

## EVBO Paper of the month, January 2023

Biswas L, Chen J, De Angelis J, Singh A, Owen-Woods C, Ding Z, Pujol JM, Kumar N, Zeng F, Ramasamy SK, Kusumbe AP. **Lymphatic vessels in bone support regeneration after injury.** *Cell*. 2023. 186(2):382-397.e24.

Blood and lymphatic vessels are jointly involved in regulating tissue-specific functions and homeostasis. In bone, blood vessels are important regulators of osteogenesis without a suggested role in bone for lymphatic vessels. Our current paper of the month challenges this dogma by combining high-resolution light-sheet imaging and cell-specific mouse genetics. Biswas and colleagues demonstrate the presence of lymphatic vessels in mouse as well as human bones. They were able to determine that lymphatic vessels in bone expand during genotoxic stress. VEGF-C/VEGFR-3 signaling and genotoxic stress-induced IL6 are capable of driving lymphangiogenesis in bones. During lymphangiogenesis, secretion of CXCL12 from proliferating lymphatic endothelial cells is critical for hematopoietic and regenerative processes within bone. Lymphangiocrine CXCL12 triggers expansion of mature Myh11<sup>+</sup>CXCR4<sup>+</sup> pericytes, which then differentiate into bone cells, thus contributing to bone and hematopoietic regeneration. In aged animals, such expansion of lymphatic vessels and Myh11-positive cells in response to genotoxic stress appears impaired. These data suggest lymphangiogenesis as a novel and potential therapeutic strategy to stimulate hematopoietic and bone regeneration.

