

Gene panel predicts lung cancer survival, study finds

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Researchers from four leading cancer centers have confirmed that an analysis involving a panel of genes can be used to predict which lung cancer patients will have the worst survival. The finding could one day lead to a test that would help determine who needs more aggressive treatment. The study, the largest of its kind, appears online in *Nature Medicine*.

The researchers looked at 442 lung cancer tissue samples collected from six cancer hospitals in North America. They tested the cancer samples to look at the expression of hundreds of genes, and factored in clinical predictors such as tumor stage and the patients' gender and age. The results showed that the lung cancers could be divided into groups with better and worse survival rates.

Typically, lung cancer patients receive chemotherapy after surgery to reduce the risk of the cancer coming back. But specialists know that some patients with stage I disease, the earliest stage, have an aggressive disease with poor prognosis while some patients with more advanced stage II disease have a relatively good prognosis. The question is how to identify which patients need the additional therapy and which patients could potentially avoid it.

"We found that looking at clinical data along with gene expression can be a more reliable indicator. Gene expression is not just a black box approach – which a lot of researchers think it is. Sometimes knowing the context actually helps you use that information more efficiently," says

study author David Beer, Ph.D., professor of surgery and radiation oncology at the University of Michigan Medical School and co-director of the Cancer Genetics Program at the U-M Comprehensive Cancer Center.

Lung cancer is particularly complex, with multiple types and subtypes, most of which are directly related to smoking. There are many genetic alterations induced by tobacco smoke exposure. To be able to offer one simple gene test for the disease, scientists would need to accurately model the known cellular diversity and the potential differences underlying the aggressiveness between lung cancers.

"Our findings suggest that there is a potential for successfully predicting lung cancer prognosis based on gene expression, but it is likely to be more difficult to develop a clinically useful test than has been suggested by previous studies. It's going to require more assay standardization and a large prospective study to identify a signature that is ready for clinical use," says study author Kerby Shedden, Ph.D., associate professor of statistics at U-M.

The researchers will continue to refine this process, identifying the important genes and testing them on tissue samples. They also plan in the future to test their predictors in a prospective trial, enrolling patients as they are diagnosed and following their progress. Enrollment for this trial has not begun.

Four institutions formed a consortium with support from the National Cancer Institute, to develop and validate gene expression signatures of lung cancers. The four institutions are the University of Michigan Comprehensive Cancer Center, H. Lee Moffitt Cancer Center and Research Institute in Tampa, Fla., Memorial Sloan-Kettering Cancer Center in New York, and Dana-Farber Cancer Institute in Boston.

Methodology: The researchers collected lung cancer tissue samples from six centers and grouped them into four sets based on the laboratories where the samples were processed. Two sets served as the "training set," in which researchers looked at several possible gene expression methods to determine whether they could be predictive of patient outcome. They then looked at the other two additional tumor sets for which all outcome data had remained unknown and blinded to the researchers, called "validation sets," to assess whether the outcome of the training set could be duplicated.

Source: University of Michigan

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