Maintenance and regeneration of the male germline

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Maintenance of male fertility is dependent on spermatogonial stem cells (SSCs) that self-renew and generate differentiating germ cells for production of spermatozoa. SSC function is dependent on growth factors produced within the testis microenvironment plus cellular factors that regulate gene expression within SSCs and modulate responses to growth factor stimulation. Despite the importance of SSCs for male fertility, the molecular mechanisms that regulate their function and maintenance remain incompletely understood. Importantly, SSC function and male fertility can be compromised by multiple factors including exposure to genotoxic drugs. However, cellular pathways mediating the regenerative response of SSCs following germline damage and loss of SSC function with age are poorly studied. Our research focuses on defining genetic controls and cellular pathways regulating SSC function and male fertility. We employ a range of *in vivo* and *in vitro* experimental systems allowing dissection of mammalian SSC function. We have defined essential roles for the developmental transcription factors PLZF and SALL4 in maintenance of SSC activity and the central importance of mTORC1 signalling in SSC fate regulation. In addition, our studies have characterised cellular heterogeneity within the SSC and progenitor cell pool using single cell approaches and demonstrated the dynamic nature of spermatogonial states with important clinical implications. Current studies are focused on understanding cellular machinery modulating the response of SSCs to stimuli from the niche and molecular mechanisms supporting germline regenerative capacity.