Thrombopoiesis is spatially regulated by the bone marrow vasculature

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In mammals, megakaryocytes (MKs) in the bone marrow (BM) produce blood platelets, required for hemostasis and thrombosis. MKs originate from hematopoietic stem cells and are thought to migrate from an endosteal niche towards the vascular sinusoids during their maturation. Through imaging of MKs in the intact BM, we demonstrate that MKs are homogeneously distributed within the dense BM blood vessel network, leaving no space for such vessel-distant endosteal niches. By combining in vivo two-photon microscopy and in situ light-sheet fluorescence microscopy with computational simulations, our study reveals surprisingly slow MK migration, limited intervascular space, and a vessel-biased MK pool. Thus, MKs do not need to migrate in order to reach the vessel. These data challenge the current thrombopoiesis model of MK migration and support a modified model where MKs at sinusoids are replenished by sinusoidal precursors rather than cells from a distant periostic niche.

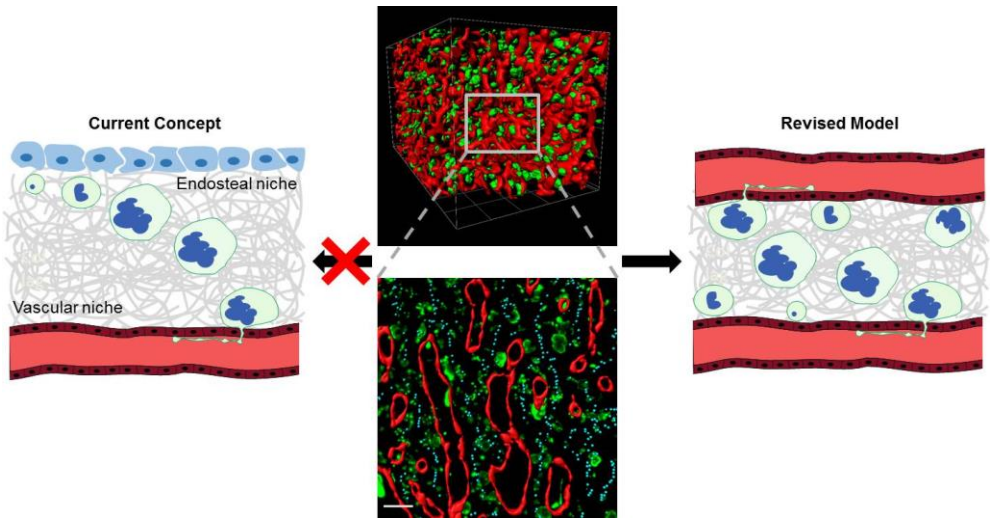

Fig. 1: Current versus revised model of thrombopoiesis