



2020 IMPACT CIRCLE

Screen for drugs that reverse reproductive aging for women

Investigators:

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Unmet Need: Did you know that in 2016 the average age for a woman in San Francisco County to give birth to her first child was 32 years old? Due to certain social and educational status changes that have taken place over time, the maternal age at first childbirth keeps increasing every year. This delayed childbearing leads to the emergence of critical social and economic challenges, as reproductive aging in women reduces fertility and increases abnormalities in offspring. The decline in fertility during aging is caused by the reduction of egg quality and the depletion of egg reserves through cell death. Therefore, there is a critical need to understand the factors that underlie reproductive aging and to develop novel methods to improve egg quality.

Background: Mitochondria is the key component in the healthy egg. Mitochondrion is known for its critical roles as the power plant and command center for cellular functions. Previous studies indicate that mitochondria are the determinants and predictors of egg competence. For example, mitochondria initiate the signaling pathways that cause the death of egg. It has been demonstrated that an increase in the amount of mitochondria by 5% in the egg by transferring isolated mitochondria can protect the aged oocyte from apoptosis¹⁰. Additionally, reproductive aging results in mitochondrial dysfunctions, which cause the maternal age-related aneuploidy in offspring. For example, the risk of having kids with chromosomal abnormalities, such as Trisomy 21 (Down syndrome), is known to increase 10 times for women at 40 years old. Therefore, improving mitochondrial function is critical to preserve egg quality and delay reproductive aging in women.

Novel Hypothesis: We hypothesize that screening for drugs that improve the mitochondrial function in aged eggs can reverse the age-related reduction of egg quality and increase the reproductive health of older women.

Proposal: To search for the Fountain of Youth, we will use the aged eggs from old mice to screen a panel of FDA-approved compounds. We will combine our expertise in

mitochondria and reproductive aging to identify the FDA-approved compounds that can be re-purposed to improve mitochondrial function in aged eggs and treat reproductive aging. The drug screen will be done using our cutting-edge imaging system that is capable of determining functional state of the mitochondria in eggs.

Impact: Mice develop similar reproductive aging phenotype as humans. The identification of FDA-approved compounds that can reverse the aging phenotype of eggs in mice is expected to shed lights on the mechanisms of reproductive aging and guide our efforts to optimize the compounds for clinical use.

Specialized Equipment Needs:

