Abstract # 1690

Uncovering A TAF4b-Dependent Gene Expression Program Required For Embryonic Oocyte Differentiation. Megan A. Gura, Brown University, USA

Proper embryonic female germ cell development is critical for the healthy establishment of the adult ovarian reserve. TBP-Associated Factor 4b (TAF4b) is a subunit of the basal transcription factor TFIID complex, which is required for RNA Polymerase II recruitment in gonadal tissues. Taf4b-deficient female mice are infertile due to several related deficits of embryonic germ cell development including increased chromosome asynapsis, excessive germ cell death, and delayed germ cell cyst breakdown. We have previously demonstrated that Taf4b mRNA and protein expression are nearly exclusive to the germ cells of the embryonic ovary from E9.5 to E18.5 and its expression is directly regulated by STRA8 and DAZL in male meiotic germ cells. Therefore, we hypothesized that TAF4b, as part of germ cell-specific from of TFIID, regulates oogenesis and meiotic gene programs. To elucidate a TAF4b-dependent program of embryonic oocyte development, we performed low-input RNA-sequencing on GFP+ germ cells sorted from Oct4-EGFP transgenic mice that were Taf4b-heterozygous or-deficient at E14.5 and E16.5. To our surprise, gene ontology analysis of our differentially expressed genes (DEGs) showed few germ cell development-related genes deregulated in the absence of TAF4b. Importantly, a few notable genes were down-regulated in the Taf4b-deficient germ cells such as Nobox, Brca2, Rhox10, and Rhox13. There were several unexpected DEGs such as Mtor, Apoe, Clock, and Igf2. Further perplexing from this RNA-seq analysis was the proportion of DEGs on the X chromosome at each time point, especially several members of the MAGE and RHOX gene families. For E14.5 DEGs in the Taf4b-deficient germ cell, there were very few down-regulated genes but many up-regulated genes located on the X chromosome. At E16.5 the trends were precisely the reverse, many down-regulated genes but no up-regulated genes were on the X chromosome. These interesting results implicate an unexpected but important role of TAF4b in regulating gene expression on the X chromosome during oocyte development. We are currently performing CUT & RUN using mouse embryonic stem cells and sorted embryonic female germ cells to clarify which genes are directly bound by TAF4b. This research may add new dimensionality to the female germ cell transcriptome as we uncover new genes that participate in the healthy development of the ovarian reserve.