

# Genetic manipulations

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# 1 Introduction

## 1.1 The subject

We decided to talk about genetic manipulations because it is an interesting subject and there are a lot of research going on. Also, the promises of this field are quite interesting but they raise some issues. We decided that we should work on one or more subjects, such as:

- Transhumanism
- Cures
- Eradication of invasive species
- GMOs
- Hybrids
- And all the problems that come along with all that

## 1.2 A short history of

### 1.2.1 How DNA works

DNA is the basic genetic material, that gives rise to our traits, like eye color or height, and that is located inside the core of all our cells. In order for the traits to be expressed, DNA must first be transcribed into RNA which is then in turn transcribed into proteins. Those proteins then leave the cells and carry on their messenger duty to transmit informations to other parts of the body. Hormones, like insulin or testosterone for example are proteins.

### 1.2.2 Genetic manipulations

Gene manipulation on plants started with agriculture as early as 10,000 B.C.<sup>1</sup>, with the farmers simply selecting plants with the most desirable traits. This knowledge was used by ancient civilizations through interspecies breeding to create new crop strains with better qualities such as increased yield, increased tolerance, and even longer storage period.

Indeed, science grew a lot since then, and ever since the start of molecular genetics, this field amazed by the many applications in the real world and the problems they could solve, and even though such applications failed to come to use quickly, we are still getting closer and closer to the day we can genetically engineer human beings.

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<sup>1</sup>[https://en.wikipedia.org/wiki/Plant\\_breeding](https://en.wikipedia.org/wiki/Plant_breeding)

## DNA replication transcription and translation

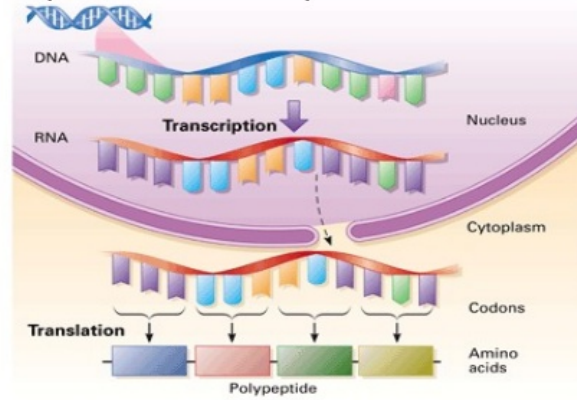


Figure 1: Picture of DNA

Quite recently, the discovery by Emmanuelle Charpentier and Jennifer Doudna of CRISPR<sup>2</sup>/Cas9, a relatively easy-to-use and cheap tool for editing DNA should allow for easier and more efficient research.

### 1.2.3 DNA sequencing

In the meantime, DNA sequencing achieved a significant victory in 2000 after the sequencing of an entire human genome.<sup>3</sup> Initially costing several million dollars this technique is now making its way to modern medicine as it is getting more and more efficient and cheaper. This helped biologists discover the mutations that cause some diseases, such as the CTFR<sup>4</sup> gene mutation causing cystic fibrosis<sup>5</sup>, a rare genetic disorder affecting mostly lungs, or haemoglobin gene mutations that can cause disease such as the sickle-cell disease<sup>6</sup>.

### 1.3 The techniques

Many techniques have been used during the past to alter DNA, such as zinc finger nuclease and TALENs, but the most promising one, CRISPR/Cas9 saw the light quite recently, in 2012. It is so promising, in fact, that it has been the American Association for the Advancement of Science's choice for breakthrough

<sup>2</sup><https://en.wikipedia.org/wiki/CRISPR>

<sup>3</sup>The Human Genome Project

<sup>4</sup>Cystic Fibrosis Transmembrane Conductance Regulator

<sup>5</sup>[https://en.wikipedia.org/wiki/Cystic\\_fibrosis](https://en.wikipedia.org/wiki/Cystic_fibrosis)

<sup>6</sup>[https://en.wikipedia.org/wiki/Sickle-cell\\_disease](https://en.wikipedia.org/wiki/Sickle-cell_disease)

in the year 2015. It makes things so much more easier than before, that by 2014, many studies have been carried out, using CRISPR/Cas9, in different fields, from biofuel engineering, to genetically modified crop strains.

