CDB SEMINAR

Frank Conlon

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Monday, November 19
16:00~17:00 C1F Auditorium

Molecular Pathways of Cardiac Progenitor Proliferation and Survival

Summary

The isolation and culturing of cardiac progenitor cells has demonstrated that growth factor signaling is required to maintain cardiac cell survival and proliferation. In this study, we demonstrate that SHP-2 activity is required for the maintenance of cardiac precursors in vivo. In the absence of SHP-2 signaling, cardiac progenitor cells down-regulate genes associated with early heart development and fail to initiate cardiac differentiation. We further show that this requirement for SHP-2 is restricted to cardiac precursor cells undergoing active proliferation. By demonstrating that SHP-2 is phosphorylated on Y542/Y580 and that it binds to FRS-2, we place SHP-2 in the FGF pathway during early embryonic heart development. Furthermore, we demonstrate that inhibition of FGF signaling mimics the cellular and biochemical effects of SHP-2 inhibition and that these effects can be rescued by constitutively active/Noonan syndrome associated forms of SHP-2. Collectively, these results show that SHP-2 functions within the FGF/MAPK pathway to maintain survival of proliferating populations of cardiac progenitor cells. A screen to identify the molecular pathways functioning downstream of FGF/SHP-2 in the developing heart has identified additional components of the SHP-2 pathway and is suggestive of a role for SHP-2 in cell polarity and cell cycle control.

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