## Heiko Enderling, Lynn Hlatky, Philip Hahnfeldt

Center of Cancer Systems Biology, St. Elizabeth's Medical Center, Tufts University School of Medicine, 736 Cambridge Street, Boston MA, 02135, USA

## The promoting role of a tumor-secreted chemorepellent in self-metastatic tumor progression

It has been proposed that cancer cells, in particular glioma tumor cells, secrete a chemorepellent factor that guides cell migration away from the tumor, facilitating migration and invasion. We present a hybrid continuous discrete mathematical model of tumor growth and the chemotropism phenomenon to show that such a chemorepellent factor can also act as a promoter of self-metastasis, a mechanism for tumor expansion we have previously shown can explain several essential kinetic dependencies of tumor growth. A sufficient criterion for this expansion was found to be the passive migration of peripheral cancer stem and non-stem cells away from the main tumor mass. The migrating cancer stem cells formed new clusters while simultaneously releasing neighboring quiescent cancer cells to proliferate and form new progeny. We show here how the introduction of an active repellent trait serves to accelerate peripheral migration, and thus, by the self-metastasis principle, accelerate tumor growth. These results provide a mechanistic basis for the proposal that chemorepellent action in gliomas may underlie their rapid growth.