



## 東北大学脳科学GCOEセミナーのお知らせ

日時 2010年3月18日(木) 16:00~18:00

会場 加齢医学研究所・大会議室

演者 西川伸一 博士

理化学研究所  
発生・再生科学総合研究センター  
幹細胞研究グループ

演題 Development of hematopoietic stem cell explained

Hematopoietic stem cell (HSC) is the most extensively studied stem cell, but yet its developmental pathway in mammals has not been fully explained. While it is established that the definitive HSC that maintains a life-long maintenance of hematopoietic system appears around E10-11 during embryogenesis, none of intermediate stages in the course of HSC differentiation from mesoderm has not been specified until recent years.

In this seminar, I will introduce our attempts to define this course. According to our model updated by the latest results, 4 distinct stages exist between mesoderm and dHSC. The first stage is  $Flk1^+Etv2/ER71^+$  population appearing in the yolk sac of E7.0-7.5 embryo. As null mutation of *etv2/er71* gene results in complete block of differentiation of endothelial and hematopoietic lineages, this is the major diverging point of those two lineages. Our analysis using *Etv2* double KO ES cells suggests that *Etv2* is involved directly in commitment of endothelial cells (EC) and HSC rather than indirectly via regulation of *Flk1*. The next stage in the HSC pathway is defined as  $Flk1^+Runx1^+GATA1^+VECAD^+$ . *Etv2* expression is also maintained in this stage. While the major population derived from this stage is primitive hematopoietic cells, a small fraction of cells proceeds to the dHSC pathway. We have evidence that *VECAD* and *GATA1* are downregulated in this stage, but definition of this stage requires further study. Subsequently, *VECAD* is re-induced in the embryo and resulting  $VECAD^+Runx1^+$  hemogenic endothelial cells are integrated into the luminal wall of developing vascular system such as dorsal aorta and umbilical artery. Finally,  $CD45^+$  cells bud out from this  $Runx1^+$  endothelial cells by the downregulation of molecules involved in maintaining cell-cell junction of endothelial cells. With this new definition of intermediate stages in dHSC differentiation pathway, we are investigating the molecules that regulate the decision making towards HSC.

連絡先：創生応用医学研究センター 形態形成解析分野 (大隅典子) 内線8203