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## Hemodynamic shear stress stimulates migration and extravasation of tumor cells by elevating cellular oxidative stress

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Circulation of cancer cells in blood flow is an important phase for distant cancer metastasis, during which cancer cells are exposed to hemodynamic shear stress. Recent studies identified shear stress as the primary factor that damages circulating tumor cells in blood flow. However, it remains unclear whether shear stress can modulate properties and functions of tumor cells in a manner that might help tumor cells to exit circulation. In our study, we demonstrate that fluidic shear stress could positively regulate migration and extravasation of surviving tumor cells in circulation, and facilitate metastasis. We established a microfluidic circulatory system to apply physiological fluidic shear stress on breast cancer cells and mimic the physical environment in blood flow. An arterial level of shear stress generated in the circulatory system significantly increased tumor cell migration in both transwell and wound healing assays. We also observed that shear stress enhanced extravasation of breast tumor cells in a transendothelial assay. The mechanistic study identified the elevation of cellular ROS as an early molecular event induced by shear stress. The excessive cellular ROS subsequently activates ERK1/2 pathway, which leads to tumor cell migration and extravasation. Finally, by using a zebrafish model, we demonstrated that application of antioxidants could suppress shear stress-enhanced tumor cell extravasation in vivo. This new understanding of how fluidic shear stress promotes metastatic potential of tumor cells has important implications in cancer treatment and can help us identify latent therapeutic targets for inhibiting tumor progression.

### Biography

Ma Shijun received his BS from Wuhan University in China. He is currently a PhD candidate in School of Chemical and Biomedical Engineering, Nanyang Technological University. His current research work focuses on the how hemodynamic shear stress influences tumor cell migration and adhesion.

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