How steady states analysis helps cancer therapies

<u>Chiara Fornari</u>, Francesca Cordero, Marco Beccuti, Gianfranco Balbo Department of Computer Science, University of Torino

fornari@di.unito.it, fcordero@di.unito.it, beccuti@di.unito.it, balbo@di.unito.it

Raffaele A. Calogero, Department of Molecular Biotecnhologiy and Life Sciences, University of Torino raffaele.calogero@unito.it

Recent studies in cancer biology have changed the traditional view of tumor progression, showing that the growth and evolution of many cancers are driven by a population of cells named Cancer Stem Cells (CSCs) [3]. In detail, the CSCs theory describes these tumors as hierarchically structured, and characterized by different subpopulations of cells. This heterogeneity is considered the cause of the failure of many conventional treatments. Indeed, even if many current treatments are able to kill the differentited tumor cell populations, they do not have the same positive effect on CSCs. In fact, cancer stem cells resist to most of the common cancer therapies, causing the tumor relapse. Therefore, it is fundamental to fully understand mechanisms underlying these type of tumors, in order to better understand their progression and treatments responses.

Mathematical models about cell populations dynamics ([4], [5] and [1]) provide a useful tool to achieve these goals. In particular, in this paper we present a compartmental mathematical model which describes the progression of a type of malignant tumors characterized by the stem-differentiation hierarchy. In our model the dynamics of cell populations are described by a system of non linear ordinary differential equations (ODEs), on which we perform both a qualitative and quantitative analysis. More precisely, we start fixing the qualitative behavior of the system through the equilibria structure definition and the stability investigation. Then, we analyze model temporal evolution by its numerical integration. Furthermore, before this quantitative phase, we set up model parameters in order to describe data related to the breast cancer evolution [2]. We find some interesting analytical properties of system equilibria that allow us to reduced the huge parameters space. Eventually, we apply this tool to a real breast cancer case study [2], in order to predict the vaccination effects on its progression.

References

- [1] R. Molina-Peña, M. A. Álvarez, A simple mathematical model based on the cancer stem cell hypothesis suggests kinetic commonalities in solid tumor growth, PLoS ONE, 7, e26233, 2012.
- [2] A. Porzia, S. Lanzardo, A. Citti, F. Cavallo, G. Forni, A. Santoni, R. Galandrini, R. Paolini, Attenuation of PI3K/Akt-Mediated Tumorigenic Signals through PTEN Activation by DNA Vaccine-Induced Anti-ErbB2 Antibodies, The Journal of Immunology, 184, 4170–4177, 2010.
- [3] M.F. Clarke, J.E. Dick, P.B. Dirks, C.J. Eaves, C.H. Jamieson, D.L. Jones, J. Visvader, I.L. Weissman, G.M. Wahl, Cancer stem cells' perspectives on current status and future directions: AACR Workshop on cancer stem cells, Cancer Res, 66, 9339–9344, 2006.
- [4] X. Zhu, X. Zhou, M.T. Lewis, L. Xia, S. Wonk Cancer stem cell, niche and EGFR decide tumor development and treatment response: A bio-computational simulation study, Journal of Theoretical Biology, 269, 138–149, 2011.
- [5] C. Fornari, F. Cordero, D. Manini, R.A. Calogero, G. Balbo Mathematical approach to predict the drug effects on cancer stem cell models, Proceedings of the CS2Bio 2nd International Workshop on Interactions between Computer Science and Biology, Reykjavik, Iceland, 2011.