April 30 2023

Research Description of the Wu Lab:
Master Program

I. Contact information

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II. Research title

What do sperm piRNAs do?

III. Project description

Medically assisted reproduction *via in vitro* fertilization is a widely adopted solution to infertility and diverse family structures such as those with same-sex couples. Despite advancements, success rates of *in vitro* fertilization remain suboptimal with no clear scientific explanations. Between 2017–2020, 6,024 women in Switzerland received *in vitro* fertilization treatments every year, with only 34% resulting in live births. The current standard-of-care procedure in Switzerland is transferring one embryo from a maximum of 12 embryos for each treatment. Determining which embryo to transfer to the mother and which ones to discard is critical, but current criteria for embryo selection do not fully predict the outcome of embryo development, challenging patients and clinicians. One solution is to seek additional predictors for embryo viability, such as **epigenetic paternal factors**. Upon fertilization, the new embryo instantaneously inherits all maternal materials from the oocyte, which are known to be indispensable for embryo development. By contrast, whether and how paternal or sperm information is utilized by embryos is poorly understood. In our lab, we study how paternal non-coding RNA influences embryo viability by investigating sperm **PIWI-interacting RNAs (piRNAs)**. piRNAs are abundant, germline-enriched small RNAs that do not encode proteins. As tiny (~30 nt) as they are, piRNAs are vital for male fertility in mice and humans, regulating protein-coding genes important for spermatogenesis. Despite their well-established role in spermatogenesis, what led our lab to study sperm piRNAs is the unexpected finding of their contribution to the development of embryos that the sperm fertilizes. How sperm piRNAs act intergenerationally remains a mystery, which we aim to solve by characterizing paternally inherited piRNAs, sperm long RNA dynamics, and embryos fertilized by mutant sperm lacking piRNAs using mouse genetics, sequencing, imaging, and other molecular and cellular biology techniques. We want to test the big idea that sperm small RNAs can serve as a paternal predictor of embryo viability, aiding the evaluation of embryos in medically assisted reproduction.

IV. References

1. Wu PH*, Fu Y, Cecchini K, Ozata DM, Arif A, Yu T, Colpan C, Gainetdinov I, Weng Z*, Zamore PD*. (2020) The evolutionarily conserved piRNA-producing locus *pi6* is required for male mouse fertility. *Nature Genetics* 52(7):728-739. **Co-corresponding authors*
2. Wu PH* and Zamore PD*. (2021) Defining the functions of PIWI-interacting RNAs. *Nature Reviews Molecular Cell Biology*. **Co-corresponding authors*
3. All publications: https://scholar.google.com/citations?user=JOqwP1IAAAAJ&hl=en