CDB SEMINAR

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Stowers Institute for Medical Research

Monday, June 18, 2012

16:00~17:00 A7F Seminar Room

Non-canonical Wnt Signaling Maintains Hematopoietic Stem Cell through Flamingo and Frizzled8 in the Niche

Abstract

Wnt signaling is involved in self-renewal and maintenance of hematopoietic stem cells (HSCs); however, the particular role of non-canonical Wnt signaling in regulating HSCs in vivo is largely unknown. Here we show, Flamingo and Frizzled8, members of non-canonical Wnt signaling, both express in and functionally maintain quiescent long-term HSCs. Flamingo regulates Frizzled8 distribution at the interface between HSCs and N-cadherin+osteoblasts (N-cad+OBs that enrich osteoprogenitors) in the niche. We further found that N-cad+OBs predominantly express non-canonical Wnt ligands and inhibitors of canonical Wnt signaling under homeostasis.Under stress, Non-canonical Wnt signaling is attenuated and canonical Wnt signaling is enhanced in activation of HSCs. Mechanistically, non-canonical Wnt signaling mediated by Frizzled8 suppresses the Ca2+-NFAT- IFNγ pathway, directly or indirectly through the CDC42-CK1a complex; and also antagonizes canonical Wnt signaling in HSCs. Taken together our findings demonstrate that non-canonical Wnt signaling maintains quiescent long-term HSCs through Flamingo and Frizzled8 interaction in the niche.

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