

Human germline genome editing: fact sheet

Purpose

- To contribute to evidence-informed discussions about human germline genome editing.

KEY TAKEAWAYS

- Gene editing offers the potential to improve human health in ways not previously possible.
- Making changes to human genes that can be passed on to future generations is prohibited in Australia.
- Unresolved questions remain on the possible long-term impacts, unintended consequences, and ethical issues associated with introducing heritable changes by editing of the genome of human gametes (sperm and eggs) and embryos.
- AusBiotech believes the focus of human gene editing should remain on non-inheritable changes until such time as the scientific evidence, regulatory frameworks and health care models have progressed sufficiently to warrant consideration of any heritable genetic edits.

Gene editing

Gene editing is the insertion, deletion, or modification of DNA to modify an organism's specific genetic characteristics. New and evolving gene editing techniques and tools (e.g. CRISPR) allow editing of genes with a level of precision that increases its applications across the health, agricultural, and industrial sectors.

These breakthrough techniques potentially offer a range of different options for treating devastating human diseases and delivering environmentally sustainable food production systems that can feed the world's growing population, which is expected to exceed nine billion by 2050.

The current primary application of human gene editing is on non-reproductive cells ('somatic' cells) where any changes to the DNA cannot be passed on to the next generation. Most human body cells are somatic – kidney, heart, brain, skin, bones, blood and connective tissue are all made up of somatic cells.¹

Somatic cell gene modification is delivering transformational health outcomes that have been elusive for traditional therapies.² The first trials for somatic cell gene editing procedures are now being approved and there is broad consensus that CRISPR may help precipitate treatments for previously untreatable conditions such as haemophilia, cystic fibrosis, and Duchenne muscular dystrophy.³ There is only one approved *gene therapy* for retinal dystrophy (Luxturna – Spark Therapeutics) plus Kymriah (Novartis) for Lymphoblastic Leukemia being only example of *cell-based gene therapy* ('gene editing') to date.

Germline cells are those involved in reproduction (i.e. sperm or egg cells) and editing these cells, their precursors or the cells of an early embryo means those changes would be passed on to future generations.

¹ <https://alliancerm.org/bioethics/>

² National Academy of Sciences: Human Genome Editing: Science, Ethics and Governance. Washington, DC, USA: National Academies Press; 2017. <https://www.nap.edu/read/24623/chapter/6>

³ [https://www1.health.gov.au/internet/main/publishing.nsf/Content/011C554B9847D6F0CA258169000FCBBE/\\$File/Final-Report-Oct2018.pdf](https://www1.health.gov.au/internet/main/publishing.nsf/Content/011C554B9847D6F0CA258169000FCBBE/$File/Final-Report-Oct2018.pdf)

In Australia, making heritable changes to the human genome is prohibited by the Prohibition of Human Cloning for Reproduction Act 2002: ⁴:

“15 Offence—heritable alterations to genome

(1) A person commits an offence if:

- (a) the person alters the genome of a human cell in such a way that the alteration is heritable by descendants of the human whose cell was altered; and
- (b) in altering the genome, the person intended the alteration to be heritable by descendants of the human whose cell was altered.

Penalty: Imprisonment for 15 years.

(2) In this section:

human cell includes a human embryonal cell, a human fetal cell, human sperm or a human egg.”⁵

The World Health Organisation has reinforced that ‘it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing.’⁶

Current issues/considerations

Early research into CRISPR has focused on gene editing of somatic cells, with consequences of any changes introduced limited to individuals being treated as the genetic modifications cannot be passed on to future generations. Risks associated with gene editing of somatic cells are therefore limited and (more) controllable.

Recently, researchers in the UK, China and USA have started to explore whether it would be possible to safely edit the genome of human embryos in laboratory studies – where there was no attempt to establish a pregnancy. However, in 2018 Chinese researcher Dr He Jiankui went one step further announcing the birth of twins following CRISPR genetic editing at fertilisation in an attempt to introduce a mutation associated with HIV immunity.⁷ Although the extent of the heritable changes remains unverified, this controversial announcement highlighted the significant scientific, ethical and regulatory implications of the use of such technologies.

