Gene signature helps identify risk of relapse in lung cancer patients

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A new genetic signature identified by Spanish researchers may provide doctors with robust and objective information about which patients with early stage lung cancer are at low or high risk of relapse following surgery, investigators report at the 3rd European Lung Cancer Conference in Geneva. Their work also opens new avenues for immunotherapy for lung cancer.

Non-small cell lung cancer is a disease that is often not diagnosed until it has grown and spread throughout the body. Even those patients who are diagnosed early enough to undergo surgical removal of the tumor still have a discouraging 30% rate of relapse.

Researchers hope that identifying which patients have the greatest risk of relapse will allow doctors to focus other treatment strategies, in order to improve their chance of being cured after surgery.

A multidisciplinary team of researchers from Hospital Clinico San Carlos, Madrid, have found a 50-gene predictor that appears to be capable of doing just that. In a study of 84 patients with stage I and II non-small cell lung cancer, who had undergone surgery to remove their tumor, the gene signature accurately predicted which patients were at low risk of relapse.

The researchers analyzed genetic expression in the tumor mass using microarray technology. Following patients for six years, they were able to correlate gene expression patterns with the clinical course of disease,

and the risk of relapse.

The Spanish research team's report at the meeting shows that the genes of the predictor were over-expressed in roughly one-third of patients, all of whom had a low risk of relapse. Further analysis showed that these genes were related to the activity of important immune system white blood cells, known as B lymphocytes.

"All of these genes overexpressed in the low-risk group are highly related to B lymphocyte activity," said Dr Florentino Hernando presenting the results at the meeting. "So, the B cell-mediated immune response seems to have a very important role."

The genetic profile identified by the researchers suggests that low-risk patients have an enhanced immune response against the tumor. "Thus, treatments that may interfere with this response such as post-surgical chemotherapy must be reconsidered for the low-risk subgroup," he says.

"One third of patients show an overexpression of an 'immune' genetic signature in their tumor specimens, that is associated with better prognosis," Dr Hernando said. "The fact that this B cell-dependent immune response was associated to the good outcome suggests we should investigate its therapeutic applications in the management of these patients after surgical resection."

Commenting on the study, which he was not involved in, Prof David Carbone from the Vanderbilt-Ingram Cancer Center, member of the IASLC Board, said: "The Spanish group studied tumors from 84 patients with completely resected stage I and II lung cancer for gene RNA expression profiles using 41,000 different probes. Since over half of these patients relapse and die from their cancer in spite of complete resection, there is a pressing need for both defining those patients at the greatest risk of relapse for trials of adjuvant therapy, but also potentially

avoiding the toxicity of adjuvant therapy in patients with a low risk of relapse. This is a potentially extremely important classifier, which if independently validated, could be the basis of such a test. It is interesting that the majority of the genes in the classifier are either immune-derived or immunomodulatory, suggesting a potential molecular basis for this observation. It would be interesting to compare the results of this classifier to simple quantitation of lymphocytic infiltration into the resected tumors.

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