Numerical predictions of endothelial gaps formation: modelling the metastatic spread of cancer

J. Escribano*, F. Spill, RD.Kamm*** and JM. García-Aznar***

* Aragón Institute of Engineering Research (I3A)
Universidad de Zaragoza (UNIZAR)
Campus Río Ebro, 50018 Zaragoza, Spain
e-mail: jmgaraz@unizar.es

** School of Mathematics
University of Birmingham
Birmingham, B15 2TT, UK
e-mail: f.spill@bham.ac.uk

*** Department of Biological and Mechanical Engineering
Massachusetts Institute of Technology, USA
e-mail: rdkamm@mit.edu

ABSTRACT

Cancer or immune cells within the vasculature may usually interact with the endothelial cells through which they can transmigrate. In fact, cancer and immune cells are the most common cells that usually transmigrate presenting different strategies.

In inflammation it is assumed that leukocytes interact with the endothelial cells of the vasculature, weakening the VE-cadherin-mediated cell-cell junctions and subsequently inducing the gap formation between the endothelial cells.

Although there are not many numerical models that have simulated this process of cell transmigration in the endothelial layers, a couple of previous models have focused on that topic. On the one hand, a particle-based model was proposed by Ramis-Conde et al (2009) in which authors assume that the tumour cell interacts with endothelial cells weakening these junctions. On the other hand, Cao et al (2016) proposed a chemo-mechanical model assuming that the limiting condition for transmigration is the deformation characteristics of the nucleus in the tumour cells.

However, more recently, Escribano et al (2019) proposed that endothelial gap formation occurs spontaneously without interaction with transmigrating cells. To test this assumption authors elaborated a novel particle-based model to investigate how contractile and protrusive cell forces in the endothelium are able to regulate gap formation. To simulate cell-cell junctions, a force-based model was considered, assuming a catch-bond constitutive law. This model is able to predict the formation of endothelial gaps between cells preferentially at vertices according to experimental measurements.

REFERENCES

[1] Ramis-Conde, I., Chaplain, M. A., Anderson, A. R., & Drasdo, D. (2009). Multi-scale modelling of cancer cell intravasation: the role of cadherins in metastasis. Physical biology, 6(1), 016008.

[2] Cao X, Moeendarbary E, Isermann P, Davidson PM, Wang X, Chen MB, Burkart AK, Lammerding J, Kamm RD, Shenoy VB. A Chemomechanical Model for Nuclear Morphology and Stresses during Cell Transendothelial Migration. Biophys J. 2016 Oct 4;111(7):1541-1552. doi: 10.1016/j.bpj.2016.08.011. PMID: 27705776

[3] Escribano J, Chen M, Moeendarbary E, Cao X, Shenoy V, Garcia-Aznar JM, Kamm RD, Spill F. Balance of Mechanical Forces Drives Endothelial Gap Formation and May Facilitate Cancer and Immune-Cell Extravasation. PLOS Computational Biology, in press.