HUMANIZED MICE AND THE DELEUZIAN DIFFERENTIATION BETWEEN SCIENCE AND PHILOSOPHY

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ALTHOUGH MICE HAVE been an important part of the biomedical research for almost a century, the ways in which they are produced for research have multiplied over the years. This article seeks to question what the latest attempts to create humanized mice models, meaning mice that have been engrafted with human cells, tissues or organs in order to better mimic human conditions, can tell about the contemporary biomedical practices. The basis for my analysis is Gail Davies's article "What is Humanized Mouse?" (2012), in which she argues that the aims to produce humanized mouse models create "a vocabulary which considers humanized mice as a contingent **assemblage** or **becoming**" (Davies, 2012, p.130, my emphasis). The concepts of "becoming" and "assemblage" connect Davies's analysis of the notion of humanized mouse to a Deleuzian worldview that argues for a more fluid and complex understanding of the material world. However, these concepts are also linked to the philosophical approach in Deleuze's work, which he differentiates from a scientific endeavor. As Todd May explains in his article "When Is a Deleuzian Becoming?" (2003), "the point of a philosophical perspective is not to tell us what the world is like – that is the point of science – but to create a perspective through which the

world takes a new significance" (May, 2003, p.142). How does the production of humanized mouse, which is a scientific undertaking, create "a vocabulary" that connects them to Deleuzian philosophy? In this paper, my aim is to locate Davies's analysis of the humanized mice to a broader question of the difference between science and philosophy. What kind of vision of scientific research does the notion of the humanized mouse create?

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In their book *What Is Philosophy?* (1994), Gilles Deleuze and Felix Guattari argue that philosophy and science have a different kind of approach to the immanent world. While Philosophy, according to them, is able to work in the field of immanence through abstract concepts, science aims to locate functions by stabilizing particular variables (Deleuze & Guattari, 1994, p.118). In order to understand why this is so, it is important to connect it with the overall works of Deleuze, as Todd May has done in his article "Gilles Deleuze, Difference, and Science" (2005). May states that in order to examine Deleuze's vision of science, it is important to understand his definition of immanence. The general definition of immanence refers to the denial of the transcendental idea that there is a God outside of the physical world. Instead, God is inherent in the world. However, instead of connecting immanence with a theological God figure Deleuze approaches it with the notion of multiplicity. By connecting the notion of immanence with the idea of multiplicity, Deleuze highlights how the physical world should be considered as complex, relational and dynamic - terms that defy the possibility to explain the world as a sum of distinct entities. Deleuze calls this irreducible character of the world as virtual

(May, 2005, p.240-243). While philosophy is able to communicate the fluid character of the world via abstract concepts, science explains functions with the concrete categorization of the world in order to answer the questions it wishes to ask, thus losing the virtual character of the world in its explanations.

Deleuze's notions of "becoming" and "assemblage" are philosophical concepts that aim to explain the formation and co-existence of things in the world. However, as Deleuze and Guattari highlight in A Thousand Plateaus (1987), this does not mean that world would consist of relations of distinct entities such as animals or women but becoming-animal refers to the movement in which heterogeneous assemblages are formed. Within these assemblages the meanings of things are actualized. In other words, becoming refers to a process of meaning making that is tied to the virtual immanence of the world. Becoming can never be finalized since it marks an actualization of things that gain their material form as well as their social meaning within a temporary alliance of multiplicity (Deleuze & Guattari, 1987, p.238-242). Although this is only a partial explanation of a much broader and complex philosophical network, this examination helps to underline how these Deleuzian concepts tie the experienced world with a broader understanding of a fluid material ontology. Scientific practices, in Deleuzian reading, cannot tackle this dynamic materiality because they stabilize their objects in order to study them. In this light, Davies's definition of the humanized mouse models is intriguing since it seems to go against the stabilizing effect of science. Davies explains her usage of Deleuzian terms by stating that they help to "conceptualize humanized mice less as an object, even a relational object, and more as a series of overlapping vectors, which have direction and velocity, but no singular identity" (Deleuze & Guattari 1987, p.238-242). What makes humanized mice such an evasive category?

