

Regulation of cybrids and chimaeras

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Executive summary

Health Council of the Netherlands



More and more opportunities are arising to do studies with what are known as human-animal combinations, in which human and animal cells (or parts of them) are fused, for the purpose of research into early embryonic development for example. Some human-animal combinations may make it possible to grow human organs in the future. For the purposes of proper regulation of human-animal combinations, the Minister of Health, Welfare and Sport asked the Health Council of the Netherlands for advice, specifically about two of these forms: cybrids and iPS chimaeras. In this advice, the council's Ethics and Law Committee discusses the medical and scientific necessity and the ethical and societal aspects of these techniques and gives recommendations about their regulation. The Committee used a 'fact sheet', in which the Royal Dutch Academy of Science presented the current scientific knowledge of cybrids and chimaeras, and a report by the Rathenau Institute, which has examined the societal debate about these human-animal combinations.

Cybrids

Cybrids are made by inserting a human nucleus into an enucleated animal egg. This creates an embryo with 99.9% human DNA (in the nucleus) and 0.1% animal DNA in the mitochondria (which handle energy management in the cell). The chance that a cybrid could grow into a viable organism is virtually nil. Initially, cybrids were intended as an alternative to studies with human embryos. The idea was that patient-specific embryonic stem cells could be derived from them. That did not turn out to be possible. Cybrids do not play an important role in current scientific research, among other reasons because there is now a better alternative in the form of iPS cells ('normal' cells that have been reprogrammed into stem cells with embryonic properties).

iPS chimaeras

iPS chimaeras are created by inserting human iPS cells into an animal embryo. This can be done in an early embryonic stage when the cells are still pluripotent (i.e. able to develop into

many tissue types) or by injecting the cells into the foetus in the womb. There are many variations and gradations in chimaeras. At the moment, studies with chimaeras are at the stage of fundamental scientific research. The most convincing clinical promise is the potential for growing human organs for transplant surgery. However, this use is uncertain and still a long way off. Safety is also a source of concern.

Ethical and societal aspects

The ethical considerations for assessing human-animal combinations such as cybrids and chimaeras are complex. There is no single argument that is decisive: every application demands its own considerations. This is also in line with the views within the societal debate. One value that plays a role in the discussion about the ethical acceptability of human-animal combinations is their naturalness or lack thereof. This argument often indicates that there are strong moral intuitions involved (spontaneous judgements about what is or is not right). (Human) dignity is also important. The more



chimaeras become humanized, the greater their dignity and the more they are worthy of protection/concern. Further points that the authorities and scientists need to consider are proportionality (whether the importance of the research is in proportion to the negative consequences, the burden and the risks – including health risks – for humans and animals) and subsidiarity (whether any less burdensome approach is available). Finally, the value of the animal and animal welfare must be respected in human-animal combinations that are mostly animal.

The Committee considers cybrids as almost as worthy of protection as human embryos but they have little scientific promise at the moment. No general statement can be made about chimaeras or iPS chimaeras because of the large amount of variation between them. Cybrids and chimaeras are only some examples of the existing and potential combinations of human and animal embryonic material; there are major differences between these and the Committee

believes that they will need independent individual consideration of arguments every time/each.

Recommendations

The need for ethical consideration for each study or application places demands on the regulations. The current legal framework for human-animal combinations is complex and not sufficiently attuned to future scientific developments. It would be possible to regulate iPS chimaeras and cybrids temporarily via the Embryo Act, but this is not the route preferred by the majority of the committee's members. The Committee recommends that the Minister should arrange individual judgement of studies using controversial biotechnological developments, such as human-animal combinations and similar entities, in a future-proof and broad regulation.

They recommend that the minister should include an assessment framework in that regulation and should appoint or establish a body that will assess the ethical and societal acceptability and safety risks of scientific

research and the actual or possible clinical use of controversial biotechnological developments on a case-by-case basis.

The Committee also advises the authorities and scientists to take into consideration the general public's moral intuitions, as well as the underlying values and reasoning. Societal dialogue is a good way of identifying these moral intuitions and considerations. The Committee agrees with the conclusions of the Rathenau Institute about the lack of public debate about cybrids and chimaeras.



The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare and Sport, Infrastructure and Water Management, Social Affairs and Employment, and Agriculture, Nature and Food Quality. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

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