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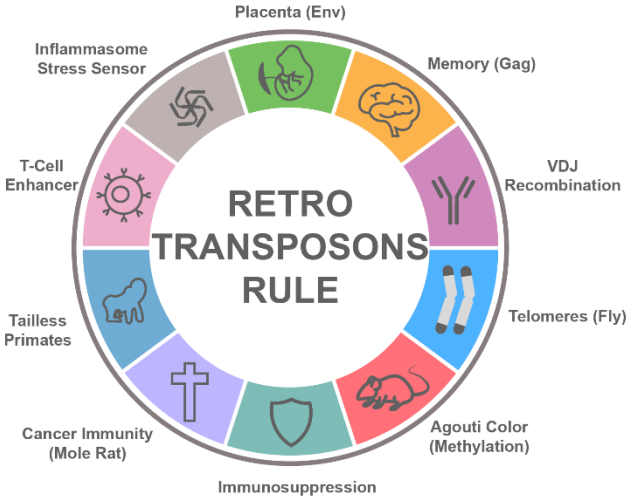

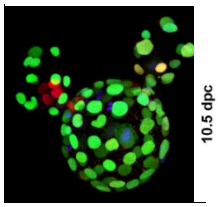

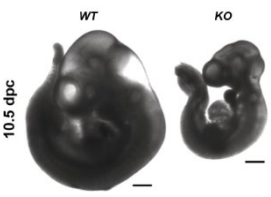

The Modzelewski Lab at the University of Pennsylvania Department of Biomedical Sciences School of Veterinary Medicine is recruiting postdoctoral researchers to join an exciting new NIH-NICHD funded project. Our work focuses on understanding the exciting and emerging role of retrotransposons in early development (and beyond). We are currently looking at how retrotransposons impact fertility and preimplantation development in mice but with comparative biology studies using various placental mammalian species to learn about human health and reproduction.

The lab has two major but linked focuses:
Developmental Biology and **Genome Editing**.

Nearly half of all mammalian genomes originate from ancient retroviral integrations. While silenced in nearly all cells, retrotransposon reactivation is a well-known phenomenon in preimplantation embryos and the germline. Many retrotransposons have retained regulatory and structural features that can influence nearby genes. In the embryo, these events are transient and span less than a cell cycle. A subset of these events splice with nearby protein coding genes, generating embryo and species specific “chimeric transcripts” that form hundreds of novel promoters, exons and polyadenylation sites. Disruptions made in the lab have led to arrested global protein synthesis, cell fate specification errors, stress induced arrest, fertilization failure, embryonic lethality and improper implantation that resembles human pregnancy complications (*Cell 2021*). This highly collaborative project adapts proteomics, genetics, bioinformatics and CRISPR/Cas9 editing to reveal this overlooked but essential form of retrotransposons-based regulation in development, fertility, and disease.

As no current cell culture system faithfully represents the preimplantation development, the majority of research at this stage must be done directly in the embryo, and sometimes animal models are necessary. Even with the advent of CRISPR/Cas9 gene editing, generating mouse models is cost prohibitive and largely inaccessible. To circumvent this, I developed a highly efficient electroporation-based editing technique called CRISPR-EZ (CRISPR Electroporation of Zygotes). I showed that CRISPR-EZ is at least 3-4x more efficient than the gold standard of microinjection, is inexpensive, works in all species tested, and can be mastered quickly, making this technology uniquely accessible to many academic labs (*JBC 2016*, *Nature Protocols* 2018). While small insertions and deletion strategies have been highly optimized, there is still room to improve in larger insertions, deletion and sophisticated model designs. Current efforts include the use of AAV, CRISPRa/i (activation/interference), humanized models to study conserved developmental regulatory networks.

Qualifications:

- PhD in various degrees of biological sciences as well as bioengineering, biostatistics, etc.
- We encourage applications with experience in developmental biology and/or non-coding RNA
- Previous mouse handling experience is a plus but not essential.
- Ideal candidate should be highly motivated and passionate about biology, development, expecting the unexpected and not afraid to challenge assumptions.

Application Documents:

- CV or NIH BioSketch (with contact information for 2-3 references)
- Cover Letter detailing interest and experience

Interested applicants are invited to submit their application documents directly to Dr. Modzelewski at amodz@upenn.edu.