# Human Genome Editing

## Background on the Science

Innovation in the biotechnology sector has led to a critical scientific breakthrough – genome editing. Genome editing is an umbrella term for a range of tools[1] that enable precise changes to the genome, the organism's code of life. Applied worldwide by researchers in academia, governmental research institutions and industry, genome editing represents a promising next step in research towards beneficial uses in medicine, agriculture and the bio-economy aimed at addressing some of society's grand challenges.

This document provides background information on the science of this emerging technology.

### How the Genome Editing Process Works

The genome is comprised of DNA and functions as the "instruction book" of a cell. Genes are specific strands of DNA, which provide the cell instructions for making different proteins. Genome editing is a process by which a strand of DNA is modified to produce a desired outcome.

Genome editing is based on a naturally occurring system that directs a molecular scissor, called a nuclease, to a target region of DNA. The DNA is targeted by a recognition signal that is specific to a fragment of DNA. Once the nuclease has been directed to the appropriate region of DNA, it cuts the DNA. The DNA is then repaired by a process found naturally in each of our cells. This repair machinery is used to fix any break that may occur within the DNA. Once the DNA is cut, the cell can be directed to repair that region of DNA in three different ways:

[1] Genome editing methods allow for changes at targeted sites and include *inter alia* ODM (oligonucleotide directed mutagenesis), and a range of site directed nucleases (SDNs) such as CRISPR-Cas (Clustered regularly interspaced short palindromic repeats) and TALEN (Transcription activator-like effector nucleases) and ZFN (Zinc Finger Nucleases).

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1. Insertion of a DNA sequence, when a template DNA is provided to the cell in parallel with the targeted cutting.
2. Deletion of a DNA sequence, when two regions of DNA are cut.
3. Change of a DNA sequence, when a corrective template DNA is provided.

## Human Genome Editing

Humans have approximately 20,000 genes, and there are more than 6,000 genetically based diseases. In human health, researchers are exploring ways to use genome editing of somatic (non-heritable) cells to treat or prevent genetically-based human diseases.

### Somatic versus Germline Cells

The ICBA shares the view reached by other leaders in the scientific and regulatory community, including the National Academies of Sciences and Medicine (NAS/NAM), that clinical applications of genome editing in somatic (non-heritable) cells can be appropriately evaluated within existing, well established regulatory frameworks. As regards germline (heritable) genome editing, the ICBA views the science as having not advanced sufficiently for clinical applications to be appropriate at this time.

#### Somatic Cells

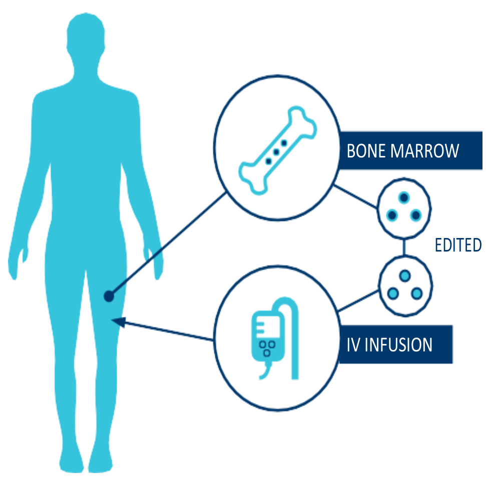
Somatic cells are cells whose genetic material cannot be passed on to future generations. The vast majority of cells in the human body are somatic cells.

#### Germline Cells

Germline cells (or germ cells) are cells whose genetic material may be passed on to future generations; these include sperm, egg cells, or fertilized embryos.

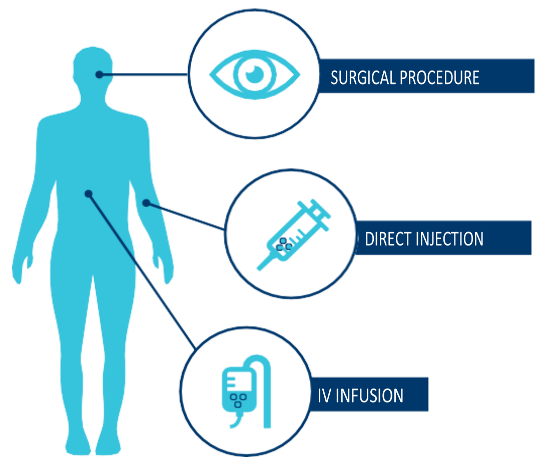
How Somatic Cell Genome Editing Works in Patients

Somatic cell genome editing can happen outside the body (ex vivo) or inside the body (in vivo). Each method has benefits and limitations, and the preference of method depends on the disease being treated.




