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Editorial

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Preface: A Physical Sciences Perspective of the Evolution of Drug Resistance in Cancer

In this day and age with advanced technologies for the detection and diagnosis of cancer, the treatment to cure or even to control cancer remains a challenge greatly due to the evolution of resistance to available treatments. It is estimated that in the United States 1,530,000 people were diagnosed with and 570,000 people died of cancer of all sites in 2010 [http://seer.cancer.gov/csr/1975_2007/results_single/sect_01_table.01.pdf]. Most cancer-related deaths are not due to cancer in the primary site; rather, the deaths are due to disseminated disease when metastasis occurs in vital organs such as the liver, lungs, or pancreas. Relapse in cancer patients undergoing therapy is by and large due to the evolution of drug resistance in the cancer cell population. Evolutionary theory predicts that, given time, heredity, and variation, any living organisms will evolve when a selective pressure is introduced. Albeit much more complex, the evolution of drug resistance in cancer is akin to the evolution of antibiotic drug resistance in bacteria, where evolutionary theory has been applied to suggest specific strategies to delay the onset of drug resistance.

In October 2009 the Physical Sciences—Oncology Centers (PS-OCs) Program was launched by the Office of Physical Sciences—Oncology (OPSO) of the National Cancer Institute (NCI) to tackle longstanding problems in cancer biology and oncology with a physical sciences perspective. Across the country, twelve PS-OCs were established to form a PS-OC Network bringing together for the first time teams of experts from the physical and biological sciences to study cancer at a fundamental level. Thematic areas around which the PS-OCs formed are (1) the physical laws and principals of cancer; (2) information coding, decoding, transfer and translation in cancer; (3) deconvoluting cancer's complexity; and (4) evolution and evolutionary theory in cancer. A subtheme of the lattermost is the topic for this special issue of *Molecular Pharmaceutics*: Evolution of Drug Resistance in Cancer. To cover the breadth of the topic for this special issue, contributions were solicited from scientific investigators both within and beyond the PS-OC Evolution of Drug Resistance Working Group to illustrate the problem of drug resistance in cancer and describe potential solutions from multiple vantage points.

Investigators from the PS-OC Program who contributed to this special issue are conducting exciting work in the thematic area of evolution and evolutionary theory in cancer. Franziska Michor and colleagues at the Dana-Farber Cancer Institute PS-OC are using evolutionary biology in combination with theoretical mathematical modeling to shed light on the optimization of dosing schedules for cancer chemotherapy.[1,2] Colleagues at the University of Southern California PS-OC including David Agus and Parag Mallick provide experimental results for input of parameters into the evolutionary mathematical models developed by Michor that predict the penetrance of drug resistance.[9] Robert Austin at the Princeton University PS-OC is using microfabricated habitats to examine evolution of drug resistance in bacteria in response to selective pressure, and has shown that within hours bacteria can develop resistance to antibiotics which is attributed to four single nucleotide polymorphisms.[3] Ongoing work in the Princeton PS-OC is translation of the findings in bacterial drug resistance to mammalian cell systems.[4] Also part of the Princeton PS-OC, Robert Getzenberg and Donald Coffey (both at Johns Hopkins University) are investigating the effects of microenvironmental stress such as heat on drug resistant cancer cells and have demonstrated that chemotherapeutic efficacy may be enhanced by triggering certain microenvironmental stresses to which cancer cells display sensitivity.[5,6] Robert Gatenby and colleagues at the H. Lee Moffitt Cancer Center PS-OC use Darwinian dynamics and mathematical modeling to demonstrate that an evolutionary double bind strategy will greatly aid in the success of cancer chemotherapy.[7] Also from the H. Lee Moffitt Cancer Center, Robert Gillies is studying how the pH of tumor microenvironment mediates cell adaptation leading to invasion and drug resistance.[8]

The series of research articles and reviews published in this special issue of *Molecular Pharmaceutics* provides us with new insights to the applications of evolution and evolutionary theory to drug resistance in cancer. We anticipate that you will find novelty in the approach of bringing fresh perspectives from the physical sciences to obtaining a fundamental understanding of drug resistance along with new strategies for cancer therapy based on evolutionary theory.

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