Transcapillary Trafficking of Clustered Circulating Tumor Cells

BRIAN STOREY, Olin College, SAM AU, Center for Engineering in Medicine, Massachusetts General Hospital, YENG-LONG CHEN, Institute of Physics, Academia Sinica, Taipei Taiwan, FATIH SARIOGLU, Center for Engineering in Medicine, Massachusetts General Hospital, SARAH JAVAID, DANIEL HABER, SHYAMALA MAHESWARAN, Massachusetts General Hospital Center for Cancer Research, SHANNON STOTT, MEHMET TONER, Center for Engineering in Medicine, Massachusetts General Hospital — Aggregates of circulating tumor cells (CTC-clusters) are known to be more metastatic than equal numbers of singlet circulating tumor cells. Yet the mechanisms responsible for CTC-cluster dissemination and tumor seeding are still largely unknown. Without direct experimental evidence, it was assumed that because of their size, CTC-clusters would occlude and rupture capillaries. In this work, we have challenged this assumption by investigating the transit of CTC-clusters through microfluidic capillary constrictions under physiological pressures. Remarkably, cancer cell aggregates containing 2-20 cells were observed to successfully traverse constrictions 5-10 microns with over 90% efficiency. Clusters rapidly and reversibly reorganized into chain-like geometries to pass through constrictions in single file. This observation was verified by computational simulation of clusters modeled with physiological cell-cell interaction energies. Hydrodynamic analysis suggested that CTC-clusters were able to pass narrow constrictions by acting as individual cells in series, not as cohesive units. Upon exiting constrictions, clusters remained viable, proliferative and rapidly returned to typical cluster morphologies.

Brian Storey
Olin College

Date submitted: 31 Jul 2015

Electronic form version 1.4