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Poster Session B

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The Importance and Contribution of Translationally Recruited Maternal Transcripts Encoding Epigenetic Factors to Gene Expression Reprogramming in the Oocyte to Embryo Transition in Mice

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ABSTRACT

The mouse maternal-to-zygotic transition entails a dramatic reprogramming of gene expression that is essential for continued development beyond the 2-cell stage. It is thought that genome-wide epigenetic modifications significantly regulate this reprogramming. Although many of the genes that are reprogrammed have been identified, a major unresolved problem is how this reprogramming occurs through the utilization of a maternally-derived transcription machinery. Our research investigates an elegant, but simple, solution to promote the success of reprogramming: the translational recruitment of dormant maternal transcripts that encode for epigenetic factors during oocyte maturation in mice. We hypothesize that blocking this translational recruitment will disrupt the fidelity of gene expression reprogramming. Analysis of gene expression profiles of mouse oocyte and preimplantation embryos showed that a handful of epigenetic factors (Sin3a, Rbbp4, Rbbp7, and Ezh2) are maternal transcripts that are potentially recruited for translation during oocyte maturation and/or following fertilization; therefore, these maternal transcripts are ideal candidates to test our hypothesis. Western blot analysis of full-grown mouse oocytes, metaphase II eggs, and 1-cell embryos revealed that all these transcripts are in fact recruited for translation during oocyte maturation. Interestingly, following fertilization, Sin3a transcripts undergo a second temporal round of translational recruitment. SIN3A was expressed at low levels in full-grown oocytes, reached relatively high levels in the egg and 1-cell embryo and then declined as the embryo progressed into the 2-cell stage; the levels of SIN3A remained low until the blastocyst stage. The same pattern of expression was found by immunofluorescence, in which a clear nuclear staining was observed. Firefly luciferase reporter constructs under the control of the Sin3a 3’ untranslated region (UTR) demonstrated that the Sin3a 3’UTR alone drives the translation of reporter transcripts during oocyte maturation and following fertilization. These results suggest that the Sin3a 3’UTR, and most likely the cytoplasmic polyadenylation elements within it, is responsible for the translational control of Sin3a maternal transcripts during oocyte maturation and following fertilization. We chose a morpholino oligonucleotide approach to inhibit the oocyte maturation-associated increase in SIN3A. The results of knockdown experiments showed that blocking the oocyte maturation-associated increase in SIN3A impedes preimplantation development in mice. The data presented here implicate that maternally-derived SIN3A may be mediating its chromatin-modifying functions prior to the major activation of gene expression that occurs during the 2-cell stage of mouse development. The data also suggest that the translational recruitment of inactive transcripts that encode for epigenetic factors may be a mechanism that the mouse oocyte utilizes to achieve the reprogramming of gene expression. Research supported by NIH grant HD022681 to R.M.S.