

Single molecule characterization of hematopoietic stem cells homing

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Hematopoietic stem cells, HSCs, are widely used to treat various types of cancer through bone marrow transplantation. For a successful transplantation, HSCs should undergo migration and homing processes in the microenvironment of the bone marrow of the recipient. The homing is initiated by the interaction of endothelial E-selectin with surface ligands of HSCs such as PSGL-1 and CD44. Here we investigate the relevance of PSGL-1 dynamics on tethers and slings, thin and flexible structures protruding out of HSCs formed during the homing, to the initial step of the homing, rolling of HSCs on endothelium by means of single-molecule live cell imaging and scanning electron microscopy (SEM).

Single-molecule tracking analysis of PSGL1 molecules on tethers and slings of HSCs showed diffusion coefficient twice faster than of the ones localized on microvilli. Also, mean square displacement analysis showed random diffusional motion of the molecules on tethers and slings and a confined diffusion on microvilli. We found that the observed random diffusional motion of the selectin ligands on the tethers and slings is a result of the detachment of actin cytoskeleton from the cell membrane, which occurs during the formation of the tethers. Further, SEM images of the rolled cells revealed that the width of the tethers and slings (50 nm in diameter) becomes smaller during their formation from the microvilli (110 nm in diameter). We will discuss how the diffusion behavior of PSGL-1 on the tethers and slings affect the rolling of HSCs on E-selectin [1, 2].

References.

- [1] AbuZineh, K., Joudeh, L. I., Al Alwan, B., Hamdan, S. M., Merzaban, J. S., & Habuchi, S. (2018). Microfluidics-based super-resolution microscopy enables nanoscopic characterization of blood stem cell rolling. *Science Advances*, 4(7), eaat5304.
- [2] Al Alwan, B., AbuZineh, K., Nozue, S., Rakhmatulina, A., Aldehaiman, M., Al-Amood, A. S., Serag, M. F., Aleisa, F. A., Merzaban, J. S., Habuchi, S. Stable hematopoietic stem cell rolling is enabled by spatial confinement and temporal dynamics of selectin ligands. Submitted.