# Inadvertently Crossing the Germ Line

Researchers have announced "the first case of human germline genetic modification resulting in normal healthy children."* Specifically, the researchers transplanted ooplasm from donor eggs into the eggs of women whose infertility was due to ooplasmic defects. One side effect of those transplants was the transfer of mitochondria, introducing new mitochondrial DNA (mtDNA) into the eggs. This news should gladden all who welcome new children into the world. And it should trouble those committed to transparent public conversation about the prospect of using "reprogenetic" technologies to shape future children.

The Recombinant DNA Advisory Committee (RAC) was created to oversee and publicly discuss federally funded gene transfer research. RAC's guidelines say that it "will not at present entertain proposals" for germline interventions. Given RAC's de facto ban on germline intervention, what reasons might have moved highly respected researchers to announce that they had achieved just that?

First, their intervention did not use recombinant DNA (rDNA). When RAC's guidelines, which apply only to interventions using rDNA, were articulated in the late 1980s, no one was thinking about transplanting ooplasm to treat a form of infertility. Insofar as the ooplasmic transfer technique does not involve rDNA, it falls outside of RAC's purview. However, as a recent American Association for the Advancement of Science (AAAS) report suggested,† RAC's purview is unduly restricted to a consideration of techniques that now are more than two decades old. The AAAS working group (of which we were a part) argued that if new techniques raise the same ethical concerns as those raised by "traditional" germline gene transfer techniques, then either RAC's purview should be expanded to encompass them, or a new, RAC-like body should be created to oversee them. The working group argued that even though some inheritable genetic modifications (IGMs) might not involve rDNA, might not alter single genes, and might not alter nuclear DNA (nDNA), they should be subject to the same public scrutiny if they raise the same ethical questions as the traditional germline interventions. Examples of IGMs in the report included the introduction of artificial chromosomes, the use of oligonucleotides to repair genes in situ—and the transfer of mtDNA.

**"Reprogenetic" technologies should be subject to public scrutiny.**

Second, federal funds did not support this ooplasmic transfer experiment. RAC guidelines are binding only on those who receive federal funds. If, however, their protocol had aimed at achieving traditional germline interventions, they probably would have felt compelled to approach RAC, as do other privately funded researchers whose work raises novel issues. Given their recognition that they were engaged in "germline modification," it is unfortunate—though perfectly legitimate—that they did not bring their protocol before RAC.

Third, gene transfer was an inadvertent effect of their intervention. Since the creation of the RAC guidelines, however, researchers have had to demonstrate that the chances of inadvertent germline gene transfer are miniscule. When an in utero gene transfer pre-protocol was recently put before RAC, the idea was rejected largely because the chances of inadvertent germline effects were too great. If the ooplasmic transplantation protocol had been within RAC's official purview, it probably would not have received RAC's blessing. We will never know.

A final reason for the researchers' apparent indifference to the ban may be that transferring mtDNA does not appear to raise the worry about controlling gross phenotypes that transferring nDNA does. Indeed, mtDNA is usually ignored in policy debates about genetic engineering, on the basis of the weak assumption that it does not have significant phenotypic effects. But mitochondria do govern cellular energy production, and we are learning more about the downstream and far-reaching effects of that function on human physiology and (through the brain) on human behavior.

We admire the therapeutic result of ooplasmic transfer and also think we ought not to drift across the germ line. The authors of RAC's guidelines thought this line too important to cross inadvertently, and the AAAS working group argued that embarking on IGMs is too important a step to be left to the consciences of individual researchers. We hope that before any other inadvertent steps are taken toward making IGMs, those interventions will receive the public discussion they deserve.

**Erik Parens and Eric Juengst**

Erik Parens is at The Hastings Center, Garrison, NY 10524-5555, USA. Eric Juengst is at the Center for Biomedical Ethics, Case Western Reserve University, Cleveland, OH 44106-4976, USA.

*J. A. Barritt *et al.*, *Human Reprod.* **16**, 513 (2001). †M. Frankel, A. Chapman, *Human Inheritable Genetic Modifications: Assessing Scientific, Ethical, Religious, and Policy Issues* (AAAS, Washington, DC, 2000).