Published in final edited form as:

Mol Reprod Dev. 2017 October ; 84(10): 1024–1026. doi:10.1002/mrd.22869.

Report from the 2016 UCSF Center for Reproductive Sciences Retreat

Paolo Rinaudo¹ and **Marco Conti¹**

¹Department of Obstetrics, Gynecology and Reproductive Science, University of California, San Francisco, 513 Parnassus Avenue, HSW 1656, Box 0556, San Francisco, Ca 94143-0556

On June 2–3, 2016, the Center for Reproductive Sciences at the University of California, San Francisco (UCSF), hosted its annual meeting in partnership with the Wiley-Blackwell Journal *Molecular Reproduction and Development (MRD)*. The meeting was held at the Observation Post at the Presidio of San Francisco, in the Golden Gate National Recreation Area. Meeting participants included clinicians, scientists, students, and post-doctoral fellows.

The retreat began with a Mini-Symposium on “Reproductive Health and the Environment”, held on the afternoon of the first meeting day. After initial opening remarks from Drs. Patricia Hunt (Center for Reproductive Biology, Washington State University) and Marco Conti (Director, Center for Reproductive Sciences, UCSF), several presentations on a variety of topics were given, focusing on the impact of the environment on gonadal development and reproductive function.

Dr. Tracey Woodruff, Director of the Program on Reproductive Health and the Environment at UCSF, provided a timely history and insightful overview of environmental exposure to industrial chemicals. Several key points worth emphasizing include: first, exposure to a variety of industrial chemicals is ubiquitous in our current society, and occurs through food, water, air, and consumer products. A minority of these chemicals introduced into the environment (~200) are well tested in terms of biological effects, whereas the majority of them (~80,000!) have unknown effects. One example of such a hazardous chemical is the flame retardant polybrominated diphenyl ether (PBDE), which is found at detectable levels in polar bears living in the wild, demonstrating its widespread contamination in the environment. Secondly, there are times of heightened sensitivity to chemicals, particularly when exposures occur during vulnerable periods of fetal development, such as periconception. One particularly worrisome study indicated that 43 of these environmental chemicals are found in pregnant women, with unknown effects on the offspring's health. Given the increasing burden of chronic disease due to exposure to these chemicals, Dr. Woodruff emphasized that leading health care, professional, and scientific societies declared industrial chemicals as a concern for reproductive and developmental health (Di Renzo et al. 2015). Indeed, her main message was that the medical profession has a duty to act, and must

Corresponding author: rinaudop@obgyn.ucsf.edu, Paolo F Rinaudo, MD, PhD, Reproductive Endocrinology and Infertility, University of California San Francisco, 513 Parnassus Ave, HSW 1463E, Box 0556, San Francisco, CA, 94143, tel:415-476 2704, fax:415-353 7744.

use its influence to benefit the health of all patient populations and future generations (Sutton et al. 2016).

Dr. Carmen Williams, from the Reproductive Medicine Group at the National Institute of Environmental Health Sciences, presented her work on epigenetic reprogramming of female reproductive tract function in the mouse following developmental exposure to estrogenic chemicals. She discussed how fetal exposure to the isoflavone genistein, a phytoestrogen, affects epigenetic marks at the genome-wide level. Further, specific genes (*Pitx1* and *Six1*) showed genistein-induced epigenetic modifications and altered expression in ways that could predispose women to uterine cancer. A fascinating aspect of her studies was that estrogen exposure may affect a subpopulation of cells possessing regenerative capabilities.

Several investigators from UCSF demonstrated how different environmental chemicals affect stem cell development and differentiation. Drs. Josh Robinson and Susan Fisher showed how PBDEs affect neurogenesis, using neuronal stem cells, and placentation, using cytotrophoblast stem cells. Dr. Boris Reznik, from Dr. Diana Laird's laboratory, revealed how phthalates administered *in utero* disrupt germ cell development and the piRNA pathway. Finally, Dr. Roy Gerona discussed his data on how human hair samples may provide an average and temporal record of an individual's daily exposure to xenobiotics. He suggested that hair provides an excellent alternative for assessing chronic and average exposure to endocrine-disrupting organic pollutants.

The second day of the retreat expanded on the main theme, with presentations on array of research topics from scientists across the nation.

Drs. Gloria Brar (University of California, Berkley) and Jennifer Fung (UCSF) presented their work on the meiotic translational program and chromosome trafficking in yeast models of meiosis. Dr. Brar performed genome-wide measurements of translation using ribosome profiling, and showed that nearly every gene in the yeast genome was translated during meiosis in a strongly stage-specific manner – including thousands of genes with no previously known meiotic role. Interestingly, she found meiotic translation of thousands of novel, short open reading frames, which necessitates a broader view of what constitutes a coding region, even in the most well-annotated eukaryotic genome. Dr. Fung reported how disruption of telomere-led motion during yeast meiosis leads to a reduction in the fidelity of chromosome association, resulting in reduced gamete viability. Using *TLC1*, which codes for the RNA template of telomerase, Dr. Fung found that protection of sister telomeres is a key feature of meiosis; alteration to this process could explain the increased incidence of chromosome-segregation errors that generate aneuploid gametes.

