

Johns Hopkins University

Department of Biology Seminar Series

Thursdays, 4:00pm

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Zoom link: <https://zoom.us/j/97925356454?pwd=6jNuTlY1dU9BcXcrRFdleis2TVNadz09>

May 2nd, 2024 - Mudd 100



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National Primate Research Center,
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Host: Rajiv McCoy

“Diverse monogenic forms of spermatogenic failure”

Non-obstructive azoospermia (NOA) is the most severe form of male infertility and typically incurable with current medicine. Due to the biological complexity of sperm production, defining the genetic basis of idiopathic NOA has proven challenging. In this talk we will describe over 10 years of work to identify and understand Mendelian forms of NOA in humans using a variety of genetic and genomic approaches. Exome sequencing of over 1,500 cases shows that a recessive Mendelian cause can be identified in 20% of the cases. The disrupted genes are primarily on the autosomes, enriched for undescribed human “knockouts”, and, for the most part, have yet to be linked to a Mendelian trait. Single-cell RNA sequencing shows that, rather than affecting a single cell type or pathway, azoospermia genes can be grouped into molecular subforms with highly synchronized expression patterns, and analogs of these subforms can be found in mice. We identify unrecognized subforms, such as a set of genes expressed specifically in mitotic divisions of type B spermatogonia, as well as gene sets with unclear function. Our findings highlight NOA as a largely understudied Mendelian disorder and provide a conceptual structure for organizing the complex genetics of male infertility, which may serve as a basis for designing novel diagnostics and therapies for infertile men.