Runx1 and Runx2 inhibit fibrotic conversion of cellular niches for hematopoietic stem cells

In bone marrow, special microenvironments, known as niches, are essential for the maintenance of hematopoietic stem cells (HSCs). A population of mesenchymal stem cells, termed CXC chemokine ligand 12 (CXCL12)-abundant reticular (CAR) cells or leptin receptor-expressing cells are the major cellular component of HSC niches. The molecular regulation of HSC niche properties is not fully understood. The role of Runx transcription factors, Runx1 and Runx2 in HSC cellular niches remains unclear. Yoshiki Omatsu, Takashi Nagasawa (IFReC/Graduate School of Frontier Biosciences, Osaka University) and the research group show that Runx1 is predominantly expressed in CAR cells and that mice lacking both Runx1 and Runx2 in CAR cells display an increase in fibrosis and bone formation with markedly reduced hematopoietic stem and progenitor cells in bone marrow. In vitro, Runx1 is induced by the transcription factor Foxc1 and decreases fibrotic gene expression in CAR cells. Thus, HSC cellular niches require Runx1 or Runx2 to prevent their fibrotic conversion and maintain HSCs and hematopoiesis in adults.

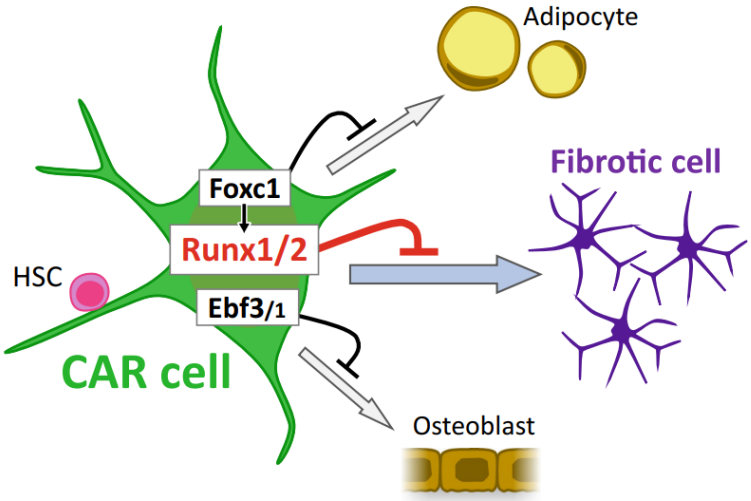

Figure.
CAR cells are specialized mesenchymal stem cells, which express the specific transcription factors, including Runx1/2 as well as Foxc1 and Ebf1/3. Runx1/2 prevents fibrotic conversion of CAR cells to maintain HSC niches.

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