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Polar Body Genome Transfer for Prventing the Transmission of Inherited Mitochondrial Diseases

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Abstract:

Inherited mtDNA diseases transmit maternally and cause severe phenotypes. Currently, there is no effective therapy or genetic screens for these diseases; however, nuclear genome transfer between patients' and healthy eggs to replace mutant mtDNAs holds promises. Considering that a polar body contains few mitochondria and shares the same genomic material as an oocyte, we perform polar body transfer to prevent the transmission of mtDNA variants. We compare the effects of different types of germline genome transfer, including spindle-chromosome transfer, pronuclear transfer, and first and second polar body transfer, in mice. Reconstructed embryos support normal fertilization and produce live offspring. Importantly, genetic analysis confirms that the F1 generation from polar body transfer possesses minimal donor mtDNA carryover compared to the F1 generation from other procedures. Moreover, the mtDNA genotype remains stable in F2 progeny after polar body transfer. Our preclinical model demonstrates polar body transfer has great potential to prevent inherited mtDNA diseases.

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