Apelin signaling restricts the blood stem cell-forming hemogenic endothelium in the dorsal aorta

Jean Eberlein, Christian S.M. Helker
Philipps-University Marburg, Faculty of Biology, Cell Signaling and Dynamics
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The process of hematopoiesis is highly conserved among vertebrates. During definitive hematopoiesis hemogenic endothelial cells (HECs) in the aorta-gonad-mesonephros region/ the dorsal aorta (DA) differentiate into multipotent hematopoietic stem cells (HSC) in a process called endothelial to hemogenic transition. Although only a small pool of HSCs is formed during embryonic development, these HSCs will generate all blood lineages throughout life. Previous work has shown that HECs and arterial endothelial cells (ECs) share a common lineage. Using a novel transgenic reporter line for the Apelin receptor (Aplnr) we found that already during the differentiation of the DA HECs exhibit a distinct expression pattern compared to arterial ECs. Live imaging of the reporter identified two subpopulations of ECs within the DA. The main population is expressing the *aplnr* while a small subset of ECs does not express the *aplnr*. *aplnr* expressing ECs are evenly distributed over the DA, but we detected *aplnr* negative ECs exclusively in the ventral wall of the DA. RNA sequencing analysis confirmed that these *aplnr* negative ECs represent HECs. Furthermore, the zonation by *aplnr* expression in the DA not only defines but functionally restricts the fate of the hemogenic endothelium. Loss of the ligand Apelin or the receptor leads to an enlarged size of the hemogenic endothelium and subsequently to an increased generation of HSCs within the DA. These HSCs leave the DA and colonize the hematopoietic tissues leading to an increased number of HSCs in the vascular stem cell niche. Our findings suggest that Apelin signaling has the potential to modulate the hemogenic endothelium fate and thereby HSC numbers. This provides new insights into the process of hematopoiesis, enabling a better understanding of hematopoietic disorders to improve treatment possibilities.