

共催:新学術領域研究「配偶子産生制御」

Identification of Slow Cycling Spermatogonial Stem Cells and their Regulation by PLZF

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A small population of GFRA1+ spermatogonial stem cells (SSCs) supports long-term maintenance of mammalian spermatogenesis. We show here that overexpression of GDNF, the ligand for GFRA1, increases functional SSC numbers in control mice but not in *Plzf^{tu/lu}* (*luxoid*) mice, which exhibit age-dependent germ cell loss. Taking advantage of the difference in SSC potential in these backgrounds, we used RNAseq to identify a subpopulation of SSCs that express EOMES, a T-box transcription factor. EOMES+ SSCs are resistant to busulfan-induced germ cell death and have a lower proliferation index than EOMES– GFRA1+ spermatogonia. PLZF controls this 'slow-cycling' state, as EOMES+ cells have a higher proliferation index in *luxoid* mutants. We propose there are two populations of SSCs, an EOMES+ slow cycling, long-term SSC (A_{s-LT}) and a highly proliferative EOMES- short-term SSC (A_{s-ST}). Loss of *Plzf* deregulates the slow-cycling status of A_{s-LT} cells, leading to stem cell exhaustion and eventual failure of spermatogenesis.

Seminar will be given in English.