

Abstract

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Selenium in mammalian spermiogenesis.

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BACKGROUND: The role of selenium in male fertility is reviewed with special emphasis on selenoprotein P and phospholipid hydroperoxide glutathione peroxidase (GPx4) in spermiogenesis.

RESULTS: Inverse genetics reveal that selenoprotein P is required for selenium supply to the testis. GPx4 is abundantly synthesized in spermatids. As a moonlighting protein it is transformed in the later stages of spermiogenesis from an active selenoperoxidase into a structural protein that becomes a constituent of the mitochondrial sheath of spermatozoa. The transformation is paralleled by loss of glutathione. Mechanistically, the process is an alternate substrate inactivation of GPx4 resulting from reactions of its selenenic form with thiols of GPx4 itself and other proteins.

DISCUSSION: Circumstantial evidence and ongoing experimental genetics indicate that the mitochondrially expressed form of the GPx4 gene is the most relevant one in spermiogenesis, with the nuclear form being dispensable for fertility and the role of cytosolic GPx4 remaining unclear. Clinical data reveal a strong association of low sperm GPx4 with infertility.

CONCLUSION: Thus, impaired GPx4 biosynthesis, due to selenium deficiency or to genetic defects in gpx4 itself or in proteins involved in Se distribution and selenoprotein biosynthesis, causes male infertility, but can also be an epiphenomenon due to any perturbation of testicular function.

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