Predicting The Effects of Cancer Therapies Targeting Angiogenesis Signaling Pathways

Stacey D. Finley
Department of Biomedical Engineering
University of Southern California

Angiogenesis, the formation of new blood vessels from pre-existing vasculature, is a tightly regulated biological process involved in physiological function such as wound healing and exercise, as well as in pathological conditions, including preeclampsia, ischemic heart disease, and cancer. Inducing angiogenesis is a hallmark of cancer, as tumors cannot grow beyond 1 mm in diameter without eliciting the formation of blood capillaries to supply oxygen and other nutrients. Vascular endothelial growth factor (VEGF) is a key regulator of angiogenesis and its role in cancer biology has been widely studied. Given the action of VEGF in promoting angiogenesis, it has been targeted in various cancer treatments.

Systems biology approaches, including experiment-based computational modeling, are useful in gaining insight into the complexity of tumor angiogenesis. Computational models provide a framework to test biological hypotheses and optimize effective therapies that aim to inhibit tumor vascularization and growth. Here, I describe the development of whole-body, molecular-detailed compartment models of VEGF kinetics and transport and the application of these models to predict the effect of various anti-angiogenic therapies that inhibit VEGF. The models reproduce experimental observations and predict the dynamics of VEGF in the body and can be applied to interpret pre-clinical and clinical data. Importantly, the models simulate the effects of intravenous administration of anti-VEGF agents. Model predictions are relevant to the clinical application of VEGF-targeting therapies and generate testable hypotheses that can aid in elucidating the mechanism of action of anti-VEGF agents. This work is useful for the development and optimization of personalized cancer treatment strategies that target the VEGF pathway.