Determining the replication factory settings

Saner et al. describe how neighboring DNA regions stochastically assemble into replication factories in budding yeast.

A replication organelle is a stretch of DNA duplicated from a single replication origin. In eukaryotes, multiple replication organelles assemble into sub-nuclear structures called replication factories, where the replication organelles are duplicated by DNA polymerases and other replication proteins. Replication factories help to coordinate efficient DNA synthesis, but how replication organelles are organized into these structures is unclear.

Saner et al. used live-cell imaging to follow the replication of different replication organelles along a budding yeast chromosome.

KASH5 helps meiotic chromosomes LINC up

Horn et al. identify a protein that helps homologous chromosomes pair up in meiosis by connecting them to the microtubule cytoskeleton.

Early in meiosis, chromosomes cluster together so that homologous chromosomes can find each other and pair up to undergo recombination. Clustering is controlled by LINC complexes, which span the nuclear envelope to couple chromosomes to the microtubule-based motor protein cytoplasmic dynein. Dynein can therefore pull chromosomes toward the centrosome on one side of the nucleus.

LINC complexes are formed by members of the SUN and KASH protein families. SUN1 is an inner nuclear membrane protein that, in most organisms, attaches to the telomeres of meiotic chromosomes. A member of the KASH family of outer nuclear membrane proteins links SUN1 to cytoplasmic dynein, but which KASH protein performs this function in mammals is unknown.

Horn et al. focused on KASH5, a recently identified KASH protein expressed in testes and ovaries. KASH5 colocalized with SUN1 at sites where telomeres attached to the nuclear envelope in mouse spermatocytes. Mice lacking KASH5 were infertile. Males, for example, couldn’t produce mature sperm because their spermatocytes arrested early in meiosis after failing to form homologous chromosome pairs. Telomeres were still attached, via SUN1, to the nuclear envelope, but dynein was no longer recruited to these attachment sites, thus abolishing chromosome clustering and homologue pairing.

Having established KASH5 as a member of the meiotic LINC complex in mammals, senior author Brian Burke now wants to identify proteins that connect telomeres to SUN1 at the nuclear periphery.

RNA granules act as egg timers

Kotani et al. reveal how RNA granules control the timing of cyclin B translation during oocyte maturation.

Fully grown oocytes initially arrest in prophase I, and mRNAs required for meiotic progression are translationally repressed. In response to maturation hormones, mRNA translation is activated so that the oocytes can progress to metaphase II, ready for fertilization. One key mRNA is the cyclin B transcript, whose translation induces germinal vesicle (nuclear) breakdown and assembly of the first meiotic spindle. Exactly how cyclin B translation is controlled is unclear, however.

Kotani et al. found that cyclin B mRNA is assembled into granules in the cytoplasm of immature zebrafish and mouse oocytes. Maturation hormones induced disassembly of these granules at the same time that cyclin B began to be translated. The researchers discovered that granule assembly was promoted by actin filaments and by the protein Pum1, which bound to cyclin B transcripts. Disrupting granule assembly—by depolymerizing actin or expressing a mutant cyclin B mRNA unable to bind Pum1—caused cyclin B to be translated sooner after stimulating oocyte maturation. Inhibiting granule disassembly, on the other hand, delayed cyclin B translation and germinal vesicle breakdown.

Lead author Tomoya Kotani says that granule assembly isn’t required to repress cyclin B translation; even in the absence of granule formation, Cyclin B isn’t produced until oocyte maturation is initiated. Instead, granules control the timing of cyclin B translation in maturing oocytes. Kotani now wants to investigate what triggers granule disassembly and translation activation and to follow the process in real time using live imaging.

Kotani, T., et al. 2013. J. Cell Biol. http://dx.doi.org/10.1083/jcb.201302139.