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Autologous adipose stem cells mitochondria transfer improves the developmental potential of cryopreserved oocytes and develops healthy offspring

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Oocyte cryopreservation is becoming prevalent in assisted reproductive technologies, among the women who facing age related decline in fertility or receiving antineoplastic therapies, to increase the possibility of bearing children using their own gametes. Though the composition of cryoprotectants and the protocols of cryopreservation have been significantly improved over time, the overall success of the development rate is still far behind that of fresh ones. The oocyte cryopreservation can adversely affect oocytes' developmental potential by increasing intracellular oxidative stresses and damage to the mitochondrial structure and function. In this study, we studied whether autologous adipose stem cell (ASC) mitochondria supplementation to oocytes could restore post-fertilization development in cryopreserved oocytes. Further, we have analyzed whether this mitochondria supplementation may cause any disorders in the offspring generated by mitochondria-supplemented oocytes. As the results, we found that ASC mitochondria showed similar morphology to oocytes' mitochondria and had a higher ATP production capacity. The cryopreserved-thawed oocytes were supplemented with ASC mitochondria at the same time as intracellular sperm injection (ICSI). And then, we compared their developmental capacity with the control group and the mitochondria quality in 2-cell embryos. We found that, compared to their counterpart, mitochondria supplementation significantly improved development from 2-cell embryos to blastocysts and ATP production in 2-cell embryos while reactive oxygen species levels were comparable. And we have developed 3 generations of offspring from the embryos developed after mitochondria supplementation and found that all the offspring show no congenital disorders arising due to mitochondria supplementation. With these results, we propose that ASC mitochondria supplementation could restore the quality of cryopreserved oocytes and enhance the embryo developmental capacity, signifying another possible approach for mitochondrial transplantation therapy.