

Introduction

"Well it is scary, isn't it, all this genetic engineering?"

"Is it?"

"Yeah, you know, messing about with the body. They reckon there's a gene for intelligence, sexuality-practically everything, you know? Recombinant DNA technology" said the girl using the term cautiously as if testing the water to see how much Marcus really knew. Seeing no recognition in his face she continued with more confidence. "Once you know the restriction enzyme for a particular, like, bit of DNA, you can switch anything on or off, like a bloody stereo. That's what they are doing to those poor mice. It is pretty fucking scary".¹

Zadie Smith

Why a book about mice?

What made me, a philosopher and a biologist, decide to write a book on mice? The answer to this question can be found in the quotation cited above, taken from Zadie Smith's novel *White Teeth*. In this book one of the characters, Marcus, a scientist, has created FutureMouse©. In this animal he implanted custom-designed genes that can be 'turned on' and 'off'. This gives Marcus the absolute control over its life and death. In collaboration with a novelist, he has written a pop science book called *Time Bombs and Body Clocks: Adventures in Our Genetic Future* that also includes a chapter on this mouse. The girl who is quoted above is reading this book, unaware that the person she is addressing is one of the authors. While the girl is 'lecturing' him about the scary aspects of recombinant DNA technology, Marcus is wondering why it is that people fail to see his mouse as a laboratory entity that is determining the future of cancer, of reproductive life cycles, of the human life-span and ageing, but rather continue to see it merely as a mouse, an animal. They focus on the mouse 'as mouse', in a manner that never failed to surprise him: 'They seemed unable to think of the animal as a site for experimentation into heredity, into disease, into mortality. The mouseness of the mouse seemed inescapable' (Smith 2000:

1. Zadie Smith (2000) *White Teeth*, New York, Vintage Books, p. 345.

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346). This fictitious scene taken from a popular novel illustrates a number of interesting aspects of the laboratory mouse.

First of all, it illustrates the different perspectives from which different individuals can perceive the genetically engineered mouse. On the one hand, we see a girl who is definitely not as hysterical as Marcus takes her to be. On the contrary, she is amazingly well informed, and expresses genuine feelings of moral concern. According to her views, a genetically engineered mouse is *unnatural* and the idea that you can *program* the mouse....is experienced as 'pretty fucking scary'. On the other hand, we have Marcus who represents the rather stereotypical image of a scientist, seemingly unable to understand the feelings and reactions of lay people. He has a very instrumental view on laboratory mice connected with a deep faith in scientific progress. There is no such thing as mutual understanding between Marcus and the girl. Secondly, when we listen carefully to what the girl says, and consider what Marcus thinks, a whole variety of moral values emerges: a fuzzy set of morally relevant notions that are somehow involved in mouse biotechnology. The genetically engineered mouse is a complex phenomenon, from a moral point of view. Yet, in the end, although they seem to disagree considerably over the value and moral status of the mouse, both Marcus and the girl seem to agree about one thing: namely, the fact that a biotechnological revolution is taking place,

here and now, at this very moment, and that FutureMouse© is one of the main characters in this revolution. To Marcus this is progress; to the girl there is 'something a little fascist about the whole deal' (Smith 2000: 346). Today, in laboratories all over the world, genetically engineered mice like Future/Mouse are being produced and used for biomedical research. These mice are determining the future of medicine. Mouse geneticists have sequenced ('cracked') the mouse genome and added genes coding for fluorescent proteins to it. In addition to the thousands of mouse models that mimic human diseases they have created mice that are smarter, stronger and live longer than ordinary mice. In the biotech revolution that is taking place, the mouse plays a central role. The biotech revolution is a radical change in terms of the way 'we' are taking control over living entities. Biotechnologists are challenging nature. Or, to put it more precisely, the biotech revolution challenges *traditional beliefs about nature*.

