DEPARTMENT OF PEDIATRICS
COLLEGE OF MEDICINE

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PROJECT TITLE: Post-transcriptional regulation of spermatogonial stem cells

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Project Description

The germ line – the cell lineage that gives rise to egg and sperm – represents the quintessential stem cell population that propagates a species. Within the testis, the germ line forms spermatogonial stem cells. These stem cells self-renew and produce progenitors that undergo rapid mitotic divisions to expand their population within the testis. Progenitors then undergo terminal differentiation, which involves meiosis or the specialized reductive division that produces haploid cells, followed by cellular differentiation into sperm. In this way, one mitotic division from a mammalian spermatogonial stem cell produces hundreds of terminally differentiated sperm.

Post-transcriptional mechanisms that regulate mRNA stability and translation play a major role in the function of stem cells, but remain poorly characterized. We focus on post-transcriptional mechanisms that facilitate two distinct stages of spermatogonial stem cell differentiation:
1. spermatogonial stem cell differentiation into mitotically dividing progenitors and
2. progenitors’ initiation of meiosis, the specialized cell division that halves the genome to produce gametes.

The testis is a complex tissue with all stages of sperm development present at the same time. To overcome this developmental complexity, we use two complementary approaches: single-cell sequencing and a specialized approach that developmentally synchronizes spermatogenesis. By combining these approaches with mouse genetics, biochemistry, functional genomics, and bioinformatics, we are able to make powerful insights into stem cell function within the testis.

Understanding the molecular foundations of spermatogonial stem cell function will provide new opportunities to treat and prevent infertility and

testicular cancers. Over the long term, the insights made from these fundamental studies have the potential to improve technologies to produce sperm and egg in a dish. The application of this technology in regenerative medicine will revolutionize the treatment of infertility.

Students will develop basic lab skills for working with mouse models as well as basic computational skills for analysis of large datasets. Project can also be tailored to meet the specific interests of the student.