The 8th European Congress on Computational Methods in Applied Sciences and Engineering
ECCOMAS Congress 2022
5-9 June 2022, Oslo, Norway

Relocation of VEGFR2 and integrin during adhesion and spreading of endothelial cells

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Keywords: *Mechanobiology, Advecting Membranes, Receptor Dynamics, Non-equilibrium Thermodynamics, High Performance Computing, Finite Elements*

Tumor angiogenesis is a pathological event triggered by the chemical interplay between growth factor proteins (or ligands), released by cancer cells, and proteins placed on Endothelial Cells (ECs) membrane (i.e. receptors). We here focus on the interaction of the VEGFR2, the main receptor regulator of the angiogenic stimulus on ECs, with gremlin, a non-canonical ligand, and integrin a further kind of receptor. In addition to play a pivotal role in the mechanical response of EC, integrin promotes the long-lasting activation and polarization of the intracellular signaling released by the gremlin-VEGFR2 complex [1]. Despite the biochemical pathways resulting from VEGFR2 activation is well documented, the role of cell mechanics to angiogenesis deserves additional quantitative studies. Therefore, we present a chemo-mechano-transport model embedded in the field of continuum thermodynamics, which accounts for two coupled chemical reactions, VEGFR2 with gremlin and VEGFR2-gremlin(-complex) with integrin. No structural capability is here attributed to the cell membrane, which is thus idealized as the edge of a deformable body whose morphological response reflects complex biological mechanisms arising within the ECs volume. Constitutive relationships are deduced from suitable Helmholtz free energies and by means of the Coleman-Noll procedure [2]. Governing equations are written in weak forms as a prelude to the approximation schemes implemented in the finite element library *deal.ii*. In-vitro and in-silico experiments have been co-designed to study the relocation of VEGFR2 and integrin along the membrane of an EC that spreads onto an enriched gremlin substrate.

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