Gene editing in the germline: pros and cons

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Genetic editing refers to the possibility to modify a specific DNA sequence by inserting, modifying or deleting genetic material to regulate or correct genes of interest. These gene editing technologies can be applied to modify the genome of somatic cells, stem cells or the germline. Several gene editing technologies have been established, however the CRISPR/Cas9 gene editing technology rapidly became the preferred choice. CRISPR/Cas9, which stands for 'clustered regularly interspaced short palindromic repeats' and the 'CRISPR-associated protein 9' is a gene editing technique based on an intrinsic defense mechanism found in bacteria. CRISPR/Cas9 has taken the world by storm in just a few years due to its high efficiency and user friendliness, providing vast opportunities for genetic modifications, even in the germline.

With this technology, hereditary diseases could be stopped in their tracks, as a possible alternative to pre-implantation genetic diagnosis. There are only few medical indications where gene editing in the germline is the only way to prevent inheritance of genetic disorders. For instance, an autosomal recessive disease in which both parents are homozygous (e.g. cystic fibrosis) or an autosomal dominant disease where at least one parent is homozygous (e.g. Huntington's disease) is likely to be considered for gene editing in the germ line. More importantly, CRISPR/Cas9 holds tremendous potential for elucidating crucial underlying processes regulating early embryogenesis in both human and mouse, as has recently been shown for the gene OCT-4. There is concern that embryo gene editing could spiral out of control, allowing parents to order a designer baby. This is highly unlikely since most of our talents and even or general phenotypic characteristics do not arise from a single gene, or even from an easily identifiable number of genes. Still, the first genetically edited babies have been claimed to be born in China. In human, several applications of CRISPR/Cas9 in embryos were described as a proof of concept, until recently only in research context. Due to some remaining safety issues and the thus far preliminary data on efficiency, the clinical application of CRISPR/Cas9 is not recommended at this moment in the human germline.