

75th IRCMS Seminar

Date **January 31, 2022 (Monday)**

Time **13:00-14:00**

On-site+
Online

Venue **1F Conference Room, IRCMS**

- To prevent the spread of COVID-19, the seats will be limited to 20.

Title:
**Hematopoiesis ~developmental,
normal, and leukemic~**

Speaker:

**Yosuke
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Abstract:

Hematopoietic stem cells (HSCs) are the most studied tissue stem cells. However, there are still many unresolved issues such as, development of HSCs in mouse embryos, dormancy regulation of adult HSCs and their leukemic aspects.

Hematopoiesis in mouse embryos begins at around embryonic day 7.5 (E7.5). First hematopoietic cells (embryonic type) appear from mesoderm and later hematopoietic stem cells (HSCs) appear at E10.5. The developmental pathway of HSCs from mesoderm has not yet been elucidated. We clarified that Runx1+Gata1- angioblastic cells at E7.5 are origin of HSCs through lineage tracing analysis and time-lapse live imaging analysis. In addition, we resolved single-cell gene expression profiles during development of hematopoietic cells from mesoderm.

Most of the HSCs are dormant (in the G0 phase of the cell-cycle). G0 marker, which can visualize G0 cells by mVenus expression, and single-cell analysis showed that the conventional HSC fraction contains three cell types; dormant, active, and phenotypic HSCs (lacking HSC potential). Furthermore, dormancy of HSCs is regulated by concentration of cytosolic calcium. This dormant state causes leukemia stem cells (LSCs), which are malignant hematopoietic stem cells due to genetic mutations, to be resistant to treatment. We clarified that inflammatory pathway activation is responsible for the resistance and its blockade is effective in eliminating LSCs.

References:

1. Tanaka, Y. et al. Early ontogenic origin of the hematopoietic stem cell lineage. *Proceedings of the National Academy of Sciences* **109**, 4515-4520 (2012).
2. Scialdone, A. et al. Resolving early mesoderm diversification through single-cell expression profiling. *Nature* **535**, 289-293 (2016).
3. Fukushima, T. et al. Discrimination of Dormant and Active Hematopoietic Stem Cells by G0 Marker Reveals Dormancy Regulation by Cytoplasmic Calcium. *Cell Reports* **29**, 4144-4158.e7 (2019).
4. Tanaka, Y. et al. Eliminating chronic myeloid leukemia stem cells by IRAK1/4 inhibitors. *Nat Commun* **13**, 271 (2022).



* Anyone in Kumamoto Univ. is welcome, but **please pre-register** by IRCMS web page (the QR code or search "IRCMS registration").



IRCMS registration 

Organizer:
Distinguished Prof. Toshio Suda

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