

**Title:** Immune privilege of the hematopoietic stem cell niche

造血幹細胞微小環境の免疫特権

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**Abstract:** Stem cells reside in a specialized regulatory microenvironment or niche that provides signals to maintain self-renewal and multi-lineage differentiation capacity and to protect stem cells from environmental insults. Despite rapid advances in our understanding of adult stem cell biology, the immunological attributes of stem cell niches have been overlooked and largely unexplored. Notably, the testis, hair follicle, and placenta are all sites of residence for stem cells and are immune suppressive environments, called immune privileged (IP) sites, where multiple mechanisms conspire to prevent stem cells from immune attack, even enabling prolonged survival of foreign allografts without immunosuppression (IS). We sought to determine if somatic stem cell niches more broadly are IP sites by examining the hematopoietic stem/progenitor cell (HSPC) niche in the bone marrow (BM), a site where immune reactivity exists. We observed persistence of allo-HSPCs in non-irradiated recipients for 30 days without IS with the same survival frequency compared to syngeneic HSPCs. These HSPCs were lost after the depletion of FoxP3 regulatory T cells (Tregs). High resolution in vivo imaging over time demonstrated marked co-localization of HSPCs with Tregs that accumulated on the endosteal surface in the calvarial and trabecular BM. Tregs appear to participate in creating a localized zone where HSPCs reside and where Tregs are necessary for allo-HSPC persistence. In addition to processes supporting stem cell function, the niche will provide a relative sanctuary from immune attack.