Ex Vivo Genome Editing

In Ex Vivo Genome Editing, the target cells — for example, blood cells — are first removed from the patient. The cells are then treated in a laboratory to edit the target gene, and return back to the patient.




In Vivo Genome Editing

In Vivo Genome Editing occurs inside the human body and is directly delivered to the target site — for example, a diseased liver — where the genome editing therapy would find and enter the target cells.

# Food & Agriculture Applications of Precision Biotechnology

Precision biotechnology tools, such as gene editing, hold tremendous promise to advance agriculture globally and help countries achieve key milestones in the United Nation's Sustainable Development Goals, such as zero hunger, clean water and climate action. Public and private researchers around the world are using these tools to make food healthier, more resilient, abundant and affordable, and to better protect the environment and animal welfare.

## Plant Genome Editing

Agricultural scientists and plant breeders are researching and developing gene-edited agricultural and food products. This research has the potential to address some of societies largest challenges surrounding food production and food security by making crops more abundant, resilient and further improve quality.

Gene editing is one of many different methods, including crossbreeding and grafting, that scientists can use to create improved varieties of plants. By making targeted changes in DNA, scientists are able to turn a gene's expression on or off and recreate a gene from within the plant's family. Thanks to gene editing, plants can become drought-tolerant or pest-resistant.

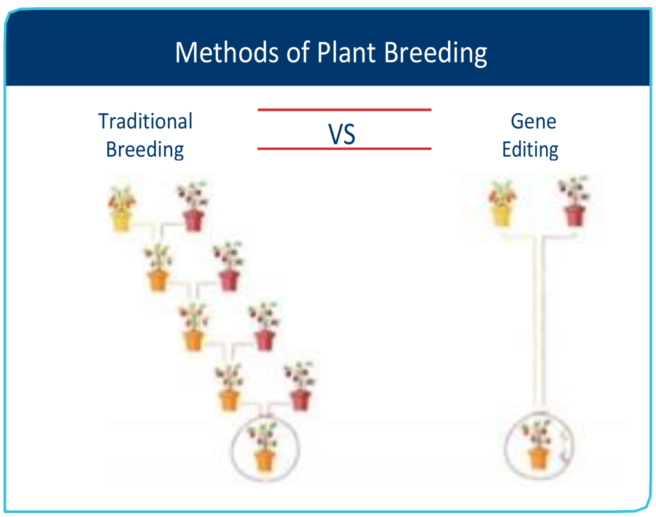
Gene editing's highly targeted approach can bring about improvements in a single generation of plant, while previous breeding methods were far less precise and could take generations to be effective.

Research is currently focusing on:

- Eggs, milk, wheat, nuts and other food products, with lower allergenic potential or to avoid food intolerances
- Healthier oils that replace trans-fat
- Pest- and disease-resistant crops and vegetables

How Does Gene Editing Work in Plants?

- Evolving methods like gene editing allow us to work within a plant's own gene pool — without the introduction of foreign DNA — to achieve the same end-result that could be achieved through more traditional plant breeding methods, but in a more targeted way.
- This added precision allows breeders to introduce specific characteristics directly into elite breeding lines without multiple cycles of backcross breeding




