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GENE EXPRESSION

RNA granules: the clock within

> translation timing in vertebrate oocytes depends on the assembly and disassembly of RNA granules

Precise timing of when specific mRNAs are translated is important for the progression of the mitotic and meiotic cell cycle, but how this is achieved is poorly understood. Kotani *et al.* now report that the timing of cyclin B1 mRNA translation in vertebrate oocytes depends on the formation and disassembly of cytoplasmic cyclin B1 mRNA granules.

Vertebrate oocytes arrest at prophase I of the meiotic cell cycle. At this stage, in which oocytes are fully grown but immature and unable to be fertilized, 'dormant' mRNAs accumulate in the cytoplasm. Upon receiving specific signals (including hormones) that induce oocyte maturation, these stored mRNAs are translated in a specific order that mediates progression to meiotic metaphase II, preparing oocytes for fertilization. Temporally controlled translation of cyclin B mRNAs is key to oocyte maturation, as it induces germinal vesicle breakdown (GVBD), assembly of the first meiotic spindle and polar body extrusion.

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The authors first observed that cyclin B1 mRNA is deposited in cytoplasmic granules that are asymmetrically distributed in mouse and zebrafish oocytes. After induction of oocyte maturation, cyclin B1 mRNA levels remained constant, but the number of granules decreased from prophase I to prometaphase I and almost disappeared by the time oocytes reached metaphase II. Importantly, this granule disassembly coincided with the activation of cyclin B1 mRNA translation.

Kotani *et al.* then analysed how these RNA granules form and whether they might affect translational control. They found that the Pumilio 1 (PUM1) protein (known to regulate cyclin B1 translation in frog oocytes) bound to cyclin B1 mRNAs in both zebrafish and mouse oocytes and that this binding was necessary for the formation of cyclin B1 mRNA granules. Furthermore, although PUM1 was not required for translational repression, its binding regulated the timing of cyclin B1 mRNA translational activation; mutant mRNAs unable to bind PUM1 were translated earlier than wild-type mRNAs following induction of oocyte maturation. Treatment with cytochalasin D, which promotes F-actin depolymerization, revealed that granule formation also depends on F-actin. Moreover, F-actin stabilization prevented granule disassembly, cyclin B1 synthesis and GVBD.

This work shows that cyclin B1 RNA granules, the formation of which depends on PUM1 and F-actin, keep cyclin B1 mRNA in a repressed state until the appropriate time during oocyte maturation and provides evidence that translation timing in vertebrate oocytes depends on the assembly and disassembly of RNA granules. The molecular mechanisms underlying granule-mediated translational control remain to be elucidated.

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ORIGINAL RESEARCH PAPER Kotani, T. *et al.* Cyclin B1 mRNA translation is temporally controlled through formation and disassembly of RNA granules. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201302139 (2013)