Abstract

Spermatogenesis is a highly orchestrated, strictly regulated cascade of events that could be divided into three major processes: mitotic expansion of diploid germ cells (spermatocytogenesis), meiotic division creating haploid cells, and spermiogenesis. Spermiogenesis, the final stage of spermatogenesis comprises a striking metamorphosis of round haploid spermatids into morphologically and functionally specialized spermatozoa designed for the fertilization. One of the proteins indispensable for proper sperm morphogenesis is centrobin, a structural component of the specialized cytoskeletal structures of the elongating spermatids (acroplaxome and manchette), executing essential role in sperm head shaping and assembly of the head-tail coupling apparatus. Disruption in *Cntrob* gene (coding for centrobin) in rats homozygous at the *hd* (hypodactyly) locus results in male infertility, with a striking morphological signature called „decapitated sperm syndrome“ with detachment of sperm head from the flagellum due to impaired head-tail coupling. However, molecular function of centrobin in spermiogenesis is still unknown. Sperm decapitation is a distinct phenotype described in several mouse mutants and importantly from infertile human males. Strikingly, in addition to proteins functioning in cytoskeletal structure/transport, there are also mutations in genes coding for LINC complex –proteins serving to connect cytoskeleton to outer and inner nuclear membranes and to nuclear cytoskeleton.

The aim of this thesis is to specify function of centrobin in the final steps of spermatid morphogenesis and detect potential centrobin-associated proteins, specifically following the hypothesis that centrobin can interact with cytoskeleton and its associated proteins, and also with proteins of the LINC complex. To achieve this goal we will employ the mutant *Cntrob*$^{hd/hd}$ males and the mutant males (partially) rescued by transgenic expression of wild-type centrobin.