

High levels of blood-based protein specific to mesothelioma

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Researchers at NYU School of Medicine have discovered the protein product of a little-known gene may one day prove useful in identifying and monitoring the development of mesothelioma in early stages, when aggressive treatment can have an impact on the progression of disease and patient prognosis.

"This gene produces a protein, fibulin-3, that is present in levels four to five times higher in the plasma of [patients](#) with mesothelioma compared to levels in asbestos-exposed patients or patients with several other conditions that cause tumors in the chest," said lead investigator Harvey I. Pass, MD, the Stephen E. Banner Professor of Thoracic Oncology, vice chair of research for the Department of Cardiothoracic Surgery and division chief of General Thoracic Surgery at NYU Langone Medical Center. "We didn't know anything about this protein's role in mesothelioma before this study, but it may be an extremely useful tool for monitoring patients under treatment and possibly even diagnosing the development of mesothelioma at early stages. This marker is as exciting as any [biomarker](#) in mesothelioma today and warrants further research and validation by the scientific community."

The study appears in the October 11 issue of the [New England Journal of Medicine](#).

Malignant mesothelioma is a rare but aggressive thoracic cancer that can develop several decades after exposure to asbestos. Diagnosis is often delayed until patients begin to show symptoms, including shortness of

breath, cough, chest pain and, in advanced stages, weight loss and night sweats.

Often, patients with mesothelioma seek treatment when the shortness of breath becomes a noticeable problem. At that point, an x-ray typically reveals fluid in the chest, but many doctors fail to inquire about asbestos exposure upon receiving this report. Rather, doctors initially associate fluid in the chest with pneumonia or other [inflammatory conditions](#), further delaying diagnosis, Dr. Pass explained.

Despite advances in chemotherapy, radiation therapy, and surgical management for [malignant mesothelioma](#), the median survival for patients diagnosed with mesothelioma remains 12 months.

"There is a great need for something – some marker or test – that will heighten the alarm that a patient presenting with new onset chest fluid could have mesothelioma," Dr. Pass said. "Our findings indicate that a simple blood test may lead physicians to ask questions about [asbestos exposure](#) and consider whether the medical history and symptoms are compatible with mesothelioma."

Dr. Pass and his team are dedicated to finding diagnostic biomarkers – genes, proteins or other molecules – that are not only different in people with mesothelioma compared with cancer-free individuals who have been exposed to asbestos, but also different when compared to individuals with a variety of conditions that could cause fluid in the chest other than mesothelioma.

Fibulin-3 is a protein that floats around outside cells, coating the cells and free floating in blood plasma and extracellular fluid. For the current study, the research team compared levels of fibulin-3 in two separate cohorts of patients who were exposed to asbestos through their jobs: a group of iron workers and other asbestos-exposed individuals in Detroit,

and a group of insulators in New York. Both cohorts included individuals who had been exposed to asbestos but did not develop mesothelioma, as well as individuals with a confirmed mesothelioma diagnosis. The researchers found that fibulin-3 expression was markedly elevated in the plasma of the patients with mesothelioma compared with the plasma of patients without mesothelioma. But the researchers wondered if maybe the elevated fibulin-3 levels were associated with other conditions, in addition to mesothelioma, that are associated with the development of chest tumors.

To test how specific the over-expression of fibulin-3 is to mesothelioma, they compared levels of the protein in the plasma of patients with mesothelioma to the plasma levels of the protein in patients afflicted by a variety of different types of cancer resulting in tumors in the chest – individuals without mesothelioma, but with conditions that "look like mesothelioma," Dr. Pass said. They found that fibulin-3 also discriminated between non-mesothelioma patients with different kinds of chest-tumor cancers and patients with mesothelioma, confirming high specificity for mesothelioma and not for conditions that "look" like mesothelioma.

To validate their results, the researchers then performed a blinded study with another cohort of patients from Toronto, Canada for whom plasma fibulin-3 was measured, but the researchers had no knowledge of whether the individuals had mesothelioma or not. Based on the fibulin-3 levels, the researchers were able to differentiate the mesotheliomas from the non-mesotheliomas with high accuracy.

In addition, the researchers discovered that post-surgery levels of fibulin-3 were drastically decreased compared to pre-surgery levels in mesothelioma patients in whom the mesothelioma was removed. In selected cases of recurrence, the fibulin-3 level rose, hinting that the marker may be useful for monitoring treatment effects.

"This marker is as good, if not better, in terms of sensitivity and specificity than other known markers for mesothelioma, and its level in mesothelioma chest fluid appears to have prognostic implications," Dr. Pass said. "Moving forward, an international effort to validate these findings is needed, as well as an effort to understand whether this marker can diagnose mesothelioma prior to the development of symptoms in high-risk individuals. This needs to be performed prospectively in a well-defined high-risk for [mesothelioma](#) cohort."

Provided by New York University School of Medicine

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