The development of drug resistance in metastatic tumours under chemotherapy: An evolutionary perspective

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We present a mathematical model of the evolutionary dynamics of a metastatic tumour under chemotherapy, comprising non-local partial differential equations for the phenotype-structured cell populations in the primary tumour and its metastasis. These equations are coupled with a physiologically-based pharmacokinetic model of drug administration and distribution, implementing a realistic delivery schedule. The model is carefully calibrated from the literature, focusing on BRAF-mutated melanoma treated with Dabrafenib as a case study. By means of long-time asymptotic and global sensitivity analyses, as well as numerical simulations, we explore the impact of cell migration from the primary to the metastatic site, physiological aspects of the tumour tissues and drug dose on the development of chemoresistance and treatment efficacy. Our findings provide a possible explanation for empirical evidence indicating that chemotherapy may foster metastatic spread and that metastases may be less impacted by the chemotherapeutic agent [1].

[1] F. Padovano, C. Villa. *The development of drug resistance in metastatic tumours under chemotherapy : an evolutionary perspective.* Journal of Theoretical Biology, **595(111957)**, 2024.

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