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EDITOR'S COMMENTARY

What we wish we knew about every embryo chosen for transfer

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On August 27, 2001, Stephen Jay Gould published an opinion piece in *The New York Times* entitled "What only the embryo knows." His typically provocative writings on this day were aimed at the nascent field of stem cell biology and in direct response to President Bush's recently announced moratorium banning the development of additional embryonic stem cell lines, but approving use of those already established for medical research. Gould had a vested interest in seeing stem cell research move forward as an avenue to the amelioration or even eradication of life-threatening diseases, and closes by noting that "…. we will marvel (someday) that we ever rejected a pathway toward knowledge so imbued with life-saving capacity." He would succumb from cancer 207 days later.

For the inquisitive, his article, which I strongly recommend for its content and prescience, traces the history of Karl Ernst von Baer who is credited with the discovery of the mammalian egg in 1827 and founding the field of scientific inquiry known today as embryology. Most importantly, though, Gould would contextualize the persona of embryonic stem cells as opportunists graced with the plasticity to transform into many of the cell types that themselves, once having served their fully differentiated duties to the mortal soma, would eventually succumb to the wear and tear of natural aging or, as in his case, the wrath of mesothelioma as a result of suspected environmental exposure to asbestos.

The influence of ARTs on the fast-paced world of regenerative medicine cannot be underestimated. And rooted in Gould's plea for measured enlightenment, a veritable litany of discoveries has brought research to a screeching halt for so many well-intentioned applications revolving around the use of stem cells of the embryonic or adult variety. To wit, starting with somatic cell nuclear transfer (SCNT) and the arrival of Dolly in the 1990s, in rapid succession, we have witnessed the debut of human embryonic stem cells derived from blastocysts, the generation of induced pluripotent stem cells (iPSCs), the delineation of the mechanisms underlying reprogramming a somatic cell nucleus, and the very real prospect of conjoining genomes from three individuals in the hopes of averting transmission of mitochondrial diseases to offspring. Along the road to exposing what science could accomplish through ARTs, public awareness of the ethical and societal implications of such research has largely been left in the hands of the popular media, until recently.

With the publication of the first study using CRISPR/Cas9 to edit genes in a human embryo a year ago (Liang et al., Protein and Cell 6:363; 10.1007%2Fs13238-015-0153-5), the global scientific community mobilized and joined forces at a recent meeting held in Washington D.C. issuing guidelines for future research, a summary of which will appear in the next issue of JARG. And, as has reached the media frontlines in recent days (http://www.nature.com/news/gene-editing-research-in-human-embryos-gains-momentum-1.19767.), a second attempt at gene editing using tripronuclear human embryos appears in this issue of JARG in a report from the Guangzhou Medical University spearheaded by Yong Fan and colleagues ("Introducing precise genetic modifications into human 3PN embryos by CRISPR/Cas-mediated genome editing," 10.1007/s10815-016-0710-8). We encourage our

Capsule Research on the human embryo continues to cast a long shadow over advances in reproductive and regenerative medicine, with the imminent goals of embryo selection for infertility treatment presently melding with those of gene editing and potential applications that warrant the utmost respect and deliberation that can be afforded by the biomedical research community.

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readership to scrutinize the underlying experimentation contributing to advances of this magnitude. Most importantly, we extend our role as educators in the field of reproductive medicine given the pivotal focus on human ARTs proffered for public consumption to an increasingly discriminant patient population wary of ethical complacency.

Accordingly, we further provide an up-to-date accounting of the means by which epigenetic modifications in the male genome influence fertility chances, a rapidly expanding field that reminds us again that our predilection towards classical genetics being at the heart of fertility-compromising disorders may be ill-founded and more distracting than demonstrating unequivocal diagnostic or therapeutic value ("The role of epigenetics in idiopathic male infertility," 10.1007/s10815-016-0682-8). And bearing in mind that our Mendelian tendencies to attribute genetic causation to pregnancy wastage, the provocative article by Dr. Coulam draws immediate attention to factors immunological and chronological that must continue to play into the debate on the origins of Recurrent Pregnancy Loss and the relative contributions of chromosome anomalies ("What about superfertility, decidualization, and natural selection?" 10.1007/s10815-016-0658-8). Finally, for the readership vested in the problem of RPL, a telling reminder of male contributions appears in the paper by Lipshutz and colleagues ("Genetic counseling for men with recurrent pregnancy loss or recurrent implantation failure due to abnormal sperm chromosomal aneuploidy," 10.1007/s10815-016-0702-8).

As the dynamic range of topics covered in JARG increases with waxing interests in the rebranding of genetics and epigenetics and the broadening of ARTs into the world of regenerative medicine, keeping Gould's perspective on what only the embryo knows will inform and guide our motivations to proceed for the benefit of all patients whose hopes rest in the successes and failures that lie ahead.