京都大学　再生医科学研究所　生体システム制御学セミナー

演者: **Prof. Tsvee Lapidot**

Department of Immunology, Weizmann Institute of Science, Israel

演題：**Regulation of normal and leukemic stem cells: Stem cell interactions with the bone marrow microenvironment.**

日時：平成 25 年 4 月 16 日（火）15：00～16：30

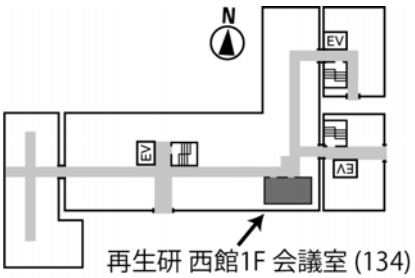
場所：京都大学　再生医科学研究所　西館 1 階会議室

講演要旨：Hematopoietic stem cells continuously replenish the blood with mature immune and blood cells on demand. These primitive cells mostly reside in the bone marrow in a quiescent, non-motile mode via adhesion interactions with stromal cells and macrophages. Quiescent and cycling stem cells have different metabolism and accordingly different amounts of intracellular reactive oxygen species (ROS). Importantly, ROS is not just a byproduct of the metabolic state, but rather has major roles in stem cell function. ROS levels are dynamic and can reversibly dictate cycling short term, ROS^{high} stem cell repopulation potential with enhanced myeloid differentiation, or quiescent long term ROS^{low} stem cell repopulation potential. Importantly, ROS^{high} short term repopulating stem cells can be converted to become ROS^{low} long term repopulating stem cells by treatment with the ROS inhibitor NAC, or with a p38 inhibitor. Low levels of ROS, are regulated by the cytokines SCF, FGF-2 and PGE_2 and connexin gap junctions with stromal cells are required for stem cell self renewal will be discussed. High ROS levels, due to stress and inflammation induced by injury, bleeding and infections, involve AKT, P38, HGF and S1P, induce stem cell differentiation, and enhanced motility. High ROS levels are also induced in clinical stem cell mobilization protocols by the cytokine G-SCF. Ultimately, balanced ROS levels are crucial for maintaining the small stem cell pool both in steady state homeostasis and during inflammation, in which the stem cells need to be shielded and protected from the toxic inflammatory insult and differentiating high ROS levels. The role of the coagulation system in regulation of stem cell migration and development via thrombin/PAR-1 and EPCR shedding, or in maintaining stem cell adhesion to BM stromal cells via APC/EPCR and PAR-1 will be presented. In addition, the role of the blood bone marrow endothelial barrier and FGF-2 signaling in promoting hematopoietic, mesenchymal and leukemic stem cell proliferation and expansion will be discussed. Finally, stem cell retention in the murine bone marrow by activated COX-2 positive monocytes and macrophages will be presented and discussed.

Lapidot 博士は、血液学、免疫学分野での有力研究者の一人です。
セミナーでは、最新の知見をご発表頂きます。

＜最近の主要論文＞

Itokin,T., et al. **Blood** 120;1843,2012.
Golan,Y., et al. **Bood** 119;2478, 2012.
Ludin, A., et al. **Nat. Immunol.** 13; 1072, 2012.
Schajnovitz, A. et al., **Nat. Immunol.** 12; 391, 2011.
Spiegel,A., et al. **Cell Stem Cell** 3; 484, 2008



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