MCB, vol.16, supplemental 2, pp.15, 2019

Immune Cells Migrating through the Brain Endothelia Junctions Served as Shuttles for Nanoparticles Delivery to Glioblastoma

Gloria B. Kim[1,†], Qiong Wei[2,†], Virginia Aragon-Sanabria[1], Sulin Zhang[2], Jian Yang[1] and Cheng Dong[1,*]

[1]Department of Biomedical Engineering, The Pennsylvania State University, University Park, PA, 16802, USA.

[2]Department of Engineering Science and Mechanics, The Pennsylvania State University, University Park, PA, 16802, USA.

[†]These authors contributed equally to this work

*Corresponding Author: Cheng Dong. Email: cxd23@psu.edu.

Abstract: Most cells survive and grow by attaching and spreading on a substrate. They generate internal tension that contracts the cell body and thus exert tractions on the underlying substrate through focal adhesions. Traction force also plays a critical role in many biological processes, such as inflammation, metastasis, and angiogenesis. Thus, measuring the cell traction force provides valuable information on understanding the underlying mechanism of these biological processes. Here, a traction force microscopy (TFM) method using super thin hydrogels composed of immobilized fluorescent beads was utilized to quantify the mechanical forces generated during the transmigration of Jurkat cells (a human T lymphocyte cell line) through the brain endothelial junctions. The mechanical forces involved during the transmigration process of Jurkat cells through the brain endothelial junctions were quantified at different stages of migration in response to brain endothelium-junction regulations. TFM also allowed continuous capturing the movement of Jurkat cells from early phases of cell spreading to post-transmigration through the brain endothelial junctions. The outcomes of this study provide insight into how mechanical forces and endothelium-junction functions change during the infiltration of immune cells into the brain. Additionally, the feasibility of using the Jurkat cells as shuttles to deliver therapeutic nanoparticles through the brain endothelial junctions has been demonstrated in an *in vitro* transwell model. Currently, traction forces are also being measured on T lymphocytes genetically modified to brain tumor targeting chimeric antigen receptors and carry therapeutic nanoparticles. Understanding such mechanisms will allow us to better design biomaterials that can be used to make drug delivery systems, which create a more favorable condition for the migration of therapeutics through physical barriers such as the blood-brain barrier (BBB).

Keywords: Traction force microscopy; human T lymphocytes; transmigration; brain endothelial cells

DOI: 10.32604/mcb.2019.07137