Homework #6

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Syntactic Modeling of Biological Systems
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Context

An organism is a species of animal or plant that is studied to understand biological, genetic, metabolic processes, etc., in order that the discoveries made on the current model organism may be extrapolated to other organisms (discoveries made to give the way of functioning / an idea of operating mode for much larger set of species). In addition, for ethical reasons, humans cannot be model organisms.

In order to provide a perspective on how biology works, a model organism must have a number of properties, such as: multiplication time (a multiplication time is desired as little as possible so that multiple generations can be studied quickly), accessibility in the environment

(it is desired a widespread organism or to which there is access without much cost), genetics (species with large chromosomes are desired, possibly with a small number of chromosomes), stability with mutations (so the child generations of a species to suffer as few mutations as possible so that the degree of genome conservation from one generation to another is maximized, in order to study the voluntary changes, made in the laboratory, not those generated by nature, such as mutations, etc.

When a link between a certain human disease and a particular gene is discovered, the gene is analyzed in a model organism in order to find out what causes that disease. In other words, if an animal model organism suffers from a natural or induced cause disease, and the disease is similar to the human condition, then it can be studied in a simplified context of the model organism (which, in principle, is not as complex as the human) and isolated. Everything is happening in a much shorter time than in humans (because a model organism has the time of multiplication, implicitly by the shorter life than the human).

Example of a model organism

Model organisms vary widely, from viruses, prokaryotic and eukaryotic bacteria to fungi, plants and animals (vertebrates and invertebrates). Below we will analyze only a few of these species, the ones that are the most studied.

The house mouse (Mus musculus)

The most beloved model organism is the mouse. Because they have a period of sexual maturity after 10 weeks, it has a period of birth of 3 weeks, it is mammal and it resemble physiologically and genetically with humans. In addition, many of the human-specific diseases exist in mice. Another advantage is that the mice can be easily manipulated with CRISPR-Cas-9. Mice served as a model organism for studying Down syndrome, heart disease, cancer and leukemia. One of the major disadvantages is that the mice do not support genetic insertion and only DNA end extension.

The fruit fly (Drosophila melanogaster)

Another highly performing model organism is Drosophila melanogaster because it has a relatively short life span of 8-14 days, makes many offspring in the form of an egg and is easily genetically modified (has very large chromosomes). In addition, it is estimated that 75% of disease-causing genes for humans have a functional counterpart in Drosophila melanogaster (Pandey and Nichols, 2011). Another important advantage is that a particular gene or series of genes can be suppressed using GAL4 / UAS and LexA technology.

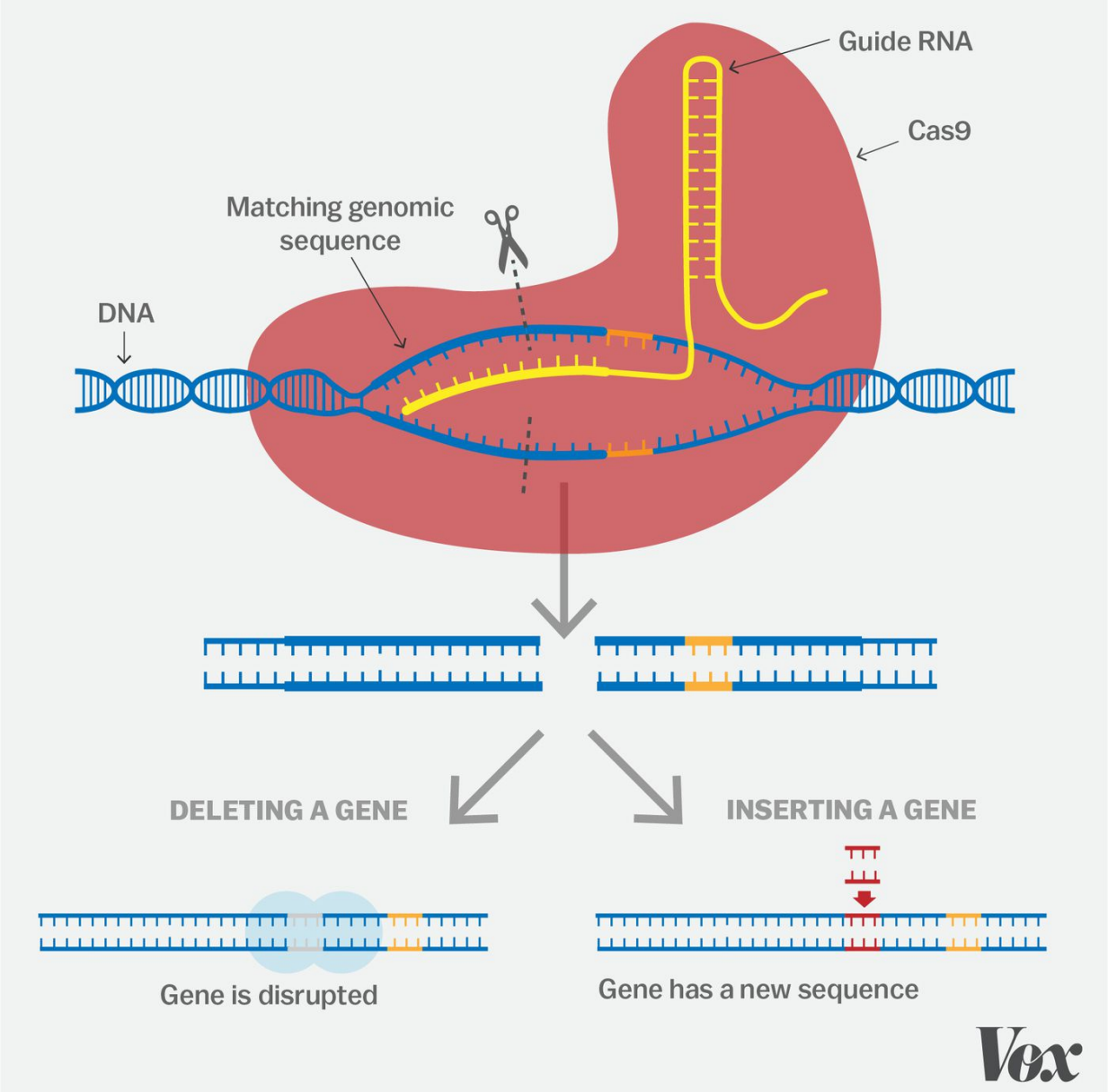
Yeast (Saccharomyces cerevisiae)

