Spatiotemporal Characterization of Ligand-Receptor Interactions in Blood Stem Cell Rolling Assay

Alabandi, Zaina (School: Dhahran Ahliyya School)

Hematopoietic stem cell (HSC) transplant failure can be attributed to graft failure, poor graft function, and the failure of the homing process in which the transplanted cells settle into the bone marrow to establish production of specialized cells. In the initial stage of tethering and rolling, signal proteins (selectins) expressed on the surface of endothelial cells attach to ligand receptor proteins found on the surface of HSCs. Projections of the cell membrane, known as tethers and slings, develop due to blood flow exerting stress on the slow-rolling cells. This project visualizes tethers/slings formation at the molecular level and characterizes the behavior of E-selectin and P-selectin glycoprotein ligand 1 (PSGL-1). E-selectin was deposited into a microfluidic chamber, where it attached itself to the bottom surface of the channel, mimicking selectins on endothelial cells. PSGL-1 was targeted using anti-PSGL-1 conjugated with fluorescent dye. Human leukemic cells modeled HSCs, because they express the same receptor proteins as HSCs do. Images of tethers/slings were analyzed using fluorescence-quantifying software. Tethers extend from the back of the cell as it slow-rolls with the blood flow. As shear stress continues acting on the tether, it flips to the front of the cell to form a sling, which retracts back to the cell membrane. This data represents a model for further studies that will be conducted to determine the role of tethers/slings formation in the failure/success of an HSC transplant. Therefore, work on preventing HSC transplant failure to improve transplant success rate may be possible.

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