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The Temporal Basis of Angiogenesis

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Through integrated agent-based computational modeling with in vitro and in vivo experimentation we have recently uncovered that the speed and specific dynamic properties of collective decision-making among endothelial cells ultimately determines the morphology of the blood vascular network that is generated. Lateral inhibition via Notch-Dll_4 signaling of neighboring cells is required to select migratory cells to lead new blood vessel sprouts. Our computational model predicted that the speed of this collective decision making process to select the cells migratory or inhibited states over time is affected by changes to tissue environment leading to drastic changes in branch spacing and vessel diameter. In experimental studies we have now validated that these predictions are correct, indicating an important new temporal mechanism for the switch to abnormal vessel growth in cancer and potentially many other diseases. Indeed we have also found first evidence that other pathways within the cells themselves can modulate collective decision deliberation times leading again to the morphogenesis if different vascular tree structures. This work has important ramifications for the field of vascular biology and therapeutic interventions targeting abnormal vascular growth in many diseases such as cancer and retinopathy.

Giovedì 6 DICEMBRE, ore 10:00, aula MAGNA, via Branze 38, 25123 Brescia

A. Salvadori, S. Mitola - Il seminario e` finanziato dall'Ateneo su fondi per attività a carattere internazionale