These genotech mice are not simply unnatural, they force us to reconsider long-held beliefs about natural species, about life and death, disease and health. In other words, these mice raise, and force us to reframe, a series of profound philosophical questions. By way of the mouse, biotechnology affects what lies at the core of humanity, of what it is to be human. For biologists these mouse technologies offer great possibilities to study the mysteries of life. For philosophers, they are a source of confusion. How does mouse biotechnology affect the way we make sense of life? Are we seizing the position of Dawkins's blind watchmaker? The mice also raise many ethical questions: 'Are we doing the right thing?' 'Where will all this 'tinkering with genes' lead to?'

The key message I want to put forward in this book is that, if we want to understand the impact of the biotech revolution, we have to look at the mouse. The mouse is the key actor in this radical series of events that is taking place in the life sciences right now. To understand the meaning of biotechnology both from a biological perspective and a philosophical perspective, we have to take a closer look at this animal's unique history and its presence in biomedical laboratories. I will do so by focussing on three central questions: an ontological, an epistemological, and an ethical one:

- 1 What is the genetically engineered laboratory mouse?
- 2 How is the mouse currently used, and what is its role and function in the pursuit of knowledge and power?
- 3 What are the moral implications of mouse biotechnology, or, how must we deal with the issues raised by the genetically engineered mouse?

As the fictitious dialogue between Marcus and the girl from *White Teeth* illustrates, there are many perspectives from which we can look at the genetically engineered mouse. All of these perspectives will produce different answers to these questions. Each perspective produces a different image of the mouse. We cannot say that one of them is more 'real', more 'adequate' more 'truthful' than the others. Rather they reveal complementary dimensions. One cannot be replaced by any of the others: they emerge on different levels. Every perspective has its own revelatory power, its own truth, its own value. At the same time every perspective on the mouse also entails a certain blindness to the aspects of the mouse that are brought to the fore by the other perspectives. A typical mouse image coming from a biologists' perspective is that of an animal which provides 'inside' information concerning the *in vivo* behaviour of our DNA. This raises a number of philosophical (notably epistemological) questions concerning the role of the mouse in the process of knowledge production in

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the field of mammalian or human genetics. What is the value of the mouse as a model organism?

Philosophical questions can also be asked about 'boundary conflicts'.

What exactly is an animal that carries genes from both mice and humans?

Such an animal not only transgresses the species boundary between mouse and man, it also transgresses the boundary between nature and culture, what is given by nature and what is man-made. This results in the ethical question whether the mouse also signifies the crossing of a moral boundary.

And, if so, why? Other ethical questions are related to animal welfare issues raised by contemporary mouse biotechnology. Do these animals suffer from the instrumental use we make of them?

By far the most intriguing questions about the mouse are those about its future. What will be the implications of these technologies, tested in and developed with the help of mice? Will they eventually be applied to humans? What can we learn about biotechnology in general by looking at the mice? What can we learn about our own future? What does the (hi) story of the mouse tell us about possible future scenarios? What can we learn from the mouse about ourselves, our genes and the role we play in the 'natural' process of evolution? I believe these are questions of vital importance precisely because a revolution is taking place right here and now that will have a radical impact on the way we view and – perhaps – reshape ourselves, in a distant future that begins today.

A short note on methodology

In order to address these questions, a variety of sources will be consulted. Being a philosopher, my main tool, my main method of investigation, is of course reading. Most of the sources I will use are written documents. In order to understand what the genetically engineered mouse is, I will study what is written and said about these mice and about animal biotechnology more general. This discourse on mice emerges at various levels. In the first place, there is a scientific discourse on mice that materialises in the form of research articles in scientific journals such as *Science*, *Nature* and the *Proceedings of the National Academy of Science* where major breakthroughs in mouse biotechnology are eagerly reported. But also important are the writings of philosophers, reflecting on the moral aspects of animal biotechnology, or of social scientists, studying the role of the mouse in the scientific practice. Besides research papers and scientific articles, I also consulted (auto) biographical reflections of scientists involved in mouse biotechnology. This latter type of written information can be found not only in scientific journals but also in the popular press such as newspapers and magazines. In addition to the reflections and reports on the mouse that originate from academic circles, there are highly relevant forms of 'mouse discourse', emerging in more popular environments. This may involve written materials, such as (science) fiction stories and articles in the media, but also works of art produced by contemporary artists. The discourse (scientific, philosophical and otherwise) on genetically engineered mice amounts to an archive of incredible proportions. Therefore, one has to be selective. Insofar as the scientific literature is taken into account, I will focus on the highlights, the breakthroughs, such as the 'birth' of the first inbred strains, the birth of the first transgenic mouse, the first human gene inserted in the mouse genome, the emergence of the first knock-out mouse, etc. To this I added a number of biographical or autobiographical publications, focussing on authors who themselves had played a major role in the mouse biotech revolution.

