Laminin-γ1 Maintains Hematopoietic Nerve-Microvascular Units

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Nerve-microvascular units (NmVUs) are an important regulatory component of the adult bone marrow niche. In elderly murine bone marrow, sympathetic neuropathy induces an aging-associated hematopoietic phenotype, the hallmarks of which are myeloid biased hematopoiesis and B-lymphopenia (Maryanovich et al., 2018). In juvenile mice, sympathectomy alone induces the same hematopoietic profile. The mechanisms that regulate and maintain NmVU organization and function in the bone marrow are unknown.

Laminin-γ1 is an important glycoprotein and regulatory factor for schwann cell, and thus peripheral nerve, development (Yu et al., 2005; Yu et al., 2009; Carlson et al., 2011). Using an inducible and global model of *Lamc1* gene deletion (encodes for laminin-γ1), we find that: (1) reduction of laminin-γ1 synthesis in adulthood depletes laminin-γ1 protein in specific bone marrow niches, (2) laminin-γ1 depletion induces a hematopoietic cell-extrinsic myeloid progenitor bias, reduction in lymphoid progenitors and peripheral b-cell lymphopenia, and (3) globally reduced laminin-γ1 synthesis reduces nerve fiber association with bone marrow arterioles.

Based on these data, we hypothesize that laminin-γ1-homeostasis regulates hematopoiesis via maintenance of bone marrow sympathetic NmVUs. Future studies will determine whether autonomic regulation of hematopoiesis is impaired in our global and inducible *Lamc1* deleted mice, whether the cell extrinsic hematopoietic changes that occur in our *Lamc1* mutant mice are the direct and exclusive consequence of NmVU dysregulation, and to what extent nonmeylinating schwann cell-expression of laminin-γ1 contributes to bone marrow NmVU structure and function.

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