A humanized mouse, for Davies, is an expression of the fact that biomedical research is

acknowledging that focus on genes or other single entities cannot, at least in most cases, offer comprehensive information about the nature of a disease. She connects the humanized mice with an ongoing change in biomedicine from genomics to post-genomics. While genomics focuses on particular genes, post-genomics aims to take into account the complexity of the organism and its relation to the environment. In mice model production, the need for such an approach becomes painfully obvious from time to time when drugs tested with mice have unforeseen complications when given to humans. Davies highlights one pre-clinical safety trial where the immune systems of mice did not react to the leukemia drug whilst human immune system reaction led to an organ failure in many patients. The humanized mice, then, are thought to minimize the possibility for such a situation by creating mouse models that would, due to the engrafted human cells, represent a human disease as closely as possible. Moreover, Davies notes that there is not only an attempt to mimic particular human diseases but also to create humanized mice that would imitate the human immune system. These humanized mice are seen as central to the future of translational research that works towards facilitating the information transfer between the clinic and the laboratory, namely that drug inventions could be speeded up and be more cost effective without compromising the safety of the human trials (Davies, 2012, p.131-135).

Although the attempts to create a humanized mouse can be seen as an example of a more holistic vision of organism taking place in biomedical research, it is not due to this that Davies connects the humanized mouse with the idea of becoming. On the contrary, the plans for the humanized mice go as far as to imagine them as possible “translational objects” (Michael, M. quoted in Davies, 2012, p.134). This implies that rather than accounting for the corporeal differences between mice and humans, the research aims to dismiss them through genetic manipulation. Instead, Davies connects the Deleuzian potentialities of the humanized

mice to the realities of the production of the models – or, more precisely, to the attempts to produce such models – in addition to the post-genetic reasons behind them. She highlights that although the aim of the humanized mouse models is to mimic humans, there is always a possibility that manipulation turns mice to something unplanned due to the practical issues, such as the cleanliness of the laboratory space, as well as corporeal differences. Thus, Davies argues that "the humanized mouse remains an experimental process, with uncertainties about precisely what is being modeled, and under what conditions" (Davides, 2012, p.140). This uncertainty is fueled by the fact that the complexities of the manipulation of the mice have required scientist to collaborate with multiple research fields, such as stem cell research and pre-clinical trials, which are more and more concerned with the personalized medicine (Ibid., p.143).[1] This leads to a situation where the question of producing animal models is not only concerned with the bodily differences between humans and animals, and their diseases, in general but also with the fact that no human is the same as another. As Davies states "biological and disciplinary multiplicity [of humanized mice] enables new forms of species co-presence and interdisciplinary collaboration, but their association constructs of individuality bring forth new forms of absence and new axes of difference" (Ibid., p.144) leading to a situation where research can only be "almost there" since "not only are there many humanized mice in the world, there are also many worlds in the humanized mouse" (Ibid., p.147).

It is clear, then, that the challenge that the humanized mice bring to the research can be connected with the Deleuzian vision of the virtual world full of complexities that cannot be explained only by referring to separate entities. Still, it is good to keep in mind that the starting point of Davies's analysis is the scientific

[1] Personalized medicine studies diseases as person-specific, taking into account individual factors that could have affected to the formation of the disease.

vision that the humanized mice could sometime in the future function as simple translational objects for human conditions. However, what seems to be missing from Davies's account is the question of the role of reductionism in the scientific research. Although scientists might dream about creating a mouse model that could fully represent human disease or the immune system, usually the aim of animal experimentation is not to create miniature humans but to form a platform that could simulate certain aspects of human diseases. As Monika Piotrowska's states in her article "From Humanized Mice to Human Disease," (2013) the humanized mouse can still be seen as functional mechanism that can offer information about the components of the human disease if the study also takes into consideration the internal, environmental as well as evolutionary context of the organism. Thus, according to Piotrowska, the complexity of the organism is not necessarily an obstacle to a mechanistic viewpoint, that is, to the vision that specific functions happening in the organism can be explained by identifying the components that take part in the formation of the disease (Piotrowska, 2013, p.453-454). In other words, there is no need to represent the whole human in a mouse but only the parts that take part in the formation of a disease. Consequently, this viewpoint reminds that humanized mice are based on narrowing down the possible causes of the disease and, hence, animal experimentation does not, as such, require a corporeal equivalence between mice and humans.

