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COMMENTARY

From the Editor

David F. Albertini

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The first decade of the "new" millennium is drawing to a close as yet another year is set to pasture. For human ARTs, 2009 has indeed been momentous. One too many "Octomoms" opened the door for a publicity spectacle that carried conversations about multiple births into the realm of everyday banter. So much so that Time magazine cites the multiple birth problem as one of the top stories in science and medicine for the year 2009. The good news was that Practice guidelines for numbers of embryos transferred were enacted upon by ASRM at the annual meeting in Atlanta, and so was the issue of no tolerance for not adhering to reason and an appropriate code of ethics. It is interesting to note that the concept of "no tolerance" seems so pervasive these days in the developed world and yet we seem to be asked to tolerate more and more. So where will the issue of multiple embryo transfers be in 10 years?

I recall vividly a meeting with Dr. Howard Jones in the spring of 2004 at the Eastern Virginia Medical Center. Peering over his desk, and with not so much as one nanosecond of delay, he asked "so when are you going tell us which egg to transfer?" The multiples problem was one he had personally championed and one he foresaw as the bane of human ARTs until a set of objective criteria could be established that would identify that perfect egg. After years of searching for sentinels, ranging from the endocrine or paracrine properties of the follicle or gene profiles of the enveloping cumulus cells, we remain ignorant as to an appropriate set of biomarkers that would be indicative of high oocyte or embryo quality at least as far as being reliable and non-invasive to the already compromised oocyte that has made its way into the IVF laboratory and awaiting fertilization. Emoting perplexity is acceptable. After all, the molecular complexity of the follicle is a log order greater than it was several decades ago and the gap between the expression of a gene or some collective we now recognize far removed from the functions of the oocyte that have bearing on embryo or offspring health.

Will the answer to this question come from technology or intellectual insight into the biology of the oocyte? Probably both as the first two papers in this issue of JARG indicate.

Browne and colleagues have assembled a set of assays that report on characteristics of follicular fluid that have been previously unappreciated and fit the criteria of sentinels that keep in mind the patients health status beyond the traditional purview of reproductive fitness. Besides offering proof of principle for the technical basis for such tests, there is at least some indication that predicting pregnancy potential may be on the horizon. At the other end of the spectrum, comes a report from Younis and coworkers suggesting that the appearance of the first polar body may have predictive value. Curiously, with the advent and adoption of polar body biopsy for genetic screening of aneuploidy, pioneered by the late Yuri Verlinsky, there arrives the prospect that right under our eyes, or those of the skilled embryologist, may lie at least a partial answer to Dr. Jones' question. Certainly efforts will continue along many paths as the quest for oocyte quality biomarkers expands into the next decade of research in human ARTs and JARG fully expects to provide a leading edge forum for keeping our readership up-to-date and in the know.

Finally, a major imperative embedded within the fertility preservation initiative(interestingly also cited in the Times

D. F. Albertini (✉)
Department of Molecular & Integrative Physiology,
University of Kansas Medical Center,
3901 Rainbow Boulevard,
Kansas City, KS 66160, USA
e-mail: dalbertini@kumc.edu

report), which will be addressed at the upcoming meeting of the International fertility Preservation Society in Brussels, regards the status of cryopreservation technology for the storage of gonadal tissues and germ cells. As momentum continues to swing in favor of vitrification over cryopreservation, this broad spectrum experimental effort additionally reveals insights into the biology of gametes and embryos that would most likely not have been uncovered for years to come. Examples of this are in evidence in the final three papers in this issue evoking potential translational value from bovine, murine, and human model system studies.

The acknowledged contribution of the "follicle of origin" to embryonic competence is shown to play a role for bovine oocytes subjected to vitrification at metaphase-2 stage as illustrated by studies of Gwazdauskas and colleagues. Moreover, they report that paternal factors influence the ability of vitrified oocytes to sustain embryonic development possibly exemplifying the beneficial effect imposed by sperm quality while rescuing deficits undoubtedly resultant from cryopreservation. That the zygote itself handles cryopreservation-induced stress in a stage specific manner is appreciated by the work from the laboratory of Tong shows again that while overall success rates for development in mouse embryos are high after vitrification, only later stages result in development to the blastocyst stage. How additional stressors such as blastomere biopsy impact on the success of cryopreservation is reported on by the Keskintepe group. Here the message is that the lesser of two evils may be vitirification rather than slow freeze technology since survival and development rates were improved in human embryos cryopreserved by the former method after having an initial round of blastomere biopsy. One wonders how many manipulations gametes and embryos can withstand without exceeding their well-honed stress management capabilities?

In summary, the challenges remain on the two fronts of fertility preservation on the one hand and identifying the optimal oocytes or embryos that should be designated for transfer. The next decade will hopefully position human ARTs as one of the many branches of modern medicine that brings improved treatment options to future generations born as a result of singleton gestations.