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HoxA3 function during blood development

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Abstract

During development, hematopoietic stem cells (HSC) are generated in the major arteries of the developing embryos. Between E8.5 and E10.5 in the caudal domain of the aorta, specialized endothelial cells, referred as hemogenic endothelium, undergo to structural changes to become blood progenitors and some of them HSC. How those specialized endothelial cells are committed and what regulates their transformation into blood progenitors is mostly unknown. Runx1 transcription factor is essential for blood development and necessary to generate HSC from the vasculature. We have discovered that HoxA3, a gene exclusively expressed in the vasculature of the embryo, controls the endothelial to hematopoietic transition. HoxA3 is expressed in the aorta prior the release of blood progenitors. By using the ES cells differentiation system, we show that HoxA3 upregulation causes blockage of the endothelial to hematopoietic transition, maintaining the cells at the hemogenic endothelium stage.The arrest of blood development is carried out by downregulation of key transcription factor including Gata1, Gfi1B, Ikaros, PU.1, and Runx1. With epistasis analysis we found that HoxA3 repression of Runx1 is sufficient to block the entire blood development process. In fact we found that when Runx1 is expressed in hemogenic endothelium, it promotes blood development by a dual function: it activates blood related transcription factors, and represses endothelial related genes. As results the hemogenic endothelium can further develop into blood progenitor cells.

Biography

Michelina Iacovino obtained her PhD at the University of Molise Campobasso, Italy in Biochemistry and Applied Chemistry. She trained as postdoc in the laboratory of Dr. Michael Kyba, studying the role of Hox genes during blood development at the UT Southwestern Medical Center in Dallas, and at the University of Minnesota, Lillehei Heart Institute. She is currently Assistant Professor at LA BioMed, at Harbor UCLA Medical Center, Los Angeles. She has 30 publications in peer reviewed journal.