GENE EDITING... QUO VADIS?

As discussed in the last editorial, modern gene editing is quite precise but it is not perfect. The procedure can be hit and miss, reaching some cells but not others. Even when Crispr gets where it is needed, the edits can differ from cell to cell, for example mending two copies of a mutated gene in one cell, but only one copy in another. For some genetic diseases this may not matter, but it may if a single mutated gene causes the disorder. Another common problem happens when edits are made at the wrong place in the genome. There can be hundreds of these "off-target" edits that can be dangerous if they disrupt healthy genes or crucial regulatory DNA.

Another controversial milestone is applying this technology in embryos with the added advantage that any edits will be passed on to future offspring [together with any undesirable off-target effects]. This is not science fiction, I repeat. In 2017, *Nature* published research relating to gene editing in embryos made with the sperm of a man who inherited a heart condition known as hypertrophic cardiomyopathy.[1] When the scientists made embryos with the man's sperm and healthy eggs from donors, they found that, as expected, about 50% of embryos carried the mutant gene. If the affected embryos were implanted into women and carried to term, the resulting children would inherit the heart condition. The researchers describe how gene editing, when performed early enough, at the same time as fertilisation, 42 out of 58 embryos, or 72%, were found to be free of the disease-causing mutation. Also in 2017, a similar technology, base editing, has been used to fix defective β-thalassaemia genes in human embryos.[2] Base editing, differs from gene editing in that it does not cut the double helix, but instead uses enzymes to precisely rearrange some of the atoms in one of the four bases that make up DNA or RNA, converting the base into a different one without altering the bases around it.

I know that discussing ethical issues merits more than a few words but let us consider the fact that today, people who carry certain genetic diseases prefer to opt for IVF and have their embryos screened for harmful mutations. If mutations are detected, these embryos are wasted. In specific scenarios, gene editing can help increase the number of embryos for implantation since this technology can eliminate such mutations.

The ramifications arising from such technology are infinite, including gene drives. Engineered gene drives have the power to propagate particular genes through an entire population of organisms, e.g. by implanting a fertility-reducing gene in malaria-carrying mosquitoes with a view to eradicate malaria. But still, this technology is controversial because it can have massive unintended ecological consequences.

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Editor-in-Chief: Dr Wilfred Galea
Managing Editor: Dr Ian C Ellul
Sales & circulation Director: Carmen Cachia

Email: mpl@thesynapse.net
Telephone: +356 21453973/4

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