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Systemic regulation of hematopoietic progenitors maintenance during Drosophila blood development

Tina Mukherjee, PhD
Department of Molecular, Cell, and Developmental Biology,
University of California, Los Angeles, CA

Tuesday, March 5, 2013
2:30 PM
Seminar Room

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Abstract

Hematopoietic stem/progenitor cells reside within a specific microenvironment or the niche, which supports their maintenance in an undifferentiated state. Signals derived from the niche have been extensively characterized and are fairly well understood. However, if blood stem/progenitor cells during development respond to systemic cues remain poorly characterized. Here, we demonstrate that hematopoietic progenitors in *Drosophila*, sense neuronally-derived GABA signal, which is released systemically into the blood from a special group of neurosecretory cells in the brain. This secreted GABA is sensed directly by the blood progenitors via functional metabotropic $GABA_B$ receptors that activate mechanisms to maintain calcium homeostasis in the progenitors to support their proliferation and maintenance. Blocking the GABA signal alters calcium homeostasis in the progenitors and leads to their loss and differentiation. These results establish the existence of a novel neuro-hematopoietic axis that links the central nervous system to the maintenance of stem-like precursors and provides insights into how behavioral/neurological disorders might be linked to immune-related dysfunctions.