



# CDB SEMINAR

Speaker: **Atsushi Miyajima**

< Institute of Molecular and Cellular Biosciences, The University of Tokyo >

Title: **“Hepatic progenitors in liver development and regeneration”**

Date:	<b>Thursday, November 25</b>
Time:	<b>16:00 - 17:00</b>
Place:	<b>7F Conference Room of Building A, CDB</b>

**Summary:**

Hepatoblasts/hepatic stem cells are known to derive from the foregut and differentiate to both hepatocytes and cholangiocytes. However, their nature still remains elusive. We searched for cell surface antigens expressed in fetal liver and developed various monoclonal antibodies that can be used to fractionate fetal liver cells. Among them, Dlk, a type I transmembrane protein with EGF-repeats, is expressed in immature hepatocytes. By using anti-Dlk antibody we isolated the Dlk<sup>+</sup> cells from fetal liver and demonstrated that they are bipotential hepatoblasts that differentiate to hepatocytes and cholangiocytes. Hepatic progenitors, also known as oval cells, develop in adult liver when it is severely injured. We found that Dlk is expressed in a subset of oval cells that are localized at the periphery of oval cell compartment and are less proliferative. These results suggest that oval cells are heterogeneous and Dlk<sup>+</sup> cells represent an intermediate stage between Dlk<sup>-</sup> oval cells and mature hepatocytes.

We have developed a culture system of fetal hepatocytes, in which hepatic differentiation can be induced by cytokines and extracellular matrices. By using this system we have been studying the molecular mechanism of hepatic differentiation. I will present recent results on the role of Notch signaling in liver development. Notch 2 is expressed in hepatoblasts, while Jagged-1 is expressed at the periportal region where cholangiocytes develop, and activation of Notch in hepatoblasts enhances differentiation to cholangiocytes whereas it suppresses differentiation to hepatocytes. These results indicate that Notch signaling plays a key role for the specification of hepatoblasts.

Fetal liver is a major hematopoietic tissue in embryo and I will also discuss unique features of fetal liver hematopoiesis.

**Host: Shin-Ichi Nishikawa <Stem Cell Biology, CDB>**

E-mail: nishikawa@cdb.riken.jp Tel: 078-306-1893 (ext:5301) RIKEN Center for developmental Biology <http://www.cdb.riken.go.jp/>