Nano-force spectroscopy: insight into intercellular de-adhesion dynamics

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Proper homeostasis of the central nervous system relies on the structural and functional integrity of the neurovascular unit (NVU). The most important physiological function of the NVU is formation and maintenance of the blood-brain barrier (BBB). Anatomically the cerebral microvascular endothelium together with pericytes, astrocytes, neurons and the extracellular matrix builds up the NVU. From a mechanical point of view, the endothelium is the most exposed to mechanical stress they represent the first defense and signaling line of the BBB. Unfortunately, most of the neoplasms found in the CNS are of metastatic origin. The first and crucial step of brain metastasis formation is the establishment of firm adhesion between the blood travelling tumor cells and the tightly connected layer of the endothelium. Amongst all tumors, the melanoma exhibits elevated frequency to metastasise to the brain.

Intercellular dynamics might present crucial nanomechanical aspects, therefore direct investigation with high accuracy provides important information. Using single-cell force spectroscopy, de-adhesion dynamics of melanoma cells with different level of malignancy (WM35, A2058 and A375) from a confluent layer of brain micro-capillary endothelial cells (hCMEC/D3) was investigated. Based on simple mechanical assumptions, hereby is presented our latest data on comparing the de-adhesion dynamics between the studied cell types. Apparent mechanical properties showed altered characteristics pointing towards cell type dependent aspects. Our results show that nanomechanical properties can be associated to higher metastatic potential and invasive characteristics may rely on stronger adhesive properties mediated by altered tether formation dynamics.