Yeast is a single-celled eukaryotic organism used primarily to study genetics. It is easy to manipulate genetically, multiplies every 2 hours and is very cheap. In addition, 23% of the yeast genes are common with those of the human (Liu et al., 2017). Due to their simplicity, these model organisms are used for the study of neurological diseases, especially Parkinson's disease but also for the study of cancer.

Zebrafish (Danio rerio)

Zebrafish is another model organism preferred by scientists because they are small, easy to maintain, produce about 300 eggs at a time. In addition, humans have a genetic similarity of about 70% of zebrafish genes. Furthermore, 85% of human disease-producing genes have a counterpart in zebrafish (Howe et al., 2013). Another major advantage is that they have chromosomes that are transparent and easy to manipulate genetically. They were studied for how insulin is produced and how embryonic development occurs.

CRISPR-Case9



How CRISPR lets us edit our DNA — Jennifer Doudna

Since ancient times there has been a continuous battle between bacteria and viruses. A number of bacteria have developed a very interesting antivirus system over time. That is, in their genetic code they inserted viral DNA (their own genetic record of the bacterium called CRISPR, or the vaccine book of the bacterium - the history of infections (of the previous generations)).

When a virus attacks such a bacterium, the bacterium will generate an RNA copy of the viral genome (from its own archive - CRISPR) and pass it on to the Cas9 protein that will search inside the bacterium for viral DNA that has matching viral RNA. generated by bacteria. When such a matching is tasted, the protein will cut the DNA of the virus making it harmless. In addition CRISPR is programmable, meaning that Cas9 protein can be given any RNA and it will search for matching to cut DNA sequences at specific locations. This works for all living cells.

This allows deletion or insertion of one DNA sequence into another DNA, which offers a huge advantage in treating genetic diseases. For example, sickle cell anemia, which is caused by a mutation - the wrong letter on a particular gene. In addition, CRISPR technology has been used to change DNA in mice, monkeys or even humans (in China). Of course, doing this raises a lot of ethical questions.

Gene editing can now change an entire species – forever — Jennifer Kahn

Malaria is one of the diseases that kills about 1000 people daily on the planet. Malaria is known to be transmitted from a series of mosquitoes to humans. So for 2 decades, researchers have been working on the genetic editing of mosquitoes so that they no longer carry malaria. This was achieved using CRISPR-Case9 technology. However, in order to perpetuate the antimalarial gene in future generations, there are 10 times more genetically modified mosquitoes than the unmodified ones, so that at one point all the temptations are anti-malaria (for 1,000 mosquitoes 10,000 mosquitoes are required), which not feasible. To solve this, mosquitoes have been modified in addition so that their genome contains CRISPR information (ie how to copy and paste oneself). Thus, a generation of mosquitoes between one modified and one unmodified one is 100% modified. and not 50% modified. In this way, the genome of any species can be modified - leaving such a modified specimen released that after a series of generations the entire species will be modified. In this way species can be eradicated, forcing the descendants of a modified specimen to be all male.

What you need to know about CRISPR — Ellen Jorgensen

CRISPR-Case9 technology is known to be cheap and easy to use. Next we will discuss each aspect separately. First, the costs are reduced relative to the costs of conventional genetic editing technologies, at present the costs range from several hundred to several thousand US dollars. In addition, the time to make a genetic modification decreases from weeks to several days. Secondly, CRISPR technology is easy to use. This is true after a few years of practice. An RNA sequence that corresponds to the searched DNA is required, the DNA segment that is to be inserted is still needed. If it is not known exactly where to make the cut (ie the nucleotide sequence before the cut) then Case9 RNA cannot be supplied to the protein. Another problem arises when generating RNA for Case9 protein. All of these things

are a series of impediments, but they are much finer than the impediments of conventional genetic editing technologies.

The ethical dilemma of designer babies — Paul Knoepfler

Because CRISPR-Case9 is a new technology - it is a few years old, the long-term consequences of genetic modification on human embryos are still unknown. Genetic editing of human embryos raises a lot of ethical questions. But when the world is doing enough in society, this will lead to even greater growth, an exponential one in the end. Moreover, in vitro fertilization, a new technology 50 years ago, was accepted by the society, and currently there are 5 million people who were conceived in vitro. At present, only one case of genetic editing on human embryos is known, in China, where children have been screened immune to HIV.