Promising Research

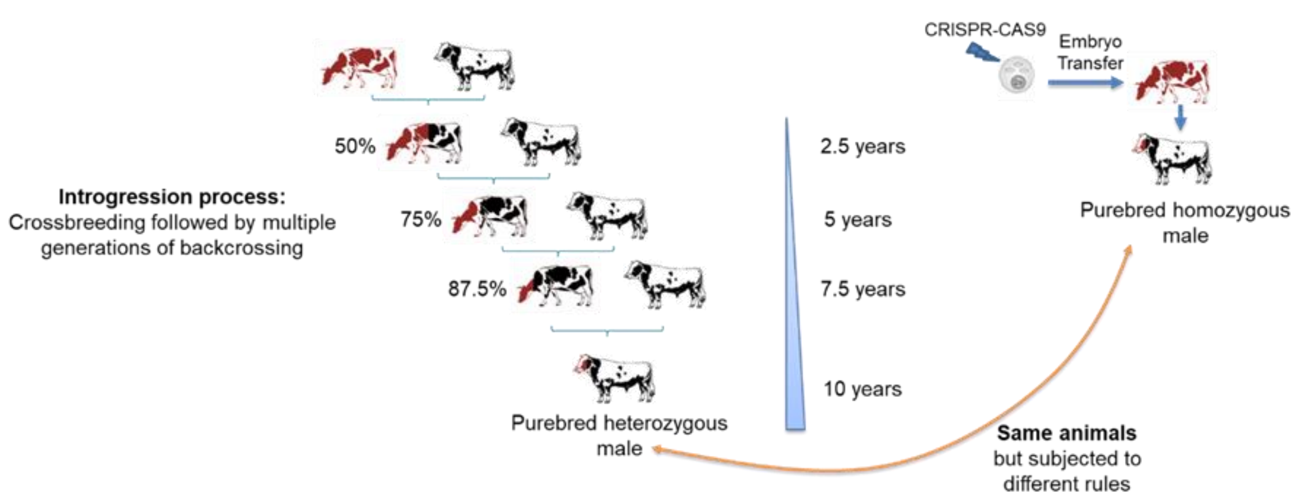
- In the pipeline are important traits that will improve plant health and reduce the use of pesticides such as varieties of spinach and grapes that are resistant to downy mildew and normally require multiple sprayings per season to control.
- Scientists are increasing crop sustainability by improving drought and heat tolerance.
- Research is underway to improve the genetics of rice to make high-yielding, disease resistant varieties that tolerate marginal soils that would particularly benefit farmers in developing nations, who lack access to many agricultural inputs and production technologies.
- Modern plant breeding tools are delivering on important consumer traits such as reduced gluten wheat and soybeans with healthier oil content and improved protein composition.

## Animal Genome Editing

Improving the welfare of animals, their sustainable production and ability to resist or transmit disease has become an area of heightened societal interest. Independent researchers and farmers are committed globally to advancing these goals and consumers are looking for more information with respect to these practices when making food choices.

The history of selecting animals such as cows, chickens, and pigs with improved genetics has provided steady improvement to their sustainability, welfare and disease resistance. However, the benefits to the animals and to society can be greatly improved using more modern breeding techniques, such as genome editing, that continue to tap into the significant genetic potential that exists in the animal's own natural genetic code. In other words, changing the genomes of animals is not new, and ultimately, neither are the results that we can achieve. The benefit of genome editing, in combination with classical breeding and genomics, is we can now do it in a manner that is more informed, and more precise and therefore can better serve our goals for the animal itself, as well as society at large, more readily. Genetic progress in animal breeding takes also a lot of time because of generational interval. Genome Editing allows to spare time and resources making this progress faster.

In terms of preservation of genetic resources, Genome Editing is a strong additional tool to keep larger population (genetic diversity) by introducing also the "new" trait from another breed or population.



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Promising Research

- In the pipeline are important animal health traits; such as diseases resistance diseases in pigs and cattle (PRRSv, African Swine Fever or bovine tuberculosis) that could be also a deal for Human Health because they are zoonosis and decrease immune response in animals; raising Antibiotics use. Diseases resistance is also an important economical trait to improve because the huge amounts of money spent in eradication programs in livestock all around the world
- Animal welfare; like hornless dairy cows, that will no longer need to have horns physically removed. This trait is already removed by classic genetic selection, but genome editing allows to spare time and resources
- Scientists are also exploring ways to use genome editing to inhibit mosquitoes' ability to transmit diseases such as malaria, dengue fever and the Zika virus.
- Research is underway to improve the genetics of cattle for hot, tropical climates so they can be more tolerant of heat, potentially boosting protein production by as much as 50 percent and thus improving people's lives in areas of extreme poverty.