Tumour phenotypic heterogeneity: the impact of mixing evolutionary trade-offs with a dynamic surrounding micro-environment

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One of the key aspects of cancer is the phenotypic heterogeneity that characterizes tumour cells at both intertumoural and intratumoural levels. In this respect, clinical evidence shows how different environmental conditions, e.g., the oxygenation level and the ECM pattern, determine the specific degree of coexistence, within a growing malignant mass, of cells characterized by different migratory abilities and metabolic/proliferation determinants. A crucial role in this dynamics seems to be played by the abnormal spatial variations in tumour microenvironment that lead to the formation of distinct local ecological niches in which highly competitive cells emerge and spread out. In this talk, some mathematical models will be presented to describe the adaptive dynamics of the phenotype of cancer cells in response to dynamic variations in the spatial distribution of abiotic factors (oxygen, glucose and lactate) and substrates (extracellular matrix) [1], [2]. The aim is to explore (evaluating the impact of the evolutionary parameters) the process that leads cancer cells to aggressive phenotypic states correlated with poor prognosis like resistance to harsh environmental conditions and metastatic abilities. The models are formulated in terms of systems of coupled nonlinear partial differential equations in the mathematical framework of population dynamics and of phenotype-structured population. The computational outcomes demonstrate that the mutual interactions between the malignant mass and the environmental variables can naturally result in the emergence within the tumour domain of subregions characterized by the presence of cells with specific biophysical determinants. This may provide a theoretical evidence of the spatial heterogeneity observed in experimental cancer studies. Finally, an interpretation in a therapeutic perspective of the obtained results will be proposed to eventually suggest some biomedical strategies to reduce tumor aggressiveness.

References

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