That being said, it is noteworthy to pay attention to the way in which Piotrowska's article highlights the problematic nature, rather than the possibilities, of the production of the humanized mice that would fulfill her requirements for this kind of revised mechanistic viewpoint. By analyzing recent research, she emphasizes that neither is the juxtaposition between humanized mice and human condition often justified, nor is the production of humanized mice usually successful (Ibid.). Piotrowska's viewpoint ties the humanized mouse more closely to Hans-Jörg Rheinberger's vision of an experimental system. In his article "Experimental Complexity in Biology," (1997) Rheinberger

argues that although experimental research needs to reduce the complexity of the organism in its approach, the complexity of the research object does not cease to exist and can "allow researchers to arrive at unprecedented, surprising results" (Rheinberger, 1997, p.247). However, it is important to make a distinction between how Rheinberger defines model organism and its function as an epistemic object in research and Davies's analysis of the humanized mouse model.

Rheinberger's definition of the model organisms, described in his book *An Epistemology of the Concrete* (2010), highlights the role of the model organism as a site to learn more about biological functions. Thomas Morgan, for example, used fruit flies, to map the functions of genes. Hence, Rheinberger points out, the relevance of model organisms is tied to a lack of knowledge and, consequently, "the emergence of certainty about a particular question abolishes the need for models altogether" (Rheinberger, 2010, p.8). Mouse models, however, do not share a similar history with fruit flies. As Jean-Paul Gaudillière argues in his article "Mapping as Tehnology," (2004) whereas researchers studying fruit flies were interested in genetic mapping, the mouse model researchers were also involved in modeling human pathologies. Hence, Gaudillière emphasizes, "The [genetic] mapping of mice did not follow the mapping of flies, **because mice were constructed as human beings**" (Gaudillière, 2004, p.200, my emphasis). The humanized mouse model production, as analyzed by Davies, follows this logic by demanding a definition for the humanized mice that would be in-between an epistemic thing and a technical object, meaning an object whose status in research would remain constant (Davies, 2012, p.137). In other words, though the humanized mouse model cannot be described being an epistemic thing, since its purpose is not only to model a human disease but to function as a replacement for human subject, for instance, in pre-clinical drug trials, the inability to stabilize the production of the humanized mice prevents its becoming a technical object either.

Nevertheless, it is important not to reduce the question about the scientific value of the humanized mice to a question

about the bodily equivalence between humans and mice models (although this certainly is the question that brings funding for the research). As Davies highlights, in some cases the mutant mice might not offer researchers the information they were looking for but they can still be valuable in other type of research. What is more, attempts to manipulate mice increase researchers' knowledge about the mice themselves. As Davies points out: "Talking to researchers, there is uncertainty about whether they are involved in model development or basic research, and indeed where these boundaries now lie" (Ibid., p. 137). The humanized mice can then be seen as a way to learn more about the complexity of an organism, if only in mice.

It is clear, then, that the role that the humanized mouse production has in the biomedical research today is not a straightforward one. The in-between status that Davies connects with the humanized mouse highlights the co-existence between Deleuzian notions of science and philosophy. As May emphasizes, even though science focuses on functions it is not separated from the virtual. Thus, according to him, science and philosophy "must inevitably come into contact; their trajectories must periodically intersect" (May, 2005, p.254). This, according to May, also explains why Deleuze uses scientists' visions of life to back up his theories about the virtual (Ibid., p.251-254). For some humanized mice can offer an example of scientific research concerned with philosophical questions about life and its forms, due to the practical problems raised by the failure to produce the aimed outcome, while simultaneously one could argue that the fact that scientific research even tries to create a humanized mouse proves that scientific research is more eager to control than understand the complexities of the organism. Seeing these two approaches as entangled in the case of the humanized mouse helps to clarify how Deleuzian vision of science and philosophy co-exists. In addition, I wish to highlight with the example of humanized mice that the logic behind scientific research cannot be seen separated form the sociohistorical context it is

produced in. This is not only to question why scientists attempt to create humanized mice for disease research today, and why they believe that it could be possible to create such a model, but also to question how scientists came to think that they need to revise their view about the organism. Although this article has not fully made justice to the complexities connected with the issue, I wish to have managed to bring forth the relevance of asking these kinds of questions when thinking about the connection between scientific and philosophical questions about life. ⊡

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