DRIVERS OF GERM CELL DIFFERENTIATION

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Spermatogenesis requires progression of a self-renewing male germline stem cell population through a precisely timed and ordered developmental sequence to form spermatozoa. For several years, we have been investigating the functional impact of signals on this progression by members of the TGFβ superfamily, follicle stimulating hormone and the bcl-2 family. For example, our lab and others have shown that activin A, bone morphogenetic protein (BMP)-4 and glial-derived neurotropic factor (GDNF) all modulate stem cell development and spermatogonial differentiation at the onset of spermatogenesis after birth. We are trying to understand how germ cells 'interpret' this plethora of competing signals to mediate maturation.

Progression through successive maturation states in response to such signals requires the movement of proteins, including transcription factors, into the nucleus to implement changes in gene transcription. We are investigating the concept that regulated transport of proteins into the nucleus is one mechanism that governs spermatogenic differentiation, and we have focused on analysis of the major class of nuclear transport factors, the importins (IMPs). A diverse family comprising at least six different α forms and 20 different β forms in the mouse, the IMP proteins selectively bind a diverse range of cargo proteins and mediate their passage through the nuclear pore complex and into the nucleus. Our immunohistochemical and *in situ* hybridisation studies have demonstrated developmentally regulated expression of many IMPs in germ cells, in the fetus, in the neonate and in the adult. This suggests that they function to transport cargo required for discrete stages of spermatogenesis. Our recent studies examined the mouse embryonic gonad around the time when specification to form either a testis or an ovary occurs. The IMPβ3 protein is present in both male and female germ cells, but the subcellular localisation and expression patterns within these cell types is gender- and age-specific. We are currently exploring the functional significance of our observations.

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