Responsible and measured development of cell-based gene therapies takes time. Advances in somatic cell treatments have come after decades of research and around 20 years after the first gene therapy clinical trials. Long term safety has still to be determined, as evidenced by 15-year follow-ups required by the European Medicines Agency and the US Food and Drug Administration for gene and gene modified cell therapies.

Germline genome editing carries additional risks and uncertainties. These include:

- **Safety** – Safety must be assessed over generations, not just an individual patient’s lifespan, to thoroughly understand possible impacts and unintended consequences (e.g. modification stability, unanticipated heritable change). A key concern is not knowing if germline editing to

⁴ ibid

⁵ <https://www.nhmrc.gov.au/research-policy/embryo-research-licensing/commonwealth-and-state-legislation>

⁶ <https://www.who.int/news-room/detail/26-07-2019-statement-on-governance-and-oversight-of-human-genome-editing>

⁷ <https://www.nature.com/articles/d41586-019-00673-1>

correct a genetic abnormality in one area will adversely affect other genes along the same DNA strand or elsewhere in the genome.

- *Efficacy* – It takes time to determine whether new therapies will be effective, which requires testing for efficacy.
- *Ethics* – Legitimate and complex ethical questions are raised such as:
 - What diseases/conditions should be gene corrected that can't be address through other approaches (monogenetic, no other co-morbidities, no other specific ongoing maintenance costs, other criteria)?
 - How is misuse to be prevented? How should this technology be regulated and by whom?
 - What is the most appropriate access equity model?
 - What does it mean for performance traits e.g. elevating testosterone, dopamine, EPO?

Regulatory and healthcare models are still catching up. Gene therapies are new and pose challenges for current regulatory frameworks and regulators. Cell-based gene editing treatments also disrupt current health models by using one-time treatments that may come with high upfront costs, as opposed to the current largely prescription-based approach. However, public opinion is beginning to show more support for such technologies when applied for therapeutic purposes.

Permitting genome editing of germline cells is a step we do not yet necessarily have to take. Once heritable changes are introduced into the genome, it will be difficult to reverse. A clear and demonstrated need is required before venturing down this path. Existing technologies, such as preimplantation genetic diagnosis (PGD) to screen embryos for specific mutations, are already available to couples at risk of passing some genetic conditions. Germline genome editing technology maybe an option when PGD is unable to assist, such the rare case where due to an autosomal dominant inheritance or expression any child will be born with major health consequences or premature death.

AusBiotech's position

Overall, AusBiotech supports a sensible, scientific, and evidence-informed approach to adoption of gene editing techniques. This should include monitoring of technological progress towards address current limitations that affect safety and efficacy as well as continued engagement amongst patients, medical researchers, bioethicists, industry and the wider community. Regulatory certainty is also important for researchers and industry.

More specifically, AusBiotech is supportive of the Alliance for Regenerative Medicine's bioethical framework approach for genetic modification consistent with these principles⁸:

1. We endorse investigation of therapeutic applications of gene editing of somatic cell gene editing.
2. We support the use of gene editing standards to facilitate the development of safe and efficacious gene editing therapies.
3. We call for the continued evolution of national and regional regulatory frameworks governing the development of somatic cell gene editing techniques.
4. We assert that germline gene editing is currently inappropriate in human clinical settings.
5. Common commitment: Unless and until ethical and potential safety questions with respect to germline gene editing are adequately addressed, we do not support or condone germline gene editing in human clinical trials or for human implantation. We believe that these are international concerns and would be supportive of an effort to discuss therapeutic gene editing issues on a global stage.

⁸ <https://alliancerm.org/press-release/the-alliance-for-regenerative-medicine-releases-statement-of-principles-on-genome-editing/>