But although this technology is showing some interesting results, experts say that it is not yet fit for human genome editing and probably won't be for the next decade. Still, CRISPR raises interesting questions, especially since it is so easy to use, compared to other technologies, that undergraduate students can use it. More than ever, bioethics debates should take place, in order to prevent misuse of genetic editing tools.

## 2 The promises of genome editing . . .

### 2.1 Preventing epidemics

For 20 years, the James Lab (University of California) tried to create malaria-resistant mosquitoes, with a success rate of about 50%. In 2015, 2 San Diego scientists, Ethan Bier and Valentino Gantz announced a new method for generating mutations on both copies of a gene in fruit flies. The mutations were then passed on to 95% of the flies' offspring. Combining the two techniques, a collaboration of both teams succeeded in creating malaria-resistant mosquitoes that pass on this ability to 99.5% of said mosquitoes' offspring<sup>7</sup>.

With more than 200 million people infected, according the World Health Organization, this technique, if used outside a laboratory could relieve the pain of poor countries with little to no medical supplies, especially on the african continent. And this technique doesn't only apply to mosquitoes, it could be used to eliminate other disease vectors like yellow fever.

### 2.2 Curing diseases

In october 2016, physicians from UC Berkeley, led by Mark DeWitt published a paper in *Science* in which they claim to have found a preliminary technique involving gene editing in stem cells in order to cure sickle cell disease.<sup>89</sup> Sickle cell diseases causes blood cells, that are produced in bone marrow, to have a "C" shape and be less flexible than regular blood cells. The conventionnal treatment to SCD involves bone marrow transplant, and chemotherapy, to supress one's immune system, followed by immunosupressant drugs, to reduce the risk that the body rejects the foreign tissue. This, of course, makes the treatment very heavy and hard to achieve, as one must, in addition wait for a compatible bone marrow donor, and then undergo a dangerous and painful surgery.

That's where genetic engineering comes to play. SCD is caused by a recessive mutation affecting a single nucleotide present on both copies of a gene coding for beta-globin, and although DeWitt's team's success will have to be improved, correcting this mutation using genetic tools could prove much an easier, cheaper and safer way to cure SCD.

Again, curing SCD is but an example of what can be achieved through genetic manipulations

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<sup>7</sup><https://news.uci.edu/research/university-of-california-scientists-create-malaria-blocking-mosquitoes/>.

<sup>8</sup><http://www.latimes.com/science/sciencenow/la-sci-sn-crispr-sickle-cell-20161012-snap-story.html#>

<sup>9</sup><http://news.berkeley.edu/2016/10/12/genome-engineering-paves-way-for-sickle-cell-cure/>

## 2.3 Improving mankind

Transhumanism is a movement that aims to take advantage of the advancement of technology, like information technology, genetic engineering and artificial intelligence, to enhance the human condition and the human organism. Of course, experiments on human beings is forbidden, so such research has to be conducted on animals. Chinese biologists at the Guangzhou Institute of Biomedicine and Health “created” beagles with double the amount of muscle mass, as you can see below.



Figure 2: Picture of improved dog

These dogs are currently used for biological and medical purposes could later serve as police dogs, for example. Other teams in China also postulated that they could modify dogs genomes in order to enhance their intelligence or cure illnesses. According to Lai Xiang, head of the Chinese beagle project, “dogs are very close to humans in terms of metabolic, physiological, and anatomical characteristics.”<sup>10</sup>. Such research opens the way for a new era for mankind.

