The Harvard Mouse

or

the transgenetic technique

Term Paper Biology

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PREFACE

What is my motivation to work on the chosen topic?

There are many reasons. One of them is that it's a very interesting topic. It is fascinating, how you can increase or decrease the functionality of organisms.

What is especially interesting?

The intricacy. And that you can use the method not only for mice but for every organism. For example in the Green genetic engineering (to make plants more resistant) or for pharmaceuticals like human insulin.
Some genes are responsible for the aging process. So if we can find those genes and deactivate them we would life longer. First successful experiments with animals where already made.
What I also like about this topic is the big ethic question behind it. I mean in the end we use animals, often mice because of their similarity to our genes, to benefit of them. We intentional make them ill and lock them into small cages. But on the other hands medicaments can be tested or invented which can save many human lifes.

What are my questions with respects to the chosen topic?

What is the process of transgenetic engineering?

What can you do with it?
Where do you use ist

INTRODUCTION

What is the context of the chosen topic?

All living organism have cells – at least one - and genes. The topic I chose is about how you can change this genes and therefore the abilitys (genotype) or the phenotype. There are many fields where you can use it.

What is the recent scientific history?

In the early 1980's a transgenetic mouse which was called the oncomouse or Harvard mouse was produced. It carried a specific gene that increased the chances that the mouse will get cancer, what made the mouse suitable for cancer research.

Scientists at Mayo Clinic College of Medicine have found a way to slow down the aging process of mice by changing a bit of the mouse genetic code.

Where and why is the technique used?

In the green genetic engineering: To make plants more useful

- resistant to pesticides
- toxic to pest insects
- more tolerant to the weather and soil

Or just more beautiful/ special like the blue rose

In the red genetic engineering: For animal testing

- to make animals less resistant against diseases
  - than its easier to do a research f.e. about cancer
- to determine a function a gene has
- …
-

Because some animals like mice are very similar to humans it is useful to know how animals react/ wich function a gene has etc.

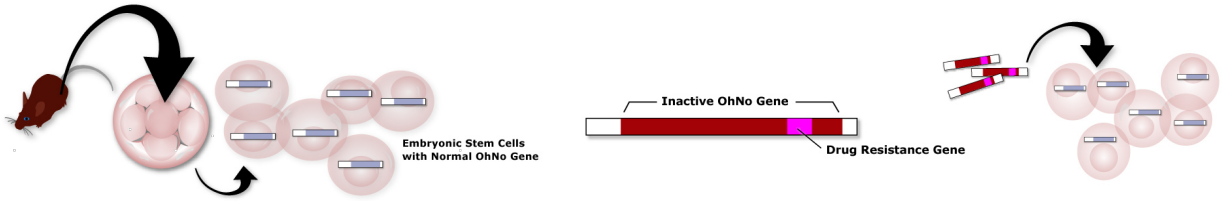
The Harvard Mouse, normally called Oncomouse is a animal wich is helpful in the field red genetic engineering (medecin, pharmacy). The Oncomouse is more susceptible for cancer than other mice, so it is used to find a cure for cancer.

Description of Engineering Technique

Explanation of the applied technique

Knock-Out:
If you want to find out what a specific gene is for, or how a animal behaves without it you use the process of Knock-Out. During that you replace the gene you want to deactivate with a mutated, not functional copy. It doesn't necessary mean that the tested animal will get a disadvantage of it. Some deactivated genes will make the animal more susceptible for diseases, others will stop that you can get stressed.

As a first step you isolate Stem Cells of a male brown mice. These stem cells will contain the not inactive gene.
After that you have to add the mutated genes, wich isn't functional and has a ability that the original gene doesn't have. For example a drug resistance (So that you can separate them later).



By a process called homologous recombination the original gene is kicked out and the inactive gene will take its place. (Why this process takes place isn't clear.)
Because not all cells have the mutated version of the gene in them, you now have to separate them. So now you add the drug the mutated gene is resistant for and the other one not. So all the cells with the old version in it will be destroyed.
Now you transplante the stem cells of the brown mice into the embryo of a white mouse. The result will be a Chimeric Mice. A Chimera inherit parts of the brown mouse and parts of the white mouse characteristics. There isn't a 100% guarantee that some of the cells with the inactive gene will develop into reproductive cells but a good chance.

Now you have to cross a male Chimera mouse with a white female mouse. The Chimera mouse can either have a mutated gene of the brown mouse (Mb) or a “normal” gene of the white mouse (Nw). The white mouse can only have the “normal” genes. If you cross the two mice and you get a white mouse you now that the mouse doesn’t have a inactive gene, because the inactive gene is dominant, whereas the white gene is recessive. If you get a brown mouse you now that the mouse has exact one mutated gene.

	Mb	**Nw**
Nw	MbNw: Brown mouse	NwNw: White mouse

To get a mouse with two inactive genes you have to cross to brown mice with a mutated gene. There is a 25% chance that you’ll get a mouse with two copies of the “knocked-out” gene. (50% will have one inactive and one functional gene and the other 25% will be a white mouse with two fully functional genes)

ilar Genes Naturally Swap

By mechanisms that are not completely understood yet, similar genes will swap places. The OhNo gene plus drug resistance marker gene is incorporated into the genome, and the normal version is kicked out. This process is called homologous recombination.

Discussion

What progress was made with the application of the chosen technique?

With the higher susceptibility to cancer is the Oncomouse therefore useful for cancer research. But not only there you can use the transgenetic technique. You can do sth. about the famines if you make a plant more profitable.

What future research steps?

In the green genetic engineering they probably will attempt to let them bear more fruits and make plants even more resistant.

Maybe there is a chance that investigators will find a way that humans can live longer. Not only the Scientist at Mayo Clinic College of Medicine but also Scientist of the hospital Saint-Antoine in Paris found a way to let mice longer life.

Discussion of ethical aspects:

Advantages:

The Oncomouse is very suitable for cancer research. So humans can benefit from them.

Humans and Mice are genetically very similar. Some genes are 99% identical. So its great to use mouse for research.

Disadvantages:

Mice are mammals. Like Humans. Anyway, researchers make sure that the mouse will have a higher chance to come down with cancer. That's a big disadvantage/ danger for the mice. The performance of animal experiments is disputed

This disadvantage has nothing to do with the process, but with a consequence of its discovery. The Oncomouse ist patented. You would have to pay something just to be allowed to use it for your research.

Summary

What is this transgenetic technique?

The transgenetic technique is a process in wich you add or remove a gene in a living organism. This changed gene will be inherited by the offspring.

Where can you use it?

You can use it in many fields.

Green genetic engineering: You can get transgene plants, which are more resistant against pesticides, the weather or wich are toxic to pest insects. You can also create plants wich have a special colour.

Red genetic engineering (medecin): You can use it to make animals more useful for animal testing, to determine the function of a specific gene,…

In the future this technique will hopefully help us to live longer and healthier.

Harvard mouse or Oncomouse

The Oncomouse, also called Harvardmouse was one of the first transgene animals. Because of a change in the genetic code it is more susceptible to cancer than other mice. Therefore the mouse is perfect for researches. It also is patented wich caused many discussion about the worth oh animal life.

Ethic questions

The transgenetic technique brings many advantages. But there are also many disadvantages, especially for the animals. There is a big ethic question about the value of life. Is it okey to kill hundreds of animals to save a human life? This question is the biggest problem with the transgenetic technique in Red genetic engineering.

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