

Overarching Principles for Governance of Human Genome Editing



Any nation considering governance of human genome editing can incorporate these principles—and the responsibilities that flow therefrom—into its regulatory structures and processes.



Example of Huntington's Disease

About **30,000** Americans have HD. **200,000** more are at risk.

BASIC RESEARCH

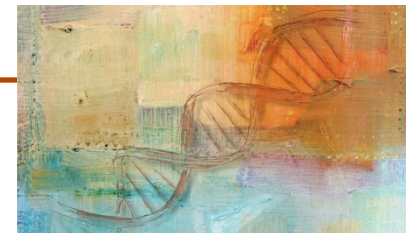
Scientists are already researching how to “delete” the genetic abnormality that causes HD.

SOMATIC THERAPIES

“Somatic cells” make up the tissues of the body. One day, doctors might be able to use genome editing techniques in somatic cells to treat someone with HD.

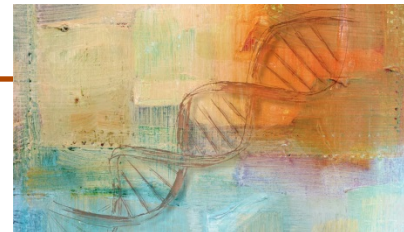
GERM CELL THERAPIES

“Germ cells” are reproductive cells that give rise to sperm or eggs. Therefore, characteristics of germ cells get passed to the next generation. One day, doctors might be able to use genome editing techniques in germ cells to ensure that parents with HD don't pass the disease to their children.



Basic Research

- **Basic research uses:**
 - somatic cells (e.g., blood, liver, heart cells)
 - germline cells (e.g., eggs, sperm, early-stage embryos)
 - pluripotent stem cells (e.g., ES and iPS cells)
- **Important to advance understanding of:**
 - gene functions and regulation,
 - DNA-repair mechanisms,
 - Cell biology, stem cells and immunity,
 - Human fertility, reproduction and fetal development,
 - Links between genes and disease,
 - Progression treatment of diseases with a strong genetic component



Somatic Therapy

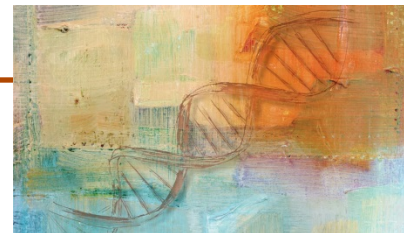
- Genome editing is a new tool for gene therapy
- Approaches for somatic interventions:
 - outside the body (*ex vivo*) by removing cells, editing them and reinserting them
 - Ex: editing blood cells for treatments of cancer (immunotherapy) or HIV
 - Ex: editing blood cells for sickle cell disease, thalassemias
 - directly in the body (*in vivo*) by injection, which carries more technical challenges at this time
 - Ex: editing liver cells for hemophilia
 - Ex: editing muscle cells for muscular dystrophy

N.B. Generally done on children/adults but might also become useful for in utero fetal therapy, e.g., using edited stem or progenitor cells



Enhancement

- Making changes beyond ordinary human capacities; or anything outside of treatment/prevention of disease and disability
- Significant public concern about fairness, if available only to some people, and about creating pressure to seek out enhancements
- But many other kinds of enhancement are tolerated or encouraged: Nutrition, education, cosmetic procedures
- Potential for uses of genome editing beyond therapy
 - Ex: curing muscular dystrophy vs becoming stronger than the normal
 - But range of possible uses of approved therapies for enhancement seems limited
- Enhancement unlikely to offer benefits sufficient to offset risks at this time



RECOMMENDATIONS

Enhancement

- Genome editing for purposes other than treatment or prevention of disease should not proceed at this time
- Do not extend genome editing to purposes other than treatment or prevention of disease without extensive public input

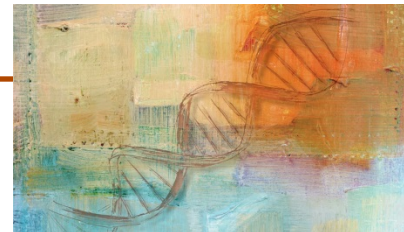


Heritable Genome Editing

- Achieved in animals, but there are currently major technical challenges for safe and predictable use in humans and will require significant further research and development before it could be considered for clinical trials.

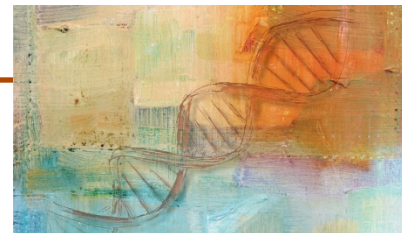
POSSIBLE METHODS:

- Editing cells that give rise to sperm or, perhaps, to eggs
- Editing the fertilised egg (zygote)
 - The first method allows verification of the edits
 - The second is more difficult to verify and currently carries a risk of mosaicism (where not all cells in the embryo carry the desired genetic alteration).



Heritable Genome Editing: Concerns

- Genetic changes may be inherited by the next generation
- Commonly viewed as unacceptable in the past:
 - multigenerational risks (but also possible benefits)
 - need for (and possible difficulty of) long term follow-up
 - lack of consent by affected persons (future child; generations)
 - the degree of intervention in nature
 - affecting acceptance of children born with disabilities
 - a step toward enhancement for “designer babies”



Heritable Genome Editing

- In light of recent advances, it is now a realistic possibility, so we need a fresh look at earlier views
- Interest driven by the thousands of inherited diseases
- Would allow individuals to have genetically related children without passing on a known risk of genetic disease
 - In many cases, preimplantation genetic diagnosis is an alternative
 - In many cases, prenatal diagnosis and selective termination is an alternative
 - For some, these alternatives are unacceptable
- In some cases, there are no alternatives that retain the parental genetic connection
 - Ex: a parent who is homozygous for Huntington's disease variant

