Notch signaling distinguishes 2 waves of definitive hematopoiesis in the zebrafish embryo.

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Public Summary:

Scientific Abstract:
Recent studies have revealed that definitive hematopoiesis in vertebrates initiates through the formation of a non-self-renewing progenitor with limited multilineage differentiation potential termed the erythromyeloid progenitor (EMP). EMPs are specified before hematopoietic stem cells (HSCs), which self-renew and are capable of forming all mature adult blood lineages including lymphoid cells. Despite their differences, EMPs and HSCs share many phenotypic traits, making precise study of their respective functions difficult. Here, we examine whether embryonic specification of EMPs requires Notch signaling as has been shown for HSCs. In mindbomb mutants, which lack functional Notch ligands, we show that EMPs are specified normally: we detect no significant differences in cell number, gene expression, or differentiation capacity between EMPs purified from wild-type (WT) or mindbomb mutant embryos. Similarly N-[N-(3,5-difluorophenacetyl)-l-alanyl]-S-phenylglycine t-butyl ester (DAPT), a chemical inhibitor of Notch receptor activation, has no effect on EMP specification. These studies establish that HSCs are the only hematopoietic precursor that requires Notch signaling and help to clarify the signaling events underlying the specification of the 2 distinct waves of definitive hematopoiesis.