Mathematical Model Could Aid Biomarker Validation

Tumors may grow for 10 years or longer before currently available blood biomarker tests can detect them, according to a mathematical model developed by Stanford researchers. Their analysis indicates that unless biomarker technology improves, it may not be possible to use blood tests to detect tumors before they metastasize.

This new model is the first to relate tumor growth to biomarker shedding and circulating levels of the molecules. "This is an uncharted area," says study author Sanjiv S. Gambhir, MD, PhD, chair of the Stanford University School of Medicine's radiology department. Gambhir and Sharon S. Hori, PhD, a postdoc in his lab, based the mathematical description on pharmacokinetic models of injected drug behavior.

Using data on ovarian cancer and the commonly employed biomarker CA125 protein, Hori and Gambhir showed that an ovarian tumor could grow for 10.1 to 12.6 years and reach roughly the size of an olive before current CA125 assays could detect it.

Gambhir says the model is applicable to any solid tumor; researchers need to input baseline values for variables such as how fast a particular cancer grows, the rate at which tumor cells shed a biomarker, the rate of shedding of the same biomarker by normal cells, the rate of the biomarker's degradation in the blood, and the sensitivity of the assay used to detect it. Varying the values allows scientists to analyze the effects of different assumptions about tumor growth and biomarker shedding.

The model makes fairly simplistic assumptions about how tumors grow and how biomarkers are shed, notes Gambhir. His lab is working on extending the model to take multiple biomarkers into account, trying to discern what effects cancer growth and circadian rhythms might have on biomarker diffusion, and determining the effects of changing tumor vasculature on biomarker levels.

Gambhir hopes that even the basic model will help guide biomarker discovery and validation. "The power of modeling is not just filling in variable values for given biomarkers but for actually helping you guide what properties you're looking for in new biomarkers," he says. He also believes the model can help determine how sensitive new detection technologies will need to be to catch cancers early enough to make a difference in treatment.

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