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FROM THE GUEST EDITORS

There is an increasing awareness that to properly understand how tumors originate and grow, and then how to develop effective cures, it must be taken into account the dynamics of tumors and its great complexity. Tumors are characterized not only by the coexistence of multiple scales, both temporal and spatial, but also by multiple and quite different kinds of interactions, from chemical to mechanical. This makes the study of tumors remarkably complicated. A genuine explosion of data concerning the multi-faceted aspects of this family of phenomena collectively called cancers, is now becoming available. At the same time, it is becoming quite evident that traditional tools from biostatistics and bioinformatics cannot manage these data. Mathematics, theoretical biophysics and computer sciences are needed to qualitatively and quantitatively interpret experimental and clinical results, in order to make realistic predictions.

Many mathematicians and physicists are approaching oncology as an ideal area of application of their competences, and recently the term Mathematical Oncology has been created. However, obtaining significant results is very difficult, since it requires the deep knowledge of biomedical phenomena as well as the knowledge of the "hot" problems currently open, which can only be guaranteed by real interdisciplinary work. On the other hand, in recent years, an increasing number of biomedical investigators more positively look at the application of mathematics to biomedicine in general, and to cancer biology and medicine in particular. Laboratories where computational scientists work together with biomedical researchers are being born, and nowadays seeing a mathematician working in a molecular oncology institution is no more a rare exception.

The present Special Issue collects contributions from the participants of the Workshop "Mathematical Oncology: New Challenges for Systems Biomedicine", held at the *Ettore Majorana Centre for Scientific Culture* in Erice (Italy), September 26 - 30, 2011, co-organized by us and by Prof. Zvia Agur. Focus of the Workshop was the formulation, analysis and computer simulation of mathematical models of cancer-related phenomena. The primary purpose of the meeting was to bring together mathematicians, biomedical researchers and clinicians to help the mutual awareness of problems and potentialities, and to promote cooperation.

Many biological processes and mathematical tools are considered in the papers here published: Billy and coworkers consider the influence of growth factors in an age-structured cellular population; Bodnar and colleagues focus on the delays involved in tumor angiogenesis by means of qualitative analysis and numerical simulations of functional differential equations; the immune system, and its interplay with immunogenic tumors, is the topic faced by Caravagna et al., who investigate this problem by defining a hybrid stochastic process; classical mathematical physics methods are employed in the work by Criaco and colleagues to model the activation and clonal expansions of T cells; systems biology of a very large biomolecular

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signaling network of relevance in breast cancer is investigated by De Ambrosi et al. by joining graph theory, sensitivity analysis and numerical simulations; d'Antonio et al. investigate the mechanics of interaction between tumor cells and extracellular matrix, and join mathematical physics to individual-based models; the interplay between a tumor and its micro-environment is studied by Dubois and colleagues by means of a multi-scale model based on hybrid cellular automata; the chemotherapy of leukemia is considered by Fimmel et al. by using the theory of optimal control; Lignet and coworkers focus on the systems biology of the VEGF signal pathway, investigating the robustness and redundancy of the network; Morales-Rodrigo focus on the modeling of anti-angiogenic therapy by means of the theory of nonlinear PDEs; genome quantitive analysis by means of highly innovative statistical procedures is the object of the study by Properzi and colleagues; the dynamics of the response to chemotherapy under a Norton-Simon-like hypothesis is investigated by Rodrigues and Mancera; cellular migration is considered by Scianna et al., who employ a tool, the cellular Potts model, that originates from the most classical model of phase transitions: the Ising model; recent experimental researches are showing that many kinds of tumors might be based on stem cells, which are here investigated by Tello by means of a systems of PDEs with non-local coefficients.

With its variety of biological problems and mathematical techniques, we hope that this volume may be of interest for a large number of readers. We are grateful to Professor Yang Kuang for hosting this collection of articles on Mathematical Biosciences and Engineering, to our co-organizer Professor Zvia Agur, and last but not least - to Prof. Franco Giannessi, director of the *International School of Mathematics 'Guido Stampacchia'* at the Ettore Majorana Centre for Scientific Culture: the conference would not have been possible without his encouragement and support. We also wish to thank all the referees for their valuable and patient job in reviewing the papers.

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