TARGETED THERAPIES

Model reveals addiction to oncogenes

Targeted therapies can produce dramatic responses in some patients, but in many cases it is difficult to tell who will respond and who will not. A mathematical model of survival and death signals has predicted which lung cancer tumors will respond to the EGFR tyrosine kinase inhibitor erlotinib, pointing the way to a more-informed use of this drug, and other drugs targeting oncogene addiction in cancer.

The Felsher laboratory has been studying the phenomenon of oncogene addiction for over 10 years. Based on this research, “we believed that it should be possible to ‘model’ oncogene addiction and thereby predict when oncogene addiction will occur,” explains Felsher.

The researchers teamed up with members of the Paik laboratory, who specialize in the measurement, quantification, analysis and modeling of imaging data. As Felsher outlines, “we decided together that we could ‘model’ imaging combined with cell signaling data to attempt to predict and define oncogene addiction.”

The team studied conditional mouse models of lung cancer and lymphoma using imaging and assessed biomarkers associated with proliferation and apoptosis. From these data they developed a mathematical model based on ordinary differential equations that predicted oncogene addiction from the differential changes in survival and cell death signals.

Crucially, the investigators were able to use this model and imaging to predict oncogene addiction and, therefore, responses of patients with lung cancer who received erlotinib as part of a clinical trial.

Going forward, Felsher says, “we plan to improve our model by incorporating other variables such as the role of self-renewal, senescence and home immune contributions and to prospectively test our models in a clinical study.”

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Original article Tran, P. T. *et al.* Survival and death signals can predict tumor response to therapy after oncogene inactivation. *Sci. Transl. Med.* 3, 103ra99 (2011)