Nature Reviews Clinical Oncology **10**, 366 (2013); published online 4 June 2013; doi:10.1038/nrclinonc.2013.96

BIOMARKERS

New VEGF model-based biomarker

Intense efforts undertaken to develop therapies that target VEGF have been hampered by the lack of biomarker-based selection of patients likely to benefit from antiangiogenic therapy. Now, researchers have developed an experiment-based computational model to investigate the distribution of two major VEGF isoforms—$VEGF_{121}$ and $VEGF_{165}$. Importantly, the levels of free VEGF in the tumour were 7–13 times greater than levels of plasma VEGF for several cancer types, with $VEGF_{121}$ being the predominant form.

Contrary to what would be expected, plasma VEGF levels increased after drug treatment, owing to intercompartment transport of VEGF, but free VEGF within the tumour decreased with anti-VEGF treatment. Thus, biochemical and transport processes deplete the tumour VEGF levels rather than circulating intravascular VEGF, explaining why paradoxical increases in VEGF levels have sometimes correlated with responses seen in the clinic.

This mathematical model is an advance in our understanding of the potential different roles of VEGF isoforms in the tumour and in the blood circulation. In an accompanying commentary, Rakesh Jain commented, "the model also predicts that tumour VEGF levels can either increase or decrease after anti-VEGF treatment depending on the tumour microenvironment. Collectively, these intriguing results suggest that the rate of VEGF secretion by tumour cells is the major determinant of response and could serve as a predictive biomarker for anti-VEGF drugs."

Lisa Hutchinson

Original article Finley, S. D. & Popel, A. S. Effect of tumor microenvironment on tumor VEGF during anti-VEGF treatment: systems biology predictions. *J. Natl Cancer Inst.* doi:10.1093/jnci/djt093