

SPERMATOGENIAL STEM CELLS: FROM BASIC RESEARCH TO CLINICAL APPLICATIONS

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The testis contains undifferentiated spermatogonia and is therefore the only adult organ populated with proliferating germline cells. Whereas the biology of these cells is quite well understood in rodents, their modes of mitotic expansion and differentiation are poorly understood in primates. The existence of these cells offers clinically relevant options for preservation and restoration of male fertility. New approaches based on male germ cell transplantation and testicular tissue grafting can be applied to generate a limited number of sperm and could therefore be considered as important new avenues applicable to a variety of disciplines like animal conservation, genetic germline modification or restoration of fertility in oncological patients. In principle, germ cell transplantation presents a removal of the stem cell from the donor's niche and a transfer into the niche of a recipient. Grafting can be considered as a transplantation of the stem cell in conjunction with its niche. Germ cell transplantation of human spermatogonia into mouse testes revealed that the stem cells survive and expand but are not able to differentiate and complete spermatogenesis. We have developed an approach to infuse germ cells into monkey and human testes and showed that germ cell transplantation is feasible as an autologous approach in primates. Furthermore, we applied germ cell transplantation in the monkey model mimicking a gonadal protection strategy for oncological patients. Ectopic xenografting of testicular tissue was applied to generate fertile sperm from a variety of species. Newborn testicular tissue was grafted into the back skin of immunodeficient mice and developed up to qualitatively complete spermatogenesis. The rapid progress in the development of novel experimental strategies to generate sperm from cryopreserved spermatogonial stem cells or immature testicular tissue will lead to many new options for germline manipulation and fertility preservation.