<sup>10</sup><https://www.technologyreview.com/s/542616/first-gene-edited-dogs-reported-in-china/>

## 3 ... and the complications they raise

### 3.1 Ethical questions

Genome editing techniques might help us cure diseases in the future, but some concerns are growing over what humans will do of it<sup>11</sup>. It has come to attention that these techniques could also be applied to “treat” unwanted physical characteristics that are in no way harmful. The first examples that come to mind are eye color, height, of physical strength, but genetic engineering could also alter DNA out of the scope of human genetic variability, by creating new eye colors (like purple). This raises the question of how to use DNA altering tools on criteria as subjective as physical appearance. Of course, we could edit one’s genome to make them more physically attractive if they suffer malformations for example.

All this means we have to draw the line somewhere, and the obvious tool to do that is indeed legislation.

### 3.2 The social issues

As discussed before, future parents wanting their child’s life to be a little easier may choose genetic enhancements that makes the child taller, for example. Indeed, being tall is seen as advantageous and evidence show that taller men earn more money and are more physically able<sup>12</sup>. Such behavior would, in practice, divide the population on numerous topics. Those who are favorable to genetic modifications, and those who are not. Those who benefited from genetic manipulations, and those who did not. Even worse, what about people who didn’t benefit from such treatment because they couldn’t afford it ?

On another topic, how do we define human “normalness” ? Suppose, the average human height is 175cm and one is considered tall if they measure 185cm or more. 55% of the people on Earth have brown eyes, while 8% have blue eyes. If we start messing around with our genes to make people taller and give them a specific eye color, how do we define the average human characteristics ? If everyone is taller than 185cm, can they still be considered tall ? Indeed, admist everyone around them, they would seem pretty average. Do we then keep making people taller and taller just to fit the desire to be taller than everyone else ? That would be unwise.

Furthermore, as of today, gene editing technologies are far from ready.<sup>13</sup>

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<sup>11</sup><https://sciencebasedmedicine.org/crispr-and-the-ethics-of-gene-editing/>

<sup>12</sup><http://www.nickbostrom.com/ethics/genetic.html>

<sup>13</sup><http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378>

### 3.3 The legislation in the European Union

#### 3.3.1 GMOs

GMOs are a good example of what can be achieved through genetic manipulations, and for that, it is interesting to briefly look at the legislation addressing them. As of now, the European Union law regarding Genetically Modified Organisms aims to ensure tracability, clear labelling and to protect the environment, as well as human and animal health. As such, genetically modified food has been authorized for agriculture use, as long as its origin, composition and properties are accurately labelled, in order for livestock farmers, for example to be able to make an informed decision when buying genetically modified food<sup>14</sup>.

By comparison, the vast majority of food in the United States comes from genetically modified animals, and the US law doesn't force them to put a label on products that indicates they come from genetically engineered sources<sup>15</sup>.

#### 3.3.2 Research

Whatever the benefits or the risks, a legislation has to be made in order to determine a legal framework for the use of genetic engineering tools. On May 2006, a conference for stakeholders and citizens debating the 25 recommendations of the European Commission Group on the ethical, social and legal applications of genetic testing took place at the European Commission in Brussels.<sup>16</sup> The Expert Group included patients organisations, pharmaceutical industries, scientists, lawyers, ... with the purpose of reaching a consensus regarding genetic testing. The following 25 recommendations are organised into 3 chapters addressing a general framework, implementation of genetic testing in healthcare systems and genetics testing as a research tool. Some of those recommendations include :

- public information
- protection from discrimination
- regulatory framework

The one we're mostly interested about is indeed the regulatory framework. Its purpose is to recognise the need for new tests and the importance of safety, clinical validity and reliability as well as passing laws obligating all tests to be conform to the standards before clinical use.

Unfortunately, we found no legislation, or official talks related to the misuse of genetic engineering tools, but it will surely become a front-end topic in the years to come.

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<sup>14</sup><http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32003R1829&from=EN>

<sup>15</sup>[https://www.ted.com/talks/paul\\_root\\_wolpe\\_it\\_s\\_time\\_to\\_question\\_bio\\_engineering](https://www.ted.com/talks/paul_root_wolpe_it_s_time_to_question_bio_engineering)

<sup>16</sup><https://ec.europa.eu/research/press/2004/pr2204en.cfm>