

Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted through the Web (www.submit2science.org) or by regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.

Marburger Makes His Position Clear

THE ARTICLE "BREAKDOWN OF THE YEAR: THE unwritten contract" (J. Mervis, "Breakthrough of the Year" Special Issue, 17 Dec. 2004, p. 2015) mischaracterizes my position regarding science colleagues who signed a statement accompanying a Union of Concerned Scientists report critical of the administration. The article implies that I dismissed the statement as "complaints from the Democrats." This quote and its implication directly contradicts the many statements I have made on this issue during the past year, including a previous *Science* article accurately quoting me as having "a great deal of respect" for the researchers who signed the statement but "considerably less for the report."

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The Ethics of Deriving Gametes from ES Cells

IN THEIR POLICY FORUM "ETHICAL ASPECTS OF ES cell-derived gametes" (17 Sept. 2004, p. 1719), G. Testa and J. Harris propose that producing gametes from embryonic stem (ES) cells derived by somatic cell nuclear transfer (SCNT) (1, 2) be considered so that same-sex couples could have offspring with genetic contributions from both partners. Their leap of faith about the technical feasibility of this proposal and their rather cavalier attitude about its health risks and social and ethical meanings demand comment.

The authors characterize risks to offspring simply in terms of whether genetic damage or misexpression (3) due to this experimental procedure is comparable to that in natural reproduction. They neglect to note that although organisms can repair DNA damage and compensate for perturbations of development, they only contain such correction mechanisms as were selected in the context of disturbances encountered in the evolutionary history of

their species. Natural selection has never acted on populations in which variants were produced by SCNT. Consequently, no specific mechanisms have evolved to deal with the associated genetic dysregulation. To learn whether general repair mechanisms can correct such damage would require experimentation on developing humans. Risks to children cannot merely be dismissed by comparisons with "other practices" as if this way of procreation was merely one more consumer choice.

Assemblages resulting from combining an ES cell-derived egg or sperm with normally produced sperm or egg via in vitro fertilization (IVF) are entities distanced not only from the physiological reproductive process but from human forebears with any socially prescribed responsibility for them. Already philosophers (4) and representatives of major research institutes (5) are claiming that human embryos produced by

“Assemblages resulting from combining an ES cell-derived egg or sperm with normally produced sperm or egg via in vitro fertilization (IVF) are entities distanced not only from the physiological reproductive process but from human forebears with any socially prescribed responsibility for them.”

—LIPPMAN AND NEWMAN

SCNT are not actually human embryos. In a culture obsessed with biological perfection, we ruefully anticipate a time when "bad" outcomes of SCNT performed with inexhaustible somatic cell nuclei and infinitely available ES cell-derived eggs and sperm are designated as not actually people.

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Response

LIPPMAN AND NEWMAN FOCUS THEIR CRITICISM on the scenario of same-sex couples parenting offspring to which both partners contribute genetically.

In the mouse, substantial progress still needs to be made to obtain bona fide gametes from ES cells and therefore much effort is required before ES-derived gametes (ESDGs) could ever be applied to human reproduction. However, we disagree that the scenario we describe constitutes a "leap of faith." Although development of science and technology has an intrinsic level of unpredictability, history of biology demonstrates that the availability of an in vitro system is a key factor to accelerate our knowledge and manipulation of biological systems. This was in fact the most salient feature of the three reports of ESDGs: not the derivation itself of so-far dysfunctional gametes, but the establishment of a system that will allow the molecular dissection of gametogenesis (1).

What other criteria should be used for evaluating risks to offspring if not the comparison with natural or currently available assisted reproduction? It is true that natural selection has never acted upon population variants generated through SCNT-derived gametes, but the same could be said for virtually every other medical or technological intervention impacting the human body. Lippman and Newman imply that SCNT would bring about a whole new sort of genetic and epigenetic damage, resistant somehow to the filter of natural repair or compensation mechanisms. The biological foundation of this prediction is unclear and should be documented. Potential defects from ESDG would be either at the genome or at the epigenome level (due to faulty reprogramming), just as for drugs, environmental factors, food, and countless other physical variables that all act, directly or indirectly, upon our genome and epigenome. Indeed, we are all new "populations variants," constantly generated by the interaction of our genomes and epigenomes with the natural and technological world. Possibly the only difference could be the scale of perturbations caused by SCNT, given our lack of understanding and control of the process of genome reprogramming. But needless to say, such issues can only be addressed through further research on scientifically and ethically appropriate models. Finally, in the case of in vitro fertilization (IVF), and especially with intracytoplasmic sperm injection, we are already curtailing natural selection to allow a "defective" genome to contribute to the offspring.

“ **It is not the enabling technology, but the choice of the word ‘assemblage,’ in its objectifying power, that distances potential humans generated through [ES-derived gametes] from the rest of society. Creatures born through ESDGs would be humans just like anybody else, whether conceived naturally or through [in vitro fertilization].** ”

—TESTA AND HARRIS

Lippman and Newman question the social implications of ESDGs and refer to the potential offspring of parents who have reproduced via ESDGs as “assemblages... distanced not only from the physiological reproductive process but from human forebears with any socially prescribed responsibility for them.” It is not the enabling technology, but the choice of the word “assemblage,” in its objectifying power, that distances potential humans generated through ESDGs from the rest of society. Creatures born through ESDGs would be humans just like anybody else, whether conceived naturally or through IVF.

