



Breaking new ground on the ovary construction project

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With fits and starts for nearly 13 years now, prospects of making an “artificial” or “synthetic” or “prosthetic” human ovary have waxed and waned through the stem cell and regenerative medicine hallways— not surprisingly greeted—to the mixed reactions expected of a three-ring circus. After all, over and above offering some much needed assistance to women whose ovarian function comes to an abrupt and premature end, what the aforementioned construction project could portend is an ever-expanding domain for extending human fecundity into the later decades of a somatic existence detached from traditional forms of reproduction. Sounds a bit Orwellian, does it not?

We have left behind a year of explosive progress. Progress measured in terms of heightened sensitivity aimed at most every molecular measure of life as we know it. And no longer must advancement await the laws of averaging many cells, tissues, organelles, or molecules to obtain sufficient datum— data mining the single cell, a solitary sperm, egg, or neuron is now theoretically comprehensible within the limits of resolution afforded by today’s technology platforms.

One notable offshoot, paralleling descriptions of oocyte-producing stem cell in mammals, has been the initiation of a branch of reproductive medicine geared specifically to meet the needs of individuals whose fertility would be lost as a result of ancillary disease conditions and treatments damaging to ovarian function [1]. As an extension of our November 2017 issue emphasizing recent advances in the field of fertility preservation, we are pleased to bring our readership a series of articles spanning breakthroughs in the quest for building a human ovary, through to the latest studies documenting the ubiquitous and parsimonious nature of maintaining the follicle reserve.

Leading off this month are several reviews, two of which take aim at the *raison d’être* for much of the impetus behind fertility preservation. Mili Thakur and her colleagues at Wayne State University in Detroit, MI, focus on galactosemia, tracing developmental implications that impact such patients as premature ovarian insufficiency later in their reproductive years (primary ovarian insufficiency in classic galactosemia: current understanding and future research opportunities, <https://doi.org/10.1007/s10815-017-1039>). Adding clarity and direction to the subject of clinical evaluation of ovarian function (when the only constant among the acronyms is an “O”—imagine) is the thorough review of this topic by Lisa Pastore and her collaborators (Reproductive ovarian testing and the alphabet soup of diagnoses: DOR, POI, POF, POR, and FOR, <https://doi.org/10.1007/s10815-017-1058>).

Our enticing menu on this ever-growing and resounding area of reproductive medicine proceeds after the plate setting with our lead article this month, a publication truly representing the power of collaboration between dedicated clinicians, scientists, and engineers. From the Catholic University of Louvain in Brussels, Belgium, comes a corpus of research in which the first principles for designing an ovary *ex vivo* were derived from studies on the physical and proteinaceous properties of fresh human ovarian tissue, resulting in reproducible formulations capable of supporting follicle health prior to removal from the engineered matrices (<https://doi.org/10.1007/s10815-017-1091-3>). Spearheaded by the collaborations of Professor Marie-Madeleine Dolmans, these studies recognize the importance of building materials, in this case mixtures of fibrin tuned to exhibit the rigidity most similar to the native ovarian tissue. That the physical nature of the ovarian cortex was a telling determinant for growth and survival of follicles was first articulated here in JARG in a paper by Woodruff and Shea [2] whose continuing contributions to this field also exemplify the utility of engineering principles when modeling tissues and organs for purposes encompassed in the area of regenerative medicine [3].

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Building out ovaries is only one dimension of the evolving fertility preservation landscape featured this month. Embedded deep within the ovarian stroma, the primordial follicle pool rests “unrested” before being launched towards a destination that few will ever attain. And encouraging an already diminishing return on the follicle reserve investment available at the time of puberty are any and all natural or iatrogenic insults imposed on the ovary that target the growing follicle fraction for demise apparently opening a floodgate of wannabes that will be to no avail. Given that the successes realized in patients receiving autologous transplants of their cryopreserved ovarian tissue are mounting [1], efforts to decipher and manipulate the consequential “burnout” of the remaining follicles would provide mechanistic insights into what has become a pressing and much needed course of investigation. Such is the objective of the contribution from Meiorin and colleagues who have established the kinetics and extent of the underlying activation of follicles from marmosets, bovines, and humans establishing animal models and experimental templates to take this research forward in the next few years (Follicle activation is a significant and immediate cause of follicle loss after ovarian tissue transplantation, <https://doi.org/10.1007/s10815-017-1079>).

And rounding out the fertility preservation focus, our readership is encouraged to take a deeper look at the implications for medically indicated egg freezing, immunomodulation strategies for ovarian transplantation in animal models, and how ovarian responsiveness is influenced by different cancers in women.

While highlighting the topical in reproductive medicine reinforces our dedication to bring readers objective and sound treatments of matters receiving immediate attention by the press, and therefore consumption by prospective stakeholders, our mission does not stop there. In a world where information is exchanged unfinished, unedited, and unrestricted through today’s media norms, it behooves us professionals to raise the flag of skepticism until the reigns of certainty can be harnessed and managed in a fashion conducive to advancing care for the fertile and infertile. Displaying discretion at every level of the publication process is a current and present imperative without which the efforts of JARG would be squandered. It is through the eyes of our many reviewers and members of the Editorial Board that we pledge to bring you, our readership, the measured excitement and enthusiasm on the agenda for reproductive medicine and biology in 2018. Happy New Year!

References

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