Doron Levy
University of Maryland

Modeling the chemotherapy-induced selection of drug-resistant traits during tumor growth

The emergence of drug-resistance is a major challenge in chemotherapy. In this talk we will present our recent mathematical models for describing the dynamics of drug-resistance in solid tumors. Our models follow the dynamics of the tumor, assuming that the cancer cell population depends on a phenotype variable that corresponds to the resistance level to a cytotoxic drug. We incorporate the dynamics of nutrients and two different types of drugs: a cytotoxic drug, which directly impacts the death rate of the cancer cells, and a cytostatic drug that reduces the proliferation rate. Through analysis and simulations, we study the impact of spatial and phenotypic heterogeneity on the tumor growth under chemotherapy. We demonstrate that heterogeneous cancer cells may emerge due to the selection dynamics of the environment. Our models predict that under certain conditions, multiple resistant traits emerge at different locations within the tumor. We show that a higher dosage of the cytotoxic drug may delay a relapse, yet, when this happens, a more resistant trait emerges. Moreover, we estimate the expansion rate of the tumor boundary as well as the time of relapse, in terms of the resistance trait, the level of the nutrient, and the drug concentration. Finally, we propose an efficient drug schedule aiming at minimizing the growth rate of the most resistant trait. By combining the cytotoxic and cytostatic drugs, we demonstrate that the resistant cells can be eliminated.