O-105 The mRNA translational program and the control of nuclear and cytoplasmic events

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After a prolonged phase of growth and accumulation of cytoplasmic and nuclear components, a fully-grown mammalian oocyte undergoes a series of more rapid changes in preparation for fertilization and acquisition of totipotency. All these changes are necessary to sustaining embryo development after fertilization, events often described in a clinical setting as changes associated with a “good quality egg”. Although the events associated with nuclear maturation are relatively well described and linked to generation of an egg of the correct ploidy, much less is known about the molecular changes in the cytoplasm of an oocyte. To investigate these processes, we have focused on defining the program of maternal mRNA translation that takes place during meiotic maturation and at the oocyte-to-zygote transition. Taking advantage of novel RNAseq strategy to quantify mRNA translation, we have generated a blueprint with genome-wide resolution of the changes in translation during both growth and maturation. Analysis of these data shows that a switch in pattern of maternal mRNA translation takes place at the time of oocyte reentry into the meiotic cell cycle. Translation of mRNAs that code for proteins required during oocyte growth, including those involved in ribosome and mitochondrial biogenesis, ceases, while translation of mRNAs that code for cell cycle components, for the transcription a machinery, and chromatin remodeling factors becomes activated. Preliminary data show that similar regulation occurs in human oocyte although with different timing. By disrupting the translation of specific mRNAs such as those coding for histone variants, we document that defects in the zygote and early embryo arise if these translation are not correctly executed. In the same vein, defective translation of cell cycle components generates aneuploid oocytes and decreased fertility. We show that oocyte manipulations known to decrease oocyte quality, including denudation or disruption of endocrine or paracrine signaling in the somatic compartment, also affect the program of maternal mRNA translation. Remarkably, oocyte quality declines with female aging affecting fertility. Preliminary data strongly suggest that translation of maternal mRNAs is disrupted in the oocytes during maternal aging. Taken together, these data demonstrate that execution of the maternal mRNA translation program during oocyte maturation is essential to produce a good quality egg and suggest that translational defects are a cause of the compromised developmental competence observed during maternal aging. Supported by NIH P50 HD055764 and R01 GM116926.