It is also unclear why ESDGs children would be “distanced... from human forebears with any socially prescribed responsibility for them.” Isn’t it exactly the opposite, since prospective parents who take the burden and cost of medical intervention to procreate are clearly demonstrating a responsibility and commitment to their offspring that is arguably stronger, for example, than in the case of fortuitous pregnancies? Infertile heterosexual couples and homosexual couples who reproduce, now through gamete donation and surrogacy, and one day possibly through ESDGs, are asserting a responsibility toward entities that they are unlikely to view as “assemblages.” The fact that this responsibility is not “socially prescribed” for homosexual couples (short of any evidence of the inadequacy of such couples to raise children) can only be described as discriminatory.

Finally, SCNT, like any other technology, does not undermine by itself the foundations of the respect we owe to people. Robust ethical reasoning indicates that self-awareness and the capacity to value

one’s own life are the foundations of the intrinsic value of persons (2). The strength of this personhood-based framework of moral status is its independence, at least a priori, from individual or species-specific connotations. So humans conceived naturally, through IVF, or one day through ESDGs are clearly all persons.

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Costs of a Rotavirus Vaccine

IN HER ARTICLE “ROTAVIRUS VACCINES’ SECOND chance” (24 Sept. 2004, p. 1890), Leslie Roberts did an excellent job of laying out the history of rotavirus vaccine development and the challenges that lie ahead in getting these vaccines to developing countries where the disease kills an estimated 440,000 children each year. Unfortunately, a quote from me may have been attributed incorrectly. In the article, she asked what would be an acceptable price for rotavirus vaccines in developing countries. She quotes me as answering, “No price is affordable for Africa.” There is a big difference between acceptable and affordable.



To arrive at an acceptable price, the value of the vaccine needs to be established. For vaccine purchasers, this requires an evidence base that includes the disease burden, the impact of the vaccine, and the cost-effectiveness relative to other interventions. Establishing the value is important to successfully engage with a manufacturer to reach agreement on a balanced price. Once an acceptable price is established, then the question of affordability can be addressed.

New vaccines, such as those against rotavirus disease, will cost more than pennies a dose. It is clear that if the poorest countries of the world are to realize the same health benefits as other countries, then the international donor community must step forward and provide financial support. The challenge to both public and private interests concerned with vaccine development and access is finding ways to meet the needs of both the consumer and the producer.

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Preserving an Important Collection

WE, TOGETHER WITH AARON KLUG AND JIM Hudson, have been trying to save the papers of some early molecular biologists. They sit in Christie's, New York and include papers from people such as Rosalind Franklin, Aaron Klug, Max Perutz, Rollin Hotchkiss, Sven Furberg, etc. They were collected by a CalTech neuroscientist, Al Seckel, for a collector named Jeremy Norman. Norman wanted to sell them one at a time. In a lawsuit we stopped the sale so they could remain as a coherent collection. Our plan is to purchase them for 2 to 3 million dollars and donate them to Cold Spring Harbor Laboratory. Jim Watson will build an adjunct to the library to hold the history of molecular biology, including his own papers. Were this to come to pass, many of us would donate our papers. We have asked 35 people, most of whom have made a fortune in biotechnology, and have failed to obtain the funds. Time is short, so we turn to the scientific community for ideas and funds. It would be tragic if the papers from which the greatest revolution in biology came were to be dispersed.

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Science and the Bush Administration

SCIENTISTS' CURRENT OUTRAGE AT THE BUSH administration's assault on science in the U.S. is understandable but might miss the real threat—the administration's subtle yet deliberate redefinition of accepted principles of what constitutes good evidence to guide policy development. For example, the Data Quality Act, signed into law in the 2000 omnibus spending bill, gives the Office of

Management and Budget license to arbitrarily vary the quality standards for evidence for regulations. Since then, the Act has been used by industry and special interest groups to challenge health and safety warnings about smokeless tobacco, sugar, fertilizer, and asbestos; findings about climate change; and regulations about endangered species.

It is acceptable for politicians to say, "We have examined the scientific evidence on this question and have weighed it against other concerns of our constituencies and public interests in making this policy." It is not acceptable for them to arbitrarily change standards of evidence to favor their ideological or campaign contributors' interests. We must denounce such violations by political operatives lest science become a set of truths subject to change every 4 years.

It is an evidence-based truism that the best predictor of future behavior is past behavior. So there is no reason to believe that the behavior of the administration that has so perturbed the scientific community will change in the coming years. Therefore, it is critical that scientists organize, choose their battles carefully, and guard against self-serving advocacy that undermines science as an objective tool to guide decisions about medicine, public health, safety, the environment, economic development, and national security.

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CORRECTIONS AND CLARIFICATIONS

News Focus: "The Indus script—write or wrong?" by A. Lawler (17 Dec. 2004, p. 2026). Farmer *et al.* did not specify the number of singletons among Indus symbols. The paper can be found at <http://compling.ai.uiuc.edu/indus>. Also, the University of Pennsylvania's Greg Possehl is an archaeologist, not a linguist.

Cover Caption: (17 Dec. 2004). The image credit in the caption on p. 1989 was incorrect. The credit should be Kees Veenbos.

News of the Week: "New TB drug promises shorter, simpler treatment" by J. Cohen (10 Dec. 2004, p. 1872). The article incorrectly stated that Johnson & Johnson was screening for a broad spectrum antibiotic. The company was screening for a TB drug from the outset. The researchers also found resistance to their new compound *in vitro*, not in the mouse model.

Cover Caption: (3 Dec. 2004). The image credit in the caption on p. 1637 was incorrect. The credit should be NASA/JPL/Cornell.

This Week in Science: "Staying mixed" (12 Nov. 2004, p. 1097). The half-life of C¹⁴ was incorrect in this item. It should be 5730 years, not 5370 years.

Science

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