientists used CRISPR to modify the gene for beta-thalassemia (a serious genetic disease) using non-viable human embryos from fertility clinics. While none of these embryos could have developed into a baby, the work raises questions about whether such techniques are ethically acceptable. In 2016, scientists in London were granted permission by the UK Human Fertilization and Embryology Authority (HFEA) to edit the genomes of human embryos for research purposes. This represents the f rst, but probably not the last, o f cial endorsement of research of this nature.

Conclusion

The CRISPR/Cas 9 gene editing technology, developed by Jennifer Doudna and Emmanuelle Charpentier was the journal Science's breakthrough of the year in 2015. There is no doubt that this technology is revolutionising genetic engineering. It has made gene editing a fast and efficient tool that can be used widely by the scientific community. Recent research also suggests that CRISPR/Cas9 system can be used as a tool to explore epigenetics and the function of non-coding parts of the genome.

To be an acceptable tool for human gene therapy, CRISPR will need to have gene editing e f ciencies close to 100% and a risk of o f -site mutations of zero. Scientists are working towards these f gures, but they may yet be unachievable. Time will tell what the full potential of this breakthrough technology will be.

Questions

1. CRISPR stands for 'Clustered Regularly Interspaced Short Palindromic Repeats'. Explain what 'Palindromic' means in the context of CRISPR's DNA base sequence. (2)

2. The CRISPR system occurs naturally in many species of bacteria. Brie f y describe what bacteria use the CRISPR system for. (2)

3. What advantages does the CRISPR/Cas9 system have over ZFN and TALEN gene editing technologies? (2)

Answers

1. Palindromic means the DNA base sequences at either end of the repeats are complementary to one another. This allows the repeat to fold and form a hairpin structure with hydrogen bonds between complementary DNA bases.

2. Bacteria use CRISPR as a defence against viral attack. A section of the virus's DNA is stored in the CRISPR array and used along with a Cas protein to recognise and cut up copies of that virus which might invade the bacterial cell.

3. CRISPR/Cas9 is easier to use because the only novel element that is required is the synthetic guide RNA that is complementary to the target DNA sequence. With ZFN and TALEN, speci f c proteins also need to be made for each gene that is to be targeted.

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