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Mitochondria transfer from adipose stem cell ameliorates the development potential of cryopreserved oocytes

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Study question: Could autologous adipose stem cell (ASC) mitochondria supplementation to vitrified-thawed oocytes, restore the post-fertilization development which has been lowered due to oocyte cryopreservation?

Summary answer: Autologous ASC mitochondria supplementation could rejuvenate the quality of vitrified-thawed oocytes and enhance the embryo's developmental capacity.

What is known already: Pre- and post-implantation developmental potential of embryos derived from vitrified oocytes are remarkedly lower than those of fresh oocytes. Despite its' low efficacy, oocyte cryopreservation is becoming prevalent in assisted reproductive technologies to respond to growing demands of 'patients' sociological and pathological conditions. Unfavorable reduction of mitochondrial membrane potential, damage to mitochondrial structures, reduced ATP production, increased reactive oxygen species (ROS), damage to meiotic spindle and microfilaments, and altered Ca^{2+} ion regulation are reported to cause detrimental damage to oocytes following the cryopreservation that adversely affect the development potential. Autologous stem cell mitochondria supplementation can rescue the aging-related oocyte mitochondrial damages.

Study design, size, duration: The young mouse vitrified thawed mature oocytes, autologous ASC, and mitochondria were collected and analyzed at Osaka City University, Japan. In total, 600 young mouse mature oocytes were occupied in this prospective study.

Participants/materials, setting, methods: The young C57BL/6JJms mouse (8weeks) mature oocytes that have been vitrified were thawed before the start of ICSI procedure. ASC specificity and ASC mitochondria function and ultrastructure were pre-analyzed. Autologous ASC mitochondria were isolated on the same day and supplemented with intracellular sperm injection (ICSI) and for the control, the mitochondrial buffer was injected. The survival rate, fertilization rate, blastulation rate, mitochondria function, and reactive oxygen species level in 2 cell embryos and live birth rates were compared between 2 groups.

Main results and the role of chance: The ASC mitochondria showed higher membrane potential compared to the somatic cells and were spherical in shape with low cristae numbers. The survival rate and the fertilization rate were comparable in both mitochondria supplemented and control groups. However, the ASC mitochondria supplementation seemed to have significantly improved the blastocyst development capacity from 2cell embryos compared to the control group ($P<0.05$; 56.8% & 38.2%, respectively). And interestingly, a significantly higher ATP level was found in the mitochondria supplemented group's 2 cell embryos than the control group ($P<0.05$; 905.6pmol & 561.1pmol respectively). And though it was not significant, higher potential of getting live birth, was found in the mitochondria supplemented group than the control group after 2 cell embryo transfer.

Limitations, reasons for caution: We acknowledge that the absence of compared data with fresh oocytes' ICSI, the detailed cellular mechanism behind the improvement of embryo development, and transgenerational safety in offspring resulted from the mitochondria supplementation were the limitations of this study.

Wider implications of the findings: With these results, we propose that ASC mitochondria supplementation could rejuvenate the quality of cryopreserved oocytes and enhance the embryo developmental capacity, signifying another possible approach of mitochondrial transplantation therapy.

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