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Mitochondria in Reproduction

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I. Mitochondrial DNA (mtDNA) Genome in Reproduction

The human mitochondrial genome comprises a circular, histone-free molecule composed of 16.6kb of DNA, present in one or more copies in every mitochondrion. Mitochondrial DNA (mtDNA) is not transmitted through Mendelian (diploid or sexual) principles, but passes from one generation to the next by way of the oocytes cytoplasm.

An individual's mtDNA is consequently entirely derived from his or her mother. Paternal mtDNA entering the oocytes with the fertilizing spermatozoon appears to be expelled from the cleaving embryo at or soon after the 2-cell stage. The fact that mtDNA replication is switched off in the oocytes by the time it becomes fertilizable ought to further discourage any leaked paternal mtDNA replicating in the zygote.

The role of mitochondria during fertilization and cleavage stages of embryo development is not fully understood. Mitochondria in oocytes and early embryos are structurally immature. Although the functional significance of this mitochondrial location is unknown, it appears to be an important part of normal development in the experimental animal. Other observations indicate that mitochondria are indeed functionally important for early embryo development.

Mitochondrial DNA is particularly sensitive to damage, as it has no protective histone proteins and minimal repair systems. This can result in an increased mutation rate and hence damage to the RNA transcripts or to the DNA itself.

Mitochondria and mtDNA are maternally inherited, whereas the transmission of paternal mtDNA is blocked in mammals. The paternal mtDNA enters the oocytes but is no longer detectable in the preimplantation embryo. Several mechanisms could be responsible for preventing the transmission of paternal mtDNA, including the down-regulation of mtDNA copy number during spermatogenesis, specific elimination of paternal mitochondria in fertilized oocytes, and the suspension of mtDNA replication in the fertilized oocytes. Mitochondrial transcription factor A (mtTFA or Tfam) is a key regulator of mtDNA copy number in mammals. Tfam could be involved in regulating the amount of mtDNA during spermatogenesis. The down-regulation of mitochondrial Tfam protein concentrations in round and elongating spermatids coincides with the reduction of mtDNA copy number. At the same time the amount of Tfam transcripts is increased.

II. mtDNA Genome and Premature Ovarian Failure, Gestational Diabetes Mellitus

Clinically premature ovarian failure (POF) is defined as the cessation of normal ovarian function in women less than 40 years of age with normal profile of growth and development. The clinical picture of POF has been well described, which is characterized by oligomenorrhea and hypoestrogenism resulted in infertility. POF is not a rare entity, seen in approximately 1-2% of the female population. However, its etiology and pathophysiology are not well established. The studies have demonstrated that a one-time test of FSH as well as checkup in anytime are not sufficient in establishing the diagnosis of the determination of this disease, and have identified the presence of intermittently normal ovarian function in patients showing the signs of POF.