Study Finds Biological Differences in Lung Tumors of African Americans and Whites

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A new study aimed at understanding why lung cancer incidence is higher in African American men than in other racial/ethnic groups has found a potential clue: Certain gene expression patterns may be different in the tumors of some African Americans than in those of whites.

The researchers also found that different biological pathways may be involved in lung cancers among African Americans and whites, according to results published in Clinical Cancer Research on December 1, 2017.

“Our research also suggests that the gene expression differences we observed could translate to different responses to therapies,” said Brid M. Ryan, PhD, MPH, of NCI’s Center for Cancer Research, who led the study.

Using a software tool called Gene Set Enrichment Analysis, the researchers predicted that patients whose tumors have certain gene signatures that are more common in African Americans would be unlikely to benefit from certain therapies.

“Our results give us some interesting leads to follow,” Ryan said, noting that the researchers can now focus on certain signaling pathways that may play a role in the aggressiveness of lung cancer in African Americans.

But she cautioned that the results need “to be replicated and investigated further—both in the laboratory and in clinical trials.”

Investigating Lung Cancer Disparities

A long-term goal of the research is to try to better understand biological factors that may contribute to disparities in lung cancer and use this information to improve the care of patients.

African American men have a higher incidence of lung cancer than other racial or ethnic groups, and they have higher death rates from the disease. “But African Americans have a lower

cumulative exposure to smoking than other groups," said coauthor Khadijah A. Mitchell, PhD, of Lafayette College, who until recently was a postdoctoral fellow in Ryan's lab. "So there may be biological factors driving the disparity that have not yet been investigated."

A recent study comparing the frequency of lung cancer-related mutations between African Americans and whites did not find meaningful differences, suggesting that differences in genetic mutations might not explain racial disparities in the disease. But few studies have looked for racial differences in gene expression in lung cancer, Mitchell said.

Comparing Gene Expression Patterns in African Americans and Whites

For the current study, Dr. Mitchell and her colleagues profiled the activity of two types of RNA molecules—those that are involved in producing proteins (mRNAs) and those that regulate gene activity (microRNAs). The analysis included samples of normal and tumor tissue from 64 African Americans and 74 whites with non-small cell lung cancer, the most common form of the disease.

To profile mRNA activity, the researchers used samples from 22 African Americans and 19 whites; the remaining samples were used to analyze microRNA expression.

In African Americans, the expression levels of 2,210 genes were different (higher or lower by at least twofold) in lung tumors and matched normal samples. In whites, 2,921 genes showed expression differences between tumor and normal tissues.

Many of the same genes were expressed at different levels between tumor and normal tissues in both groups of patients. But some genes were expressed at higher or lower levels in just one group.

The researchers hypothesized that these differences in the overall gene expression patterns between African Americans and whites were associated with biological differences in certain signaling pathways.

To investigate this hypothesis, the researchers identified the signaling pathways affected by the genes that were differentially expressed between African Americans and whites. They found that lung cancer in African Americans may involve stem cell and invasion pathways, whereas the disease in whites may involve cell proliferation pathways.

Predicting Differences in the Response to Treatments

To explore potential clinical implications of their findings, the researchers used a software tool designed to predict the response to drugs. This tool, called the Connectivity Map, predicted that tumors with the gene expression pattern found more often among African Americans might respond differently to certain drugs than tumors with the gene expression pattern found more

commonly among whites.

Specifically, the model identified 53 drugs that may not benefit patients with gene expression patterns found more often among African American patients than whites.

Noting that the sample size of this study was small, the researchers said that additional studies in a larger population are under way to validate their observations. They also stressed that many aspects of lung tumors—not just gene expression—need to be studied to better understand the biological differences among racial groups in a way that could benefit patients.

“We have additional ongoing studies where we are probing even deeper into this disease,” said Ryan. “Our goal is to map it, understand it, and then, as much as we can, leverage it to improve patients’ lung cancer outcomes, especially in minority populations.”

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