

Obesity is a growing global challenge, with nearly half of adults classified as overweight and 16% living with obesity as of 2022. This condition has significant effects on health, including fertility. Women with higher body weight (a BMI of 27 or more) are three times more likely to struggle with conceiving a baby compared to those with normal weight. This research focuses on understanding how obesity impacts early embryo development, aiming to uncover new solutions for obesity-related infertility.

Eggs carry the blueprint for life, orchestrating early developmental processes like cell division and DNA instructions. Obesity disrupts this process through hormonal imbalances, particularly involving leptin, a hormone that is released from fat and regulates satiety and metabolism. In obesity, when fat accumulates, leptin levels rise, causing resistance to its normal signals, and thus disturbance of many processes in the organisms, that were normally regulated by leptin. This also encompasses the proper functions of ovarian cells and the quality of eggs. Importantly, egg shape is tightly linked to proper embryo development. Thus, exposing eggs to disturbed obesogenic environment may have repercussions and cause delayed embryo development and affect the embryo's ability to use energy efficiently, setting the stage for health challenges in the next generation.

This study focuses on the role of leptin and a key cellular pathway called mTOR, which senses nutrients availability and regulates cell growth, in early embryo development in obese mothers using mouse model of obesity. By studying how signals mediated by aforementioned molecules are disrupted in obesity, the researchers aim to find ways to restore healthy embryo development.

Firstly, researchers will study how exposing mouse embryos to leptin during their growth and maturation, affects pace of their growth and the activity of the mTOR pathway. Cell numbers in two critical parts of the embryo will be evaluated: the trophectoderm (TE), which will give rise to the placental tissue, and the inner cell mass (ICM), which will form the fetus on later developmental stages. Then, by using eggs from three mouse models with different leptin and obesity profiles, the team will analyse how the mother's weight and hormone levels influence embryo development. They will measure the energy balance, metabolites, and gene activity in individual cells to uncover how obesity shapes the embryo's metabolic performance. Finally, the researchers will test whether insulin growth factor 1 (IGF1), a molecule that activates the mTOR pathway, can reverse developmental delays in embryos from obese mothers. By treating embryos derived from obese mice with IGF1 and modulating mTOR signals, they aim to restore normal embryo development.

This research could improve our understanding of how obesity affects fertility and early development, offering hope for new therapies to help women with obesity conceive and deliver healthy babies. By targeting key mechanisms like leptin signalling and the mTOR pathway, these findings could enhance assisted reproduction techniques and promote better health for future generations.