

Clone mammals... clone man?

What are the implications for humankind of the astounding report two weeks ago of the production of viable sheep from adult cells? The moral imperative of preserving human dignity must remain paramount.

Axel Kahn

The experiments of I. Wilmut *et al.* (*Nature* 385, 810; 1997) demonstrate that sheep embryonic eggs (oocytes) can reprogramme the nuclei of differentiated cells, enabling the cells to develop into any type. The precise conditions under which this process can occur remain to be elucidated; the factors determining the success of the technique, and the long-term prospects for animals generated in this way, still need to be established. But, of course, the main point is that Wilmut *et al.* show that it is now possible to envisage cloning of adult mammals in a completely asexual fashion.

The oocyte's only involvement is the role of its cytoplasm in reprogramming the introduced nucleus and in contributing intracellular organelles — mainly mitochondria — to the future organism. This work will undoubtedly open up new perspectives in research in biology and development, for example, in understanding the functional plasticity of the genome and chromatin during development, and the mechanisms underlying the stability of differentiated states. Another immediate question is to ask whether a species barrier exists. Could an embryo be produced, for example, by implanting the nucleus of a lamb in an enucleated mouse oocyte? Any lambs born in this way would possess a mouse mitochondrial genome.

The implications for humans are staggering. One example is that the technique suggests that a woman suffering from a serious mitochondrial disease might in future be able to produce children free of the disease by having the nucleus of her embryo implanted in a donor oocyte (note that this process is not the same as 'cloning').

Would cloning humans be justified?

But the main question raised by the paper by Wilmut *et al.* is that of the possibility of human cloning. There is no *a priori* reason why humans should behave very differently from other mammals where cloning is possible, so the cloning of an adult human could become feasible using the techniques reported.

What medical and scientific 'justification' might there be for cloning? Previous debates have identified the preparation of immunocompatible differentiated cell lines for transplantation, as one potential indication. We could imagine everyone having their own reserve of therapeutic cells that would increase their chance of being cured of various diseases, such as cancer, degenerative disorders and viral or inflammatory diseases.

But the debate has in the past perhaps paid

insufficient attention to the current strong social trend towards a fanatical desire for individuals not simply to have children but to ensure that these children also carry their genes. Achieving such biological descent was impossible for sterile men until the development of ICSI (intracytoplasmic sperm injection), which allows a single sperm to be injected directly into the oocyte.

But human descent is not only biological, as it is in all other species, but is also emotional and cultural. The latter is of such importance that methods of inheritance where both parents' genes are not transmitted — such as adoption and insemination with donor sperm — are widely accepted without any major ethical questions being raised.

But today's society is characterized by an increasing demand for biological inheritance, as if this were the only desirable form of inheritance. Regrettably, a person's personality is increasingly perceived as being largely determined by his or her genes. Moreover, in a world where culture is increasingly internationalized and homogenized, people may ask themselves whether they have anything else to transmit to their children apart from their genes. This pressure probably accounts for the wide social acceptance of ICSI, a technique which was widely made available to people at a time when experimental evidence as to its safety was still flimsy. ICSI means that men with abnormal sperm can now procreate.

Going further upstream, researchers have now succeeded in fertilizing a mouse oocyte using a diploid nucleus of a spermatogonium: apparently normal embryonic development occurs, at least in the early stages. But there are also severe forms of sterility — such as dysplasia or severe testicular atrophy — or indeed lesbian couples, where no male germ line exists. Will such couples also demand the right to a biological descent?

Applying the technique used by Wilmut *et al.* in sheep directly to humans would yield a clone 'of the father' and not a shared descendant of both the father and mother. Nevertheless, for a woman the act of carrying a fetus can be as important as being its biological mother. The extraordinary power of such 'maternal reappropriation' of the embryo can be seen from the strong demand for pregnancies in post-menopausal women, and for embryo and oocyte donations to circumvent female sterility. Moreover, if cloning techniques were ever to be used, the mother would be contributing something — her mitochondrial genome. We cannot exclude the possibility that the current direction of public opinion will tend to legitimize the resort to cloning techniques in cases

where, for example, the male partner in a couple is unable to produce gametes.

The creation of human clones solely for spare cell lines would, from a philosophical point of view, be in obvious contradiction to an ethical principle expressed by Emmanuel Kant: that of human dignity. This principle demands that an individual — and I would extend this to read human life — should never be thought of only as a means, but always also as an end. Creating human life for the sole purpose of preparing therapeutic material would clearly not be for the dignity of the life created.

Analysing the use of cloning as a means of combating sterility is much more difficult, as the explicit goal is to create a life with the right to dignity. Moreover, individuals are not determined entirely by their genome, as of course the family, cultural and social environment have a powerful 'humanizing' influence on the construction of a personality. Two human clones born decades apart would be much more different psychologically than identical twins raised in the same family.

Threat of human 'creators'

Nonetheless, part of the individuality and dignity of a person probably lies in the uniqueness and unpredictability of his or her development. As a result, the uncertainty of the great lottery of heredity constitutes the principal protection against biological predetermination imposed by third parties, including parents. One blessing of the relationship between parents and children is their inevitable difference, which results in parents loving their children for what they are, rather than trying to make them what they want. Allowing cloning to circumvent sterility would lead to it being tolerated in cases where it was imposed, for example, by authorities. What would the world be like if we accepted that human 'creators' could assume the right to generate creatures in their own likeness, beings whose very biological characteristics would be subjugated to an outside will?

The results of Wilmut *et al.* undoubtedly have much merit. One effect of them is to oblige us to face up to our responsibilities. It is not a technical barrier that will protect us from the perspectives I have mentioned, but a moral one, originating from a reflection of the basis of our dignity. That barrier is certainly the most dignified aspect of human genius. □

Axel Kahn is director of the INSERM Laboratory of Research on Genetics and Molecular Pathology at the Cochin Institute of Molecular Genetics, 75014 Paris, France.

This article is a slightly edited version of a Commentary first published on *Nature's* Web site on 27 February.