

## Next gen ARTs: what lies ahead?

David F. Albertini

Published online: 13 December 2013  
© Springer Science+Business Media New York 2013

In our last issue, my commentary drew attention to a sampling of the original papers that appeared in 2013 evidencing the ever narrowing gap between discovery in the laboratory and the resultant proximity to clinical application in the fields of reproductive and regenerative medicine. While forecasting the future in any scientific discipline is risky business, and food for critics in search of low hanging fruit, it would be remiss at this juncture to evade what lies ahead in the field of human ARTs and reproductive genetics given the platform of potential served up in the past year. *Next generation* ARTs are here and poised to change the practice of infertility diagnosis and management soon, with cogent implications of our discipline emerging for the overall benefit of reproductive health in this and subsequent generations!

Our journey into the next generation of ARTs begins with our cover illustration. The astute observer, looking beyond hues and redundancy of form, will notice the central lumen of a uterine tube in plain proximity to the surface of the ovary. This fundamental anatomical association forms the basis for ovum capture where the meeting of sperm and egg will launch the earliest stages of human development. And following fertilization within this specialized niche, one evaded in the conventional practice of ARTs as a result of our routine practices of egg retrieval and in vitro fertilization, the conceptus's sojourn down the tubes will guarantee a timely arrival in the uterus of the blastocyst, poised to implant having completed its excursion

---

*Capsule* ARTs are rapidly evolving with the introduction of powerful analytical tools to satisfy the needs of the reductionist aiming to solve the riddles of infertility on a molecular genetic level. At the same time, revisiting reproductive physiology with a deeper sense of appreciation for how we have been culturing human embryos may open avenues for improving our current methods with novel technology aimed at recapitulating the reproductive tract in the incubator.

---

D. F. Albertini (✉)  
University of Kansas Medical Center, Kansas, KS, USA  
e-mail: dalbertini@kumc.edu

over a matter of days. In human ARTs, the transformation from zygote to fully expanded blastocyst is witnessed daily in the embryology laboratory as we search for sentinels of success forecasting the likelihood of term gestation. And, our perception of cellular events by the use of time-lapse imaging is providing insights into cleavage, compaction, and blastocoel formation never before appreciated. As exciting as it is to follow this remarkable transformation from a single cell to one endowed with so much developmental potential, our perceptual license requires that our object of study remain relatively motionless, resting in an artificial environment made from ingredients reflecting our best approximation of the chemical environment an embryo would be exposed to if it was taking this journey through the uterine tubes.

Our lead article by Jason Swain this month takes the subject of *Next Gen* ARTs to a new level of comprehension and practicality (*Shake, rattle, and roll: bringing a little rock to the IVF laboratory to improve embryo development*). Jason takes on a challenging question. How well are we, as practitioners of ARTs, truly recapitulating the tubal environment experienced by embryos from the time of ovum capture through to delivery into the uterine cavity? His argument is aligned with a more introspective analysis of the biophysical forces being exerted on the embryo. The mantra “Be The Embryo” is adopted in his critical assessment aimed at improving the methodology now in use to potentially bring our *ex vivo* mentality a bit closer to one of an *in vivo* reality.

The contention that sitting in a dish as a sessile object may compromise some of the external cues to which the embryo is subjected *in vivo* is valid given how little we know about the physical conditions within the tubal lumen during embryo transport. From animal studies at least two recognizable forces have been identified. First, at the “ampullary” end of things, the highly ciliated fimbria create waves of “touchy-feely” stroking that rotate and gyrate any object of similar size and shape proportions that would liken the embryo during the first

2 days of its excursion. Second, once within the inner reaches of the less ciliated and more mucous producing parts of the tubal epithelium, the embryo is awash with secretions and enveloped by the recurrent and pulsatile contractions of the smooth muscle that will guide it for the remainder of its journey, encompassing the last 2 days of the trip. If you feel like you are being taken for a ride to nowhere, then be sure to have a close look at this article and ask yourself if we may be missing something in the design and practice of ARTs.

Of course, predicating any effort to improve an existing technology must exceed in substance the theoretical foundations upon which it is built. Swain takes this into consideration from a practical point of view, drawing on recent literature to show that a little “shake, rattle, and roll” can go a long way to improve the chances of pregnancy when a more active biophysical environment is deployed during embryo culture. As the idea of using time-lapse imaging attracts greater interest as an assessment tool, with the jury still out as to predictive utility, a not-so-subtle confounder enters the picture. Time-lapsing a moving object is a bit different from a sessile one whose every action at a cellular level can be captured easily as long as a stable focus plane can be established and maintained. Stay tuned as our deepening perspective of natural conception and embryo development melds with the desire to improve our technology.

Several glimpses of this and other *Next Gen* prospects for human ARTs are also introduced in this issue of JARG. We are pleased to bring our readership a meeting summary from the 3<sup>rd</sup> International Society for Fertility Preservation conference held recently in Valencia, Spain. This rapidly expanding field is forging the discipline of Fertility Preservation to new heights and offering alternatives to traditional ARTs likely to expand the purview and application of technology in development. The ever-perplexing issue of how to select sperm with respect to their epigenetic normalcy becomes more disconcerting with the demonstration of significant heterogeneity within healthy fertile men as described in the study by Buffone and colleagues (*Heterogeneous distribution of histone methylation in mature human sperm*). And a critical assessment of automated sperm analyzers relative to manual approaches is provided in the paper from Freour and colleagues (*Double-blind prospective study comparing two automated sperm analyzers versus manual semen assessment*).

In closing, we would like to take this opportunity to welcome our newest additions to the editorial board of JARG. Paula Amato, David Reichman, Jason Swain, and Mary Zelinski bring to JARG a blend of interests and expertise that is likely to enrich our future scope and efforts beyond the first 5 years we have had the opportunity to serve you, our readership. Happy New Year to All!