FREEZE! A REGULATORY PROTEIN PUTS MESSENGER RNA IN WAITING POSITION

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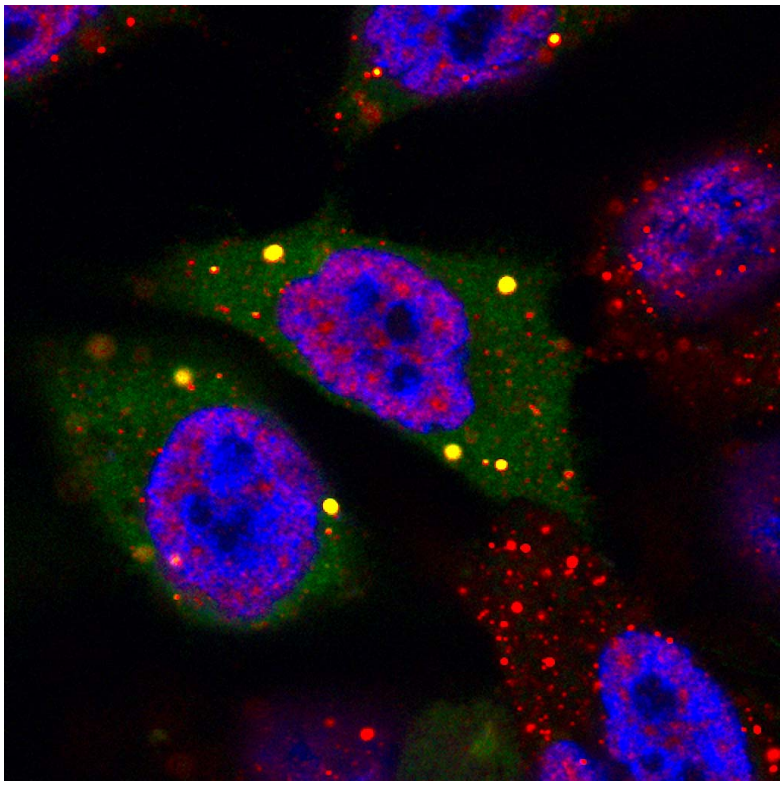
Messenger RNA plays a decisive role in the regulation of protein production in the cell. It contains the building instructions for proteins and its whereabouts are crucial for whether these protein molecules are synthesized or not. Scientists at the Max Planck Institute for Developmental Biology in Tübingen have now identified a crucial factor that ensures that messenger RNA is captured and retained for later use. They have thus discovered a key mechanism that not only explains how it is possible for egg cells or nerve cells, for example, to remain at a certain stage of development until they are needed. It is also possible that this is a hidden reason for premature ovarian failure.

The regulatory protein 4E-T (green) made visible under the microscope with fluorescent dyes.



The ova in the female body are already created at birth. But they only develop to a certain point. It is only at puberty that they begin to mature into a fertilisable egg cell - ovulation after ovulation, one after the other. To do this, they must be held at an immature stage of development until their time has come.

But what are the mechanisms by which this happens? Cátia Igreja from the Max Planck Institute for Developmental Biology in Tübingen and her doctoral student Felix Räsch have discovered that a protein called 4E-T plays a decisive role in this process. This protein is a regulatory factor in protein biosynthesis and plays a new and surprising role in this process: It prevents messenger RNA (mRNA) from reaching the ribosomes, the protein factories of the cell, and at the same time protects them from being degraded.

The mRNA is virtually the transcription of a gene on the DNA strand and contains the building instructions for new proteins to be synthesized in the ribosomes. "RNA is the most important key factor when it comes

to controlling protein production in cells," says Igreja. "We know various mechanisms that come into play when certain proteins are no longer to be produced." The most obvious way is to simply destroy the mRNA so that the blueprint does not even reach the ribosomes.

But what if the assembly instructions are needed again at a later time and need to be available quickly? In such cases, it is advantageous if the mRNA remains in the cell and remains frozen in the cell until it is needed. "We know that the regulatory protein 4E-T plays an important role in immature oocytes that remain in the waiting position for many years," said Igreja. Mutations in this protein are associated with premature ovarian failure. "Another example is nerve cells that must always be ready to form new connections to other nerve cells," said Igreja. Here, too, 4E-T has been shown to play a role.

4E-T assumes various regulatory functions in protein synthesis. "We wanted to know whether 4E-T might also be responsible for the freezing of mRNAs in the cell," said Igreja. Indeed, the experiments of the Tübingen scientists showed that 4E-T attaches itself to a protein that is crucial for the transport of mRNA to the ribosomes. This prevents the assembly instructions from reaching the protein factory. At the same time, 4E-T stabilises the stopped messenger RNA so that it is not degraded and is retained for later use.

"4E-T plays a variety of roles in protein synthesis," says Igreja. "We now know that this regulatory protein also plays a decisive role in stopping mRNA on its way to the ribosomes and preserving it for later use." Igreja adds that "4E-T plays a variety of roles in protein synthesis. The scientists are thus not only making a decisive contribution to understanding how protein synthesis is regulated and how cells such as egg cells or nerve cells are stopped in their development.

"Our findings may also explain why mutated 4E-T can cause affected women to become infertile at a relatively young age," says Igreja. Premature ovarian failure, i.e. the exhaustion of ovarian function before the age of 40, affects around 1 to 2 percent of all women. The underlying mechanisms have not yet been clarified.

This research has been dedicated to Elisa Izaurralde, who was a Director at the Max Planck Institute for Developmental Biology in Tübingen until her death in 2018.

Original publication:

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