Dr. Keith Latham (Michigan State University) discussed the role of the gene *Smchd1* (Structural maintenance of chromosome flexible domain containing 1) during preimplantation development, suggesting that it contributes to early lineage formation. In fact, transient suppression of *Smchd1* function leads to deficits in embryo size, nuclear volume, cell number, and hatching, as well as deficiencies in term development.

Several trainees and fellows presented their excellent work on the migration of primordial germ cells (Andrea Cantu, from the Laird lab, UCSF) and the regulation of transcription in

mouse embryonic stem cells (Trisha Macrae, from the Santos Lab, UCSF). Clinically oriented presentations highlighted novel insights into human folliculogenesis (Dr. Hakan Cakmak, UCSF), and how decidualization is affected by the presence of uterine fibroids (Dr. Lusine Aghajanova, UCSF). A related talk from faculty member Dr. Trevor Burt (UCSF) focused on T cell diversity and function during human fetal development, in which he provided data on how T cells display unique functional characteristics that are tuned to meet the specific needs of the developing individual.

Particularly noteworthy were the presentation of Dr. Carlos Simón (University of Valencia, Spain) and the Founders Lecture, presented by Dr. Gary Wessel (Brown University).

Dr. Simón provided some novel molecular evidence of embryonic-maternal communication. He proposed that maternal microRNAs act as transcriptomic modifiers of the pre-implantation embryo, via endometrium-derived exosomes (Vilella et al. 2015). Using microarray profiling of human endometrial fluid during the window of implantation, Dr. Simón's group identified *hsa-miR-30d* as an exosome-associated small RNA. Further, *hsa-miR-30d* was internalized by the trophectoderm of mouse embryos, resulting in an indirect overexpression of genes involved in embryo adhesion.

Dr. Wessel showed the remarkable and beautiful varieties of reproductive strategies adopted in the animal kingdom, and then focused on how the germ-line lineage is specified. He emphasized how primordial germ cells (PGC) specification occurs, with particular attention on the regulation of PCG development in the sea urchin (Fresques et al. 2014). He provided compelling evidence on how PGCs in the sea urchin are transcriptionally quiescent, yet possess a set of inherited germ-line determinant mRNAs. These mRNAs remain stable because the RNA-binding protein Nanos continually degrades the deadenylase CNOT6 (Swartz et al. 2014). As a result, PGCs are insulated from differentiation signals, allowing them to retain the molecular characteristics of a totipotent egg and early embryo – a time capsule, of sorts, that retains cellular potency within the germ line as the remaining embryo differentiates.

The retreat concluded with a lively poster session where the trainees in the Center for Reproductive Sciences showcased their research projects, which span basic, translational, and clinical aspects of reproduction. Appropriately, the meeting topics highlighted the overall mission of the Center for Reproductive Sciences: Integration of different experimental models, ranging from yeast to humans, to tackle major unanswered questions in reproduction. It also provided examples on how different research programs that explore the diversity in reproduction can converge to provide new insights into one of the most important aspects of human health.

Acknowledgments

We thank Dr. Wessel for supporting the Retreat, and for his insightful and entertaining presentation. The organizers are also indebted to Drs. Carmen Williams, Keith Latham, Patricia Hunt, Gloria Brar, and the UCSF faculty and students for presenting their work.

We would also like to thank the following entities for their support:

Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institutes of Health cooperative agreement 4P50HD055764-10, National Centers for Translational Research in Reproduction and Infertility (NCTRI)

UCSF Center for Reproductive Sciences

UCSF Mary Martin Cadieux Fund

UCSF Robert B. Jaffe Innovation Fund

UCSF Department of Obstetrics, Gynecology and Reproductive Sciences

Wiley-Blackwell.

Abbreviations

PDBE	polybrominated diphenyl ether
UCSF	University of California, San Francisco

References

- Di Renzo GC, Conry JA, Blake J, DeFrancesco MS, DeNicola N, Martin JN Jr, McCue KA, Richmond D, Shah A, Sutton P, Woodruff TJ, van der Poel SZ, Giudice LC. International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals. *Int J Gynaecol Obstet*. 2015; 131:219–225. [PubMed: 26433469]
- Fresques T, Zazueta-Novoa V, Reich A, Wessel GM. Selective accumulation of germ-line associated gene products in early development of the sea star and distinct differences from germ-line development in the sea urchin. *Dev Dyn*. 2014; 243:568–587. [PubMed: 24038550]
- Sutton PM, Giudice LC, Woodruff TJ. Moving from awareness to action on preventing patient exposure to toxic environmental chemicals. *Am J Obstet Gynecol*. 2016; 214:555–558. [PubMed: 27126615]
- Swartz SZ, Reich AM, Oulhen N, Raz T, Milos PM, Campanale JP, Hamdoun A, Wessel GM. Deadenylation depletion protects inherited mRNAs in primordial germ cells. *Development*. 2014; 141:3134–3142. [PubMed: 25100654]
- Vilella F, Moreno-Moya JM, Balaguer N, Grasso A, Herrero M, Martinez S, Marcilla A, Simon C. Hsa-miR-30d, secreted by the human endometrium, is taken up by the pre-implantation embryo and might modify its transcriptome. *Development*. 2015; 142:3210–3221. [PubMed: 26395145]