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COMMENTARY

Climate change and the morphing of human ARTs

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For some, these monthly commentaries may provide interested observers with the intended overview of what the particular issue of JARG delivers to our readership, often couched within current topics in reproductive medicine and biology that would not be evident in the conventional journals covering these fields of endeavor. For others, the stretch of the imagination afforded by editorial prerogative and cogitation of the associative variety leads more directly to head scratching-not a bad thing in this altered world of disorder we now live in. Whatever your response, that climate change above and beyond our well-worn concerns over ocean salinity and temperature, deforestation, and environmental contamination are here to stay, the same conclusion we must accept when it comes to the COVID-19 pandemic. So we at JARG continue to offer a perspective that sometimes will follow well within the purview of reproductive medicine and biology, but will at times appear to stray off limits all to induce a level of curiosity, disgust, and maybe even enlightenment when it comes to facing the challenges of the day in this strange year of 2020.

Such is the case with the latest and greatest scientific reports (should really say summaries) ranging appropriately from how SARS-CoV-2 is playing some novel and never-before-witnessed games with the cell biological management of pathogenic viruses [1] to treating the current pandemic as a catalyst for understanding its impact on the future fertility of our species [2]. Next month's issue of JARG will take these widely divergent aspects of COVID-19 to our readership through the lens of living with the pandemic today and in the not-so-distant future relative to what will happen over the long term given the already disturbing reality of broad based and lingering health deficits known to affect many survivors of the disease.

Closer to home, and the climate within which ARTs are practiced today, the overarching question has been and will continue to be selecting high quality embryos for transfer that have the best chance of producing healthy offspring. Getting from retrieved oocyte to blastocyst has created a standard of care driven historically by achieving as many retrievable follicles after an appropriate controlled ovarian stimulation (COS) regime with an attitude of "the-more-the-merrier" for stockpiling frozen embryos. That attrition during extended culture due to developmental arrest, iatrogenic elimination as poor "test-takers" (read aneuploid for example), or embryos lacking the wear-with-all to recover from cryopreservation is how we operate and only sets the stage for repeat cycles, at least for those patients lucky enough to respond well to COS.

But knowing all embryos start this journey as ovarian oocytes, has increased awareness of the importance of genetic and epigenetic determinants laid down in the blueprint for later development while the oocyte transits through the follicle. It is in this line of thought, reminding us of the classical embryology adage that "embryogenesis begins with oogenesis" that we have come to respect the importance of the molecular and cellular principles of oogenesis dictating embryo quality and chances of term pregnancy.

Enter the subcortical maternal complex (SCMC). Introduced to JARG readership in 2016 [3], a full decade after the SCMC was identified in mice by Jurien Dean and his colleagues at the NIH as the missing link between the oocyte and the embryo [4]. If there ever was a mother's legacy to her children, it would be in the form of the many proteins comprising the SCMC. And only recently is the role of the SCMC being revealed as an essential component of the maternal legacy driving the human embryo through the most critical stage of preimplantation development. Earlier genetics studies had implicated mutations in the NLRP7 gene as linked to the formation of hydatidiform moles [5, 6] even while gene products for this and other proteins were becoming recognized as integral components to the SCMC in mice and sheep. And in this issue Bebbere and colleagues now begin to trace the expression pattern for SCMC components during the course of oogenesis in the sheep model and

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find interestingly that age may be a complicit player in the story of developmental competence as enacted through the SCMC (Subcortical maternal complex (SCMC) expression during folliculogenesis is affected by oocyte donor age in sheep; https://doi.org/10.1007/s10815-020-01871). Moreover, with the aggregate clinical evidence implicating *screenable* mutations in SCMC components such as NLRP7 as causative for recurrent moles, it has become possible to offer oocyte donation to patients carrying mutations that would have otherwise been subjected to repeat conventional treatments for their condition (Pregnancy after oocyte donation in a patient with NLRP7 gene mutations and recurrent molar hydatidiform pregnancies; https://doi.org/10.1007/s10815-020-01861). These papers bridge an important gap between basic biology and ART care.

Finally, there is mounting evidence to suggest that not only as a genetically identifiable entity underlying the pathogenesis of hydatidiform moles, NLRP7 and other members of the SCMC play vital functions in the epigenetic modifications of the female genome following fertilization [7] and during the course of intraovarian oogenesis, impacting the embryo down the road [8].

We take this opportunity to introduce Denny Sakkas as our newest Associate Editor of JARG and as always welcome your feedback and insights into this and future issues of JARG.

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