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EDITOR'S COMMENTARY

Reproductive biology and medicine 2015—the year in review

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It would be an understatement to suggest that the discoveries in reproductive biology and medicine during 2015 were anything short of remarkable. And to rank these according to potential impact on our field would be a disservice to the groups that have persevered in tackling fundamental questions with the most sophisticated of techniques ensconced in the biomedical research enterprise of this decade. And so, with a measure of humility, a sense of awe, and the poetic license liberally taken by your EIC, a short summary of what might be considered a sentinel of what reproductive medicine may look like in the coming years is provided below.

Progress in the area of germline stem cells continues to dominate a research landscape aiming to define the embryonic origins of primordial germ cells (PGCs) in molecular terms while at the same time nudging this line of research into the domain of treating infertility in men and women. That the horizon indeed holds the promise of making germline stem cells in vivo and in vitro is evidenced by the latest contributions from the laboratory of Surani and colleagues who have now mapped a molecular signature for the production of PGCs in humans (Tang et al., A Unique Gene Regulatory Network Resets the Human Germline Epigenome for Development. Cell. 2015 Jun 4;161(6):1453–67. doi: 10.1016/j.cell.2015.04.053. http://www.ncbi.nlm.nih.gov/pubmed/26046444).

And the continuing quest for ways to obtain the best quality stem cells, which the field of regenerative medicine has been waiting for (as human ARTs sets the gold standards for quality embryo production), has taken an interesting twist of fate with a recent publication from the laboratory of Susan Fisher and her colleagues at UCSF (Zdavkovic et al., Human stem cells from single blastomeres reveal pathways of embryonic or trophoblast fate specification. http://dev.biologists.org/lookup/doi/10.1242/dev.122846). Taking single blastomeres from four 8-cell and one 12-cell embryos from a single individual lead to the derivation of ten ES cell lines, each of which displayed unique transcriptomic and protein heterogeneities, providing new insights into the allocation of cell lineages in the human embryo.

Gene editing in human embryos captured the attention of many this past year. The power of CRISPR/Cas9 entered the arena of reproductive medicine with much fanfare as a result of the publication by Liang and colleagues proof-of-principle case using ART generated three PN zygotes (Liang et al., CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. Protein Cell. 2015 May;6(5):363–72. doi: 10.1007/s13238-015-0153-5. Epub 2015 Apr 18. http://www.ncbi.nlm.nih.gov/pubmed/25894090). This work sparked renewed interest in prospects for genetic engineering but in tandem has brought the level of discourse to new heights in light of ethical and societal implications that are only now being subject to the degree of scrutiny they deserve.

That RNAs of the many varieties now understood to have important physiological functions have been catching their fair share of attention at both the basic and clinical levels has come as no surprise. From the Kravetz and Diamond groups, this year came the exciting finding that certain sperm-associated RNAs detected by next gen sequencing could be

Capsule 2015 was a year of unprecedented discovery in the fields of reproductive biology and medicine. Here, we take note of ten publications that have drawn upon technological advances of the past decade to bring new ways of thinking about old problems into the realm of human ARTs and reproductive genetics.

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markers for sperm quality extending the application of new technologies well beyond the more traditional semen parameters now in use (Jodar et al., Absence of sperm RNA elements correlates with idiopathic male infertility. Sci Transl Med. 2015 Jul 8;7(295):295re6. doi: 10.1126/scitranslmed.aab1287 http://www.ncbi.nlm.nih.gov/pubmed/26157032). And, so as not to overlook the role of microRNAs (MiRNAs), the discovery of MiRNA-320 in human follicular fluid was used to test the possible impact of this factor on the determination of embryo quality using a mouse model (Feng et al., MiRNA-320 in the human follicular fluid is associated with embryo quality in vivo and affects mouse embryonic development in vitro. Sci Rep. 2015 Mar 3;5:8689. doi: 10.1038/srep08689. http://www.ncbi.nlm.nih.gov/pubmed/257325130).

A similarly game-changing molecular analysis of human embryos was published by Tohonen and colleagues from Sweden (Tohonen et al., Novel PRD-like homeodomain transcription factors and retrotransposon elements in early human development. Nat Commun. 2015 Sep 11;6:8207. doi: 10.1038/ncomms9207, http://www.ncbi.nlm.nih.gov/pubmed/26360614). Above all, the aforementioned articles collectively have advanced our understanding of the inner workings of human gametes and embryos and will impact the practice of ARTs in the not-too-distant future. In parallel, investigations into the fundamentals of reproduction have revealed intricacies of a cause-and-effect nature that could only be gleaned from animal studies.

To wit, the capacity of mammalian zygotes to detect genome abnormalities of maternal or paternal origin has been poorly understood on a mechanistic level. That is, until the work of Marchetti appeared (Marchetti et al., Meiotic interstrand DNA damage escapes paternal repair and causes chromosomal aberrations in the zygote by maternal misrepair. Sci Rep. 2015 Jan 8;5:7689. doi: 10.1038/srep07689. http://www.ncbi.nlm.nih.gov/pubmed/25567288). And an elegant example of how mouse genetics can be exploited to understand the impact of maternal metabolism on offspring health was provided by the work of Wu and colleagues in Australia (Wu et al., Mitochondrial dysfunction in oocytes of obese mothers: transmission to offspring and reversal by pharmacological endoplasmic reticulum stress inhibitors. Development. 2015 Feb 15;142(4):681–91. doi: 10.1242/dev.114850. http://www.ncbi.nlm.nih.gov/pubmed/25670793). In addition to identifying an influence on oocyte mitochondria, these studies showed that a targeted pharmacological intervention in females could rescue germline deficits resulting in the production of phenotypically normal offspring.

And if you want to double your reading pleasure, two final examples of how great things can happen when the stimulus for translational biology crosses paths with problems we have known deter fertility in humans—but have escaped detection due to a lack of bravado and technology! For the oocentrics among our readership, have a close look at the structural basis of age-related aneuploidy in human oocytes as provided by Melina Schuh and her colleagues of Cambridge University in England (Holubcova et al., Human oocytes. Error-prone chromosome-mediated spindle assembly favors chromosome segregation defects in human oocytes. Science. 2015 Jun 5;348(6239):1143–7. doi: 10.1126/science.aaa9529. http://www.ncbi.nlm.nih.gov/pubmed/26045437). This truly enlightening study defines meiotic spindle dynamics in cell biological terms that materially extend what have long been suspected as defects acquired by human oocytes with advancing maternal age. From the same laboratory, and last but not least, 2241 mouse oocytes at progressive stages of development were probed by live cell RNAi screens for meiotic phenotypes yielding an unprecedented data base that attests to the power of high-throughput screening in reproductive biology (Pfender et al., Live imaging RNAi screen reveals genes essential for meiosis in mammalian oocytes. Nature. 2015 Aug 13;524(7564):239–42. doi: 10.1038/nature14568. Epub 2015 Jul 6. http://www.ncbi.nlm.nih.gov/pubmed/26147080).

We hope these highlights of the year will guide our readership into 2016 and set the stage for our goal for next year in bringing topical reviews of the many technologies being applied in reproductive medicine and biology. We thank our many supporters for their efforts during the past year and wish all a happy holiday season and new year.