The Postcopulatory Transcriptional Response In Different Sections Of The Female Reproductive Tract In Mice

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In internally fertilizing species, the first direct molecular contact between the male and female gene products occurs within the female reproductive tract – a highly complex and rapidly evolving structure in many species. While molecular interactions between sperm and oocyte have received a lot of attention, efforts to gain insight into the crosstalk happening during the sperm cells' journey to the site of fertilization have been limited, especially in mammals. The interactions between sperm cells and the female reproductive tract not only facilitate sperm guiding, storage, and protection against introduced pathogens but also comprise a sophisticated mechanism of female-mediated sperm selection. Molecular interaction partners that are involved directly in sperm assessment and selection, however, are difficult to pinpoint within the massive immunological response happening in the female reproductive tract following copulation. While we have some knowledge of sperm surface proteins interacting with the components of the female reproductive tract, the female counterparts of these interactions are still largely unknown. We characterized the murine female transcriptional response to semen following copulation comparing several lab mouse and wild-derived inbred *Mus domesticus* strains. We mated males and females from different strains and used strain-specific SNPs to distinguish semen-derived from female reproductive tract-derived transcripts. We specifically focused on the different subdivisions of the female reproductive tract, with the aim to identify female molecules directly involved in sperm assessment. Our results show a large number of differentially expressed genes in uterus, uterotubal junction and oviduct compared to unmated control and significant differences in differential expression between the subsections. In addition to the upregulation of genes related to immune activation and tolerance, we found increased expression of transmembrane and cell adhesion genes, as well as receptors involved in cell communication and migration (e.g. *Epha1* and *Adam17*). From these semen-activated genes, we selected the strongest candidates for direct interaction with sperm cells for immunohistochemical validation and sperm surface protein interaction assays. This study ultimately has the aim to test the potential of the discovered candidate proteins in *in vitro* sperm selection systems involving microfluidic chips. Given the ever-increasing need for assisted reproduction in humans and the need for specific selective breeding in agriculture, we have to make sure that the natural quality control and selection mechanisms occurring in the female reproductive tract are understood and leveraged to their full potential.