Mathematical Modeling of Tumor-Tumor Distant Interactions Supports a Systemic Control of Tumor Growth

S. Benzekry[1]*, Clare Lamont[2], Dominique Barbolosi[3], Lynn Hlatky[2], Philip Hahnfeldt[4]

[1]Inria Bordeaux Sud-Ouest and Institut de Mathematiques de Bordeaux, Talence, France
[2]Center of Cancer and Systems Biology, Tufts University School of Medicine, Boston, USA
[3]SMARTc team, Centre de Recherche en Cancerologie de Marseille (Inserm 1068), Marseille, France

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Abstract (300 words limit)

Interactions between different tumors within the same organism have major clinical implications, especially in the context of surgery and metastatic disease. Three main explanatory theories (competition, angiogenesis inhibition, and proliferation inhibition) have been proposed, but precise determinants of the phenomenon remain poorly understood. In this talk, I will present a formalized version of these theories into mathematical models and the results of biological experiments that were performed to test them against empirical data.

The main experimental finding was that in syngeneic mice bearing two simultaneously implanted tumors, growth of one and only one of the tumors was significantly suppressed (61% size reduction at day 15, $P < 0.05$). At the theoretical level, the competition model had to be rejected, whereas the angiogenesis inhibition and proliferation inhibition models were able to describe the data.

The proliferation inhibition model was identifiable and minimal (four parameters), and its descriptive power was validated against the data, including consistency in predictions of single tumor growth when no secondary tumor was present. This theory may also shed new light on single cancer growth insofar as it offers a biologically translatable picture of how local and global action may combine to control local tumor growth and, in particular, the role of tumor-tumor inhibition. This model offers a depiction of concomitant resistance that provides an improved theoretical basis for tumor growth control and may also find utility in therapeutic planning to avoid postsurgery metastatic acceleration.

References

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*Speaker; E-mail: sebastien.benzekry@inria.fr