Insofar as the philosophical and ethical literature is concerned, it was not at all that easy to steer my own course in an ocean of writings. First of all, I was primarily interested in publications on animal biotechnology

that evoke a living or 'tangible' image of the mouse. In other words, I was interested in publications that really speak about mice, rather than about philosophical concepts. Therefore, I more or less ignored philosophical writings in which, because of their level of abstraction, the mouse is lost in a jungle of words. This book is about real, living mice, the myths they evoke, their images, and their meanings.

Moreover, this book is neither about animal ethics (or animal ethics committees), nor about policy making and legislation on animal biotechnology.

Again, the focus is on the meaning of the genetically modified mouse. Therefore, I hardly discuss the writings of the various Dutch bioethicists who have tried to analyse and clarify notions such as integrity and intrinsic value in order to make them suitable for use in animal ethics committees or bioethics committees. Moreover, the focus is on the international literature, rather than on sources written in Dutch that focus on national policy development.

While reading these diverse sources of information I ask myself a number of questions: What language is used in these different sources? What do they reveal about mice? What metaphors are used? What myths are referred

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to? What kind of images of the mouse emerge in these writings or in these works of art? For this 'reading method', the writings of a number of philosophers and social scientists have served as a source of inspiration. They have provided me with basic concepts and methodological tools. Mary Midgley, for instance, has inspired me to take a closer look at metaphors and myths at work in scientific practice. Karen Rader inspired me to take a historical perspective on mouse biotechnology, and Jon Turney taught me how to connect scientific reports with public perceptions articulated in the media. These and other sources have allowed me to see the mouse as the 'right organism' for the job. They taught me that mouse images evolve along 'never-converging tracks', and that a philosophical understanding of the mouse calls for a 'palaeontology of the present'. Finally, powerful images such as Bryan Crockett's *Ecce Homo* have been of major importance for the development of my view on the genetically engineered mouse. But there is more to philosophy than reading. An important, perhaps even decisive, source of information is personal experience. Trained as a medical biologist, I have worked with laboratory animals² and, as a result, developed a 'scientific gaze' on the laboratory animal (Nuijtinck et al. 1997). I know, from 'inside' so to speak, what a scientist means when he or she says 'we study these complex phenomena in the *mouse model* because ...'. I understand what is to be deeply fascinated by small and inconspicuous processes such as cell-cell interactions or the function of a single gene in the complex process called DNA regulation that can only be made visible by technological devices such as microscopes, amplifiers, oscilloscopes and micro-arrays. On the other hand, as a philosopher I am trained to 'read' what lies behind these sentences: the so-called 'self-evident' and 'obvious' conventions of these research practices. How can an animal be a model? What is a model, and what kind of knowledge does it produce? The distance between various mouse perspectives becomes visible as soon as they come into contact, or even conflict with one another. The use of animals in experimental research is an issue of public moral debate of long-standing. Many philosophical questions about the use of mice in research are translated sooner or later into ethical questions. Can an animal be regarded as an instrument? Does it have intrinsic value, besides instrumental value? And, if it has intrinsic value, what does this imply

for the scientific practice concerned? Some of the ethical questions are

2. Albeit *Wistar* rats and goldfish, rather than mice.

related to the practice of biotechnology. Does the genetic engineering of the mouse amount to a violation of the animal's integrity?

