CXCL12a/CXCR4b acts to retain neutrophils in caudal hematopoietic tissue and to antagonize recruitment to an injury site in the zebrafish larva

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 Neutrophils are a major component of the innate immune response and the most abundant circulating cell type in humans and zebrafish. The CXCL12/CXCR4 ligand receptor pair plays a key role in neutrophil homeostasis, controlling definitive hematopoiesis and neutrophil release into circulation. Neutrophils overexpressing CXCR4 respond by migrating towards sources of CXCL12, which is abundant in hematopoietic tissues. However, the physiological role of CXCL12/CXCR4 signaling during inflammatory responses remains unknown. Here, we show that zebrafish mutants lacking functional CXCL12a or CXCR4b show disrupted granulopoiesis in the kidney and increased number of circulating neutrophils. Additionally, CXCL12a and CXCR4b mutants display exacerbated recruitment of neutrophils to wounds and not to infections, and migrating neutrophils to wounds show increased directionality. Our results show that CXCL12a/CXCR4b signaling antagonizes wound-induced inflam