Sleeping beauties: the biology behind oocyte dormancy

The maturation process of oocytes remains paused for several years. Researchers from Konstanz and Göttingen have now found out which protein ensures this state is maintained over such a long period.

The fertilization of an egg by a sperm is central to human reproduction. A complex biological process transforms immature oocytes into ones that can be fertilized. The process begins in the female embryo and pauses for the first time shortly after birth. Many years later, starting in puberty, oocytes restart the maturation process.

Astonishingly, almost no transcription takes place in fully grown immature oocytes – a process that usually is constantly taking place in our cells. During transcription, our genes are "copied" into messenger RNAs that are used as blueprints for the production of proteins. However, when oocytes restart the maturation process, they have to rely on stockpiled messenger RNAs that had already been transcribed before the process paused.

"Until now, we did not know exactly how vertebrates inhibited the translation of existing messenger RNAs, sometimes for years, thus keeping the maturation of oocytes paused", says Thomas Mayer, a molecular geneticist in the Department of Biology at the University of Konstanz.

A protein hits pause

In their recent study published in Nature Communications , Mayer and his team, along with colleagues from Konstanz and Göttingen, have come a good bit closer to solving this puzzle. They identified a protein that plays a central role in maintaining the dormant state of immature oocytes: the translation inhibitor 4E-T.

Using experiments in which they removed the 4E-T protein from oocytes of frogs and mice, the team demonstrated that this drastic reduction was enough to restart the maturation process in the oocytes. "The loss of the 4E-T protein during the pause in maturation led to a widespread increase in the translation of messenger RNA into the respective proteins. In collaboration with Florian Stengel, a mass spectrometry expert at the University of Konstanz, we were able to show that these proteins included important regulators of the maturation process and that their activation initiates the next steps in oocyte maturation", Mayer explains.

Part of a larger network of interactions

The researchers also identified important interaction partners of 4E-T that are essential for its translation inhibiting function in immature oocytes. First and foremost, this includes the RNA-binding protein PATL2 found specifically in oocytes. "Based on our analysis, we conclude that the interaction between 4E-T and PATL2 forms the core of a larger network of interactions between proteins that allows 4E-T to accumulate on specific messenger RNAs and thus inhibit their translation", Mayer explains.

Interestingly, mutations in the human 4E-T gene are associated with premature ovarian insufficiency – a particularly early onset of menopause tied to fertility problems. The results of the recent study will also contribute to a better understanding of such disorders in oocyte maturation.

Publication:

A. Heim, S. Cheng, J. Orth, F. Stengel, M. Schuh & T. U. Mayer (2025) Translational repression by 4E-T is crucial to maintain the prophase-I arrest in vertebrate oocytes. Nature Communications 16, 8051 (2025). DOI: 10.1038/s41467-025-62971-9

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