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Numerical Simulation of a Single Cell Passing through a Narrow Slit

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Abstract : Most cancer-related deaths are due to metastasis. Metastasis is a complex, multistep processes including the detachment of cancer cells from the primary tumor and the migration to distant targeted organs through blood and/or lymphatic circulations. During hematogenous metastasis, the emigration of tumor cells from the blood stream through the vascular wall into the tissue involves arrest in the microvasculature, adhesion to the endothelial cells forming the microvessel wall and transmigration to the tissue through the endothelial barrier termed as extravasation. The narrow slit between endothelial cells that line the microvessel wall is the principal pathway for tumor cell extravasation to the surrounding tissue. To understand this crucial step for tumor hematogenous metastasis, we used Dissipative Particle Dynamics method to investigate an individual cell passing through a narrow slit numerically. The cell membrane was simulated by a spring-based network model which can separate the internal cytoplasm and surrounding fluid. The effects of the cell elasticity, cell shape and cell surface area increase, and slit size on the cell transmigration through the slit were investigated. Under a fixed driven force, the cell with higher elasticity can be elongated more and pass faster through the slit. When the slit width decreases to 2/3 of the cell diameter, the spherical cell becomes jammed despite reducing its elasticity modulus by 10 times. However, transforming the cell from a spherical to ellipsoidal shape and increasing the cell surface area only by 3% can enable the cell to pass the narrow slit. Therefore the cell shape and surface area increase play a more important role than the cell elasticity in cell passing through the narrow slit. In addition, the simulation results indicate that the cell migration velocity decreases during entry but increases during exit of the slit, which is qualitatively in agreement with the experimental observation.

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