In my experience the different vocabularies used in experimental biology and philosophy do not mix very well. This has been my experience as a member of an Animal Ethics Committee (In Dutch: *Dier Experimenten Commissie* or DEC). On countless occasions, I had to explain the difference between 'intrinsic value' and 'integrity' at a DEC meeting or answer questions such as: 'Is the integrity of the offspring of transgenic mice violated at birth?' or 'Can the integrity of mice be violated in different degrees and, if so, how can you measure this *objectively*?' Between the two cultures of experimental biology and philosophy a gap seems to exist that is both epistemological and ethical. In order to deepen my understanding of this gap, I decided to do fieldwork in the mouse facility at the same institute where I was a DEC member, the Netherlands Cancer Institute (NKI). This institute plays a leading role in the Dutch mouse biotechnology. Much of the research conducted at the NKI involves transgenic mice. Mice are also created for scientists who work in laboratories outside the institute. The mice travel all over the world. At the NKI I visited the mice in the transgenic mouse facilities and talked to the biotechnicians who perform many of the surgical operations and actually do the genetic modifications, the animal caretakers who feed the mice and clean their cages, the researchers who plan the genetic modifications and use the mice for their research, and the mouse pathologists who search for the cause of death. I did this when they were all at work. I witnessed the routine procedures for breeding mice, transplantations of genetically modified embryos into foster mothers, the checking of the health and fitness status of the mice, the removal of organs as part of an experiment, and post-mortem autopsies of mice. As a result, I learned about the day-to-day 'facts of life' of these mice and the motives and visions of the people who work with them.

These experiences, together with the written sources studied, have shaped the outline of my research. It is not at all my intention to give a 'correct' or 'objective' image of the mouse. Such an image does not exist. Instead, I will present a broad variety of images in the form of photographs, quotes, artworks, visions, etc. The resulting image of the mouse is highly complex and ambiguous. Nonetheless, there is a certain amount of structure that can be discovered in this bewildering variety. Three basic (irreducible) mouse images will be identified.

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Rough outline of the book

In Chapter 1, I focus on biological science. I introduce the mouse, so to speak, by entering its 'natural' habitat, the scientific laboratory. In order to answer the questions how it got there and how it evolved towards its present form, I go back to the early 1900s when the mouse made its entrance into biomedical science. From thereon I follow its 'career' as 'the right tool for the job' in genetics research. I describe three crucial steps in the 'genealogy' of the lab mouse: 1) the transformation of the mouse from an object of study as an *animal* into a homogeneous laboratory *tool* that could be used for studying of the laws of genetics; 2) its becoming the pioneering species in transgenic technology; and 3) its transformation from a model *mouse* into a mouse *model* used for the study of human diseases. It is here, I argue, that the mouse, as a result of a long process of human interference in its genetic make-up, has become a living artefact.

In Chapter 2, I focus on the moral and social debate about mouse biotechnology. What are the moral implications of the genetic engineering of research animals, and how should we deal with the genetically engineered mouse? How are these questions addressed and answered by philosophers? In the moral debate about animal biotechnology, I see three never-converging tracks. On the first, there is a discussion about the promise of biotechnology to cure us from life-threatening diseases; on the second, a discussion about animal suffering; and, on the third, a discussion whether we humans have any right at all to tamper with genes or to 'play God'. On these three tracks, three different images of mice appear: (1) mice as high-tech laboratory tools; (2) mice as animals of flesh and blood and as victims of science; and (3) mice as monsters that resemble the one that Frankenstein created. These images do not easily converge into an unequivocal moral verdict on mouse biotechnology, since they refer to different and perhaps even incommensurable moral values, such as progress in biomedicine, animal welfare, and respect for nature. According to Bernard Rollin, one of the most influential philosophers writing about animal biotechnology, only welfare issues are morally relevant. Other objections are, as he argues, 'merely' aesthetic. Many philosophers (including me) and members of lay audiences have strong objections to this line of reasoning. There clearly seems to be more at stake in animal biotechnology than animal welfare: namely, our vision of nature, or what we take as being natural. However, in day-to-day research practice, a utilitarian balance between human benefits and animal welfare seems to be the dominant ethical framework, for biomedical scientists, as well as for members of animal experimentation committees. Why this is the case I will explain by building on Martijntje Smits's monster theory. This theory discusses public responses to the products of new technologies that at first sight challenge the nature-culture dichotomy. The genetically engineered mouse is such a 'product'. I will argue that the mouse, despite its general use in the biomedical laboratory and its apparent domestication, is still a monster for many. Its monster character is, amongst other things, revealed by the myths, metaphors and vocabularies that dominate the biotechnology debate. I will highlight the three most important ones: Playing God; the Frankenstein thing; and the yuk!-factor. What 'truths' lie behind these metaphors and myths? In order to answer these questions, I analyse these metaphors and/or myths in Chapters 3, 4 and 5 in more depth.

