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Metabolic means to preserving egg supply and fertility

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The stresses that come with aging, chemotherapy treatments, and environmental exposures all threaten fertility. But what if there were a way to preserve women's limited egg supply? Researchers reporting on studies conducted in frog and mouse eggs in the Cell Press journal *Molecular Cell* on October 3rd may have found a way.

The findings come at an important time when many women are waiting longer and longer to have children, renewing interest in the development of strategies to preserve oocytes—immature egg cells.

"Our work provides insight into how oocyte viability may be maintained and offers potential therapeutic targets for trying to prevent infertility due to loss of oocytes," said Leta Nutt of St. Jude Children's Research Hospital. "Whilst these potential therapies might be broadly applicable, they are especially important to us at our institution, as we want to ensure our pediatric patients have the opportunity to live full and normal lives as adults."

The key is a pathway involved in active metabolism and its involvement in whether an oocyte lives or dies.

Scientists knew before about some of the players involved in oocyte survival, but the link from metabolism to cell death wasn't entirely clear. Now, Nutt and her colleagues have found the key signal that keeps both frog and mouse oocytes from dying: a metabolite known as coenzyme A.

When oocytes are in a healthy, young, and "fed" state, study first author Francis McCoy explains, coenzyme A keeps an enzyme known as CaMKII on, and oocytes stay alive. When oocytes are "starved" or nutrient deprived due to age or other factors, CaMKII gets turned off, and the cells begin to die.

Because this mechanism appears to be conserved in animals, treatments designed to maintain oocyte metabolism might preserve women's egg supply and fertility. There might also be new ways to assess the health of a woman's egg reserves based on metabolic status, Nutt says, and her studies in Xenopus frog eggs could lead the way.

"The study of metabolic regulation in mammalian cells is cumbersome, as it is not feasible to introduce intermediate metabolites directly into cells unless by microinjection," the researchers wrote. "Therefore, using the Xenopus oocyte model allowed us to discover a novel connection between metabolism and oocyte viability. A better understanding of the molecular mechanisms underlying these links might provide the basis for developing novel strategies for coenzyme A in promoting oocyte longevity for increased fertility."

More information: *Molecular Cell*, McCoy et al.: "Metabolic activation of CaMKII by Coenzyme A." dx.doi.org/10.1016/j.molcel.2013.08.043

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