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MITOCHONDRIAL THEORY OF REPRODUCTION AND OVARIAN AGING

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Although oxidative stress underlies the pathogenesis of various diseases, its role in the reproduction and effective methods to inhibit aging-related pathologic events remain unknown. We studied roles of the reactive oxygen and nitrogen species and mitochondria in the mechanism of ovulation and fertilization of oocytes, their embryonal development and aging of the ovary. Kinetic analysis using site-specific superoxide dismutase and related compounds revealed that oxidative stress elicited by mitochondria and NADPH oxidase regulated the maturation of ovarian follicles and the number of ovulated oocytes in rodents. Oxidative stress in and around mitochondria was found to play critical roles in the induction of granulosa cell apoptosis to support the process of ovulation. Analysis using time-lapse cinematography revealed that fluorescence-labeled mitochondria rapidly moved within oocytes from their central area to subcortical regions and along pericortical area of plasma membranes where microtubules and microfilaments were highly enriched. Repeated ovulation and/or aging of mice induced pathologic localization of mitochondria. Oral administration of L-carnitine successfully inhibited aging-related pathologic events of oocytes and the process of ovulation, fertilization, and embryonal development. Critical roles of mitochondria and redox functions of reactive species in the sequence of events of mammalian reproduction and effective method to support safe development of embryo will be discussed.