How disparities in gamete maturity influence the nascent conceptus, and beyond

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Selecting suitors for an oocyte in waiting used to be a situation reserved for those sperm capable of making their way through the female reproductive tract with fertilization armament poised. While evidence abounds in the animal literature for the ability of female gametes to attract their would be suitors via a variety of devices, ARTs as we practice today have all but given up letting Mother Nature take her course. In the surge for selection dictated by the expanded usage of ICSI, the embarrassment of riches presented by the normospermic patient in reality becomes a wishful expectation for homogeneity.

With the name of the game being synchrony-synchrony-synchrony, no wonder launching these earliest events of embryogenesis influence immediate progress during the preimplantation phase and perhaps even into adulthood. Synchronizing genomes from mom and dad with respect to acquiring chromatin maturity states capable of working the magic of syngamy is one of the most significant processes initializing the very beginnings of human development. And the road taken by the sperm head on its way to becoming the male pronucleus is as elegant example of nuclear remodeling as can be imagined. From unraveling compacted chromatin, to protamine displacement and nucleosome assembly, to constructing a card-carrying nucleus, this remarkable process in a matter of hours yields the paternal complement to the female pronucleus that will forever-maybe-be united in the ultimate spirit of zygosity. And while the male genome demands and consumes resources stored in the oocyte cytoplasm, achieving perfect registration of chromatin states is no simple matter and failings of the slightest varieties can have both short and long term impacts on future development(1).

With this backdrop, our issue this month takes aim at the expanding repertoire of data bases bringing contemporary

sperm biology in line with prospects for diagnosis and treatment of male infertility. From genetic screening platforms, to the influence of obesity on the sperm proteome, to the impact of chronic inflammation, and on to the emerging roles of microRNAs and male fertility we see a field bursting with promise but challenged with practical situations yet to be fully resolved.

Here is where the problem of synchrony rears its ugly head. Even though we rest comfortably in attributing maturity to the status of oocytes bearing signs of having arrested at metaphase of meiosis 2 (M2s), reality is far different given when maturation is measured in its full form. Routine practices of controlled ovarian stimulation do not always yield a basket full of M2s and even if they look mature, timing is essential without an accurate estimate of just when an hCG trigger did its thing to the oocyte (2). Exactly what is regulating the differential processing of chromatin from maternal and paternal chromatin has been a mystery until recently where protamine specific patterns of phosphorylation have now been reported to make a difference in assuring the correct timing for matching chromatin states(3). Room for problems leading to asynchrony between genomes still exist. Disparities inherent in the maturation window for oocyte or sperm are likely given our inability to ascertain discriminating properties of gametes as we select them in the embryology laboratory. Besides maturation disparities, we are gradually coming to appreciate that even in the case of the normospermic individual, looks can be deceiving even in the face of our most trident measures of performance.

One example attracting attention in the autism-spectrum-disorder (ASD) field has recently appeared. Risk assessments for genetic predispositions to disease are being recognized in many fields, including reproductive medicine. Breuss and colleagues now report a potential benefit for genetic counseling given their demonstration of novel mosaic variants in human sperm (4), affirming the growing need for documenting the emergence of de novo mutations during germline or early embryonic stages of development. We hope our readership is

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guided along the pathway of male infertility and the latest breakthroughs provided in this issue.

Finally, we note our continuing commitment to the field of fertility preservation and offer coverage of the International Society for Fertility Preservation meeting held last November in New York City. Abstracts from the meeting are also included in this issue. Of the breakthrough research presented at this meeting, exemplifying again how this field has created multiple avenues for basic and applied research in reproductive medicine, are advances in the topic of oocyte in vitro maturation. With more younger patients seeking fertility preserving treatments, the particular case of how ovarian materials might be deployed beyond autologous tissue transplantation has remained of great interest (5). Now the group from Copenhagen has discovered that residual medullary tissues left over following preparation of cortical strips (for cryopreservation) are a rich source of human oocytes many of which are capable of initiating and completing maturation in vitro (***Improving the maturation rate of human oocytes collected ex vivo during the cryopreservation of ovarian tissue***; <https://doi.org/10.1007/s10815-020-01724>). Taking such a strategy into the clinic is evidenced by the case report of Kirillova and her colleagues who not only used this material to obtain mature oocytes but generated euploid blastocysts for future use (***Cryopreservation of euploid blastocysts obtained after fertilization of in vitro matured ovarian tissue oocytes: a case report*** <https://doi.org/10.1007/s10815-020-01729>).

With the Covid-19 crisis touching so many in these troubling days, we wish all of our followers good health and send our warmest greetings to those who have been affected.

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