**Investigating ribosome dynamics in the aging mammalian oocyte**

**Anna Galligos**[1], Wei-Ting Yueh[1], Joseph Varberg[1], and Jennifer L. Gerton[1]

[1]Stowers Institute for Medical Research, Kansas City, United States

The female reproductive system is the first system to experience age-dependent functional decline in mammals. In humans, advanced maternal age severely compromises the likelihood of successful conception and pregnancy, due to decreased fertility and increased risks of pre-eclampsia, miscarriage, birth defects, and pre-term birth. This age-dependent decline has become a significant concern to society, as more women than ever are delaying childbearing until their advanced maternal years.

Oocyte quality is the greatest barrier to fertility at advanced maternal age. Though the impact of oocyte quality is appreciated, our understanding of its molecular culprits is limited. One aspect of oocyte quality that remains understudied is translation, the production of proteins by macromolecular machines called ribosomes. Oocytes are unique in that they rely entirely upon ribosomes to modulate gene-regulation during meiotic maturation and the oocyte-to-embryo transition. Furthermore, the oocyte ribosomes provide for the zygote until zygotic ribosome biogenesis becomes active. Ribosomes are therefore an important - but poorly characterized - factor of oocyte quality. If ribosome production or activity is perturbed with age, oocyte quality would be significantly compromised.

To address this gap in knowledge, we conducted single-cell RNA sequencing from oocytes isolated from reproductively young and old female mice. The pathways identified to be the most enriched with age were those associated with ribosome biogenesis and translation. We then measured the levels of ribosomal RNA (rRNA), the rate limiting factor of ribosome biogenesis, within oocytes. As expected, we found that rRNA also significantly increases in oocytes with age. This observation compliments the finding that cytoplasmic ribosome populations in oocytes significantly increase with age. To determine the functional output of these ribosomes, global translation assays were conducted in germinal vesicle oocytes from reproductively young and old mice. The results revealed significantly lower translation levels in old oocytes. Taken together, we surmise that ribosome numbers increase while translation decreases. These paradoxical findings point to translation perturbations within the aging oocyte that warrant further investigation. We hypothesize that as oocytes age, the regulation of ribosome production and translation are compromised. Continued investigation of age-associated changes in ribosome production and translation activity in oocytes will provide new insight to oocyte quality and how it changes with age.