In Chapter 3, I take the artwork *Ecce Home* by Crockett as a starting point to discuss the playing God metaphor, or God talk, in biotechnology. In this sculpture, the genetically engineered oncomouse is represented as Jesus Christ. It is a very powerful visual image of the playing God metaphor. It suggests not only that scientists who are involved in mouse biotechnology play God but also that this type of science leads to salvation. Exploring this myth of science as salvation, I will argue that, regardless of whether we take the science-as-salvation idea literally or metaphorically, it reveals that biotechnology has the character of a promise. And the genetically engineered mouse represents the promise of biotechnology in flesh and blood.

Biotechnology is a future-oriented technology, a technology whose hopes and promises are more or less science fiction. But who is promising, and what is being promised? Who is playing God? What is their ultimate plan? What are the implications of mouse biotechnology for ordinary people? This takes me to the fear of monsters coming out of laboratories, to be discussed in Chapter 4. This fear is often formulated by referring to Mary Shelley's *Frankenstein*. Frankenstein's monster is more or less the archetype of popular 'biotech monster phobia'. In this chapter, I will address the question what it is that people find fearsome about biotechnology when

they refer to Frankenstein. How does the myth of Frankenstein relate to new developments in biotechnology? What is the actuality of the myth? In order to answer this question I will tell the stories of four super mice and their creators and illustrate some of the (future) possibilities of genetic human enhancement. I will argue that, in the days of the super mice,

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rereading Shelley's novel is of great importance because biotechnologists did indeed discover a monster: namely, the fact that our own DNA, our essence, is malleable. How do we distinguish between good and bad 'genetic re-creations'? Is this purely a matter of taste? Finally, in Chapter 5, I will explore more extensively the relationship between judgments of taste, aesthetic judgments and moral judgments about animal (or human) biotechnology. To do this, first, I will return to Rollin's argumentation, as it was discussed in Chapter 2. Rollin believes that moral concerns based on 'aesthetic judgements' are not genuine moral concerns. In opposition to Rollin, I will argue that we have to take aesthetic judgements very seriously. Moral convictions are always based on a mixture of both reason and feeling. People who say 'yuk!' when being confronted with animal biotechnology are expressing genuine feelings of moral concern but apparently lack the vocabulary to do so in a philosophically articulate way. What is expressed when people say 'yuk!?' I will argue that two things are involved in the yuk-response to animal biotechnology: namely, a feeling of confusion, or even disgust, that is the result of our vision of nature losing its status of being given, unquestioned and selfevident 'objectivity', and the threat that animal biotechnology imposes on what we perceive as good life, or a life worth living. The second question I address in this chapter is what the role of art could be in the age of the biotech revolution. How can contemporary art assist in the moral and social assessment of animal biotechnology, in particular where questions about visions of nature, quality of life, identity, the normal and the abnormal are concerned? To illustrate my argument, I will introduce three art projects: the *GFP Bunny project* by Eduardo Kac (2000); the *Transgenic Mice series* by Catherine Chalmers (2000); and *Genpets™* by Adam Brandejs (2005). I will argue that the most important value of bioart lies in making visible the invisible.