The role of lineage and cell interactions in the specification of blood stem cell fate during embryonic development of the zebrafish

Summary
We have used cell lineage techniques to show that during primitive hematopoiesis in the zebrafish, two different mechanisms exist for producing blood that correlate with a cell's location in the gastrula. Our results provide in vivo evidence for the existence of hematopoietic progenitors that are specified to produce either a uni-potential or multi-potential blood cell fate. After this initial specification event, cell interactions further define the final fate of blood progenitors. Zebrafish embryonic red blood cells (RBCs) develop in trunk intermediate mesoderm (IM), and early macrophages develop in the head, suggesting that local microenvironmental cues regulate differentiation of these two blood lineages. spadetail (spt) mutant embryos, which lack trunk paraxial mesoderm (PM) due to a cell-autonomous defect in tbx16, fail to produce embryonic RBCs but retain head macrophage development. In spt mutants, initial hematopoietic gene expression is absent in trunk IM, although endothelial and pronephric expression is retained, suggesting that early blood progenitor development is specifically disrupted. Using cell transplantation, we reveal that spt is required cell-autonomously for early hematopoietic gene expression in trunk IM. We also uncover an interaction between embryonic trunk PM and blood progenitors that is essential for RBC development, potentially identifying a hematopoietic microenvironment that allows embryonic RBC production in the zebrafish.