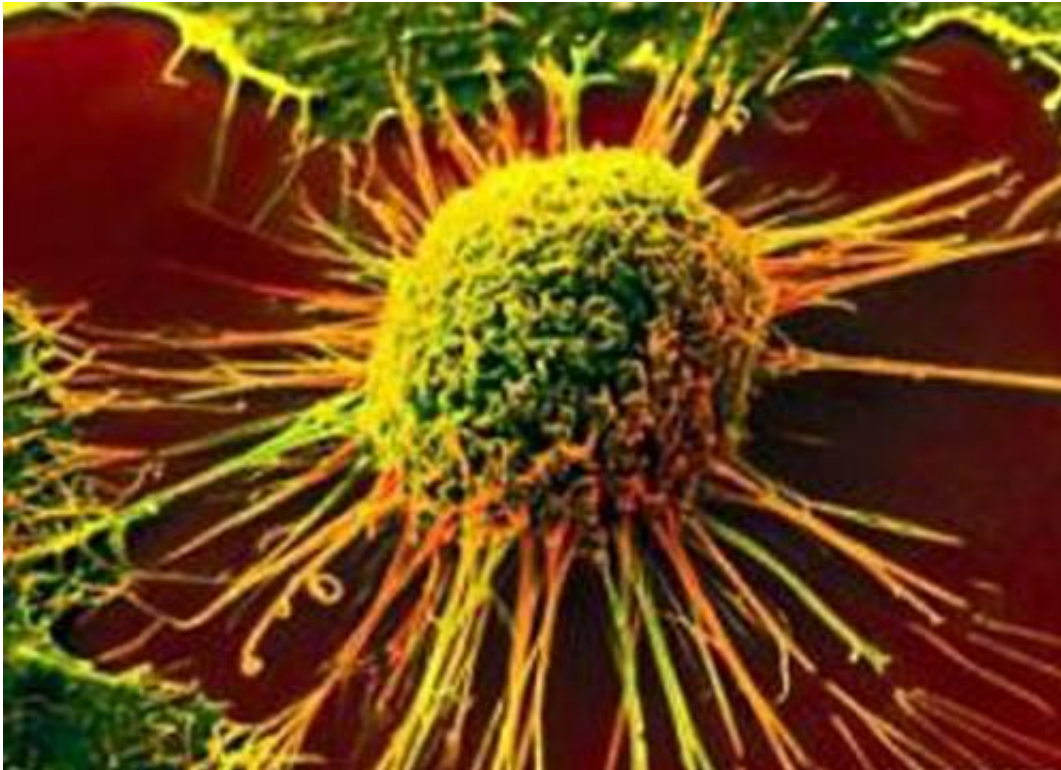


New genetic insights into mesothelioma

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Mesothelioma is a rare but deadly form of cancer: the five-year survival rate for patients diagnosed with the disease is between five and ten percent. Although aggressive surgery can help some patients with early-stage mesothelioma, current treatments for patients with more advanced mesothelioma are not effective.

Physician-researchers from the International Mesothelioma Program at

Brigham and Women's Hospital (BWH) have been caring for patients with mesothelioma for the past 25 years and, in parallel, studying the disease in the laboratory to better understand its biology and develop treatment strategies to target its vulnerabilities. In a comprehensive genomic analysis using more than 200 tumors, investigators from Brigham and Women's Hospital and scientists from Genentech have found previously unknown genetic alterations, including some that may be clinically actionable, as well as others that may improve diagnostics, screening and predictions about outcomes for patients. The team's results are published this week in *Nature Genetics*.

"By studying so many samples, we've been able to describe a spectrum of mutations for this rare disease. A small number of these mutations have been found previously in other cancers, and drugs have been developed to target these mutations," said lead author Raphael Bueno, MD, chief of the Division of Thoracic Surgery at BWH and co-director of the BWH Lung Center. "No one knew before now that these mutations might also be found in mesothelioma tumors. This new work suggests that patients with such mutations may benefit from certain existing drugs."

In collaboration with colleagues at Genentech, researchers analyzed 216 [malignant pleural mesothelioma](#) (MPM) samples, comparing DNA and RNA from normal tissue to cancerous tissue. They uncovered more than 2,500 alterations, and identified 10 significantly mutated genes. They also captured information on the presence of immune cells at the site of the tumor. Some of the [genetic alterations](#) they found suggest that targeted therapies, such as a BCR-ABL-1 inhibitor, could be matched to a patient's tumor. Other alterations and the presence of particular immune targets could serve as better markers to help pathologists accurately diagnose mesothelioma and predict which patients will have poor or better outcomes. The study also analyzed tumors for expression of PD-L1, a cancer immunotherapy target, and found that sarcomatoid

histology, a subtype of the mesothelioma, might be a good candidate for anti-PD-L1 therapy.

Each year, more than 3,200 people are diagnosed with mesothelioma, and an equal number of people die of the disease every year in the U.S. About 80 percent of mesothelioma cases are linked to exposure to asbestos, which continues to be mined and used in many countries, including China, India, Brazil, Russia and others. The International Mesothelioma Program, one of the largest mesothelioma treatment and research program in the world, provides consultation and care for hundreds of newly diagnosed patients each year. Based on their findings, Bueno and colleagues see genotyping their patients in the clinic - a process of looking for genetic differences at precise locations in the genome -as an important next step.

"When you have a cancer that has a 80 to 90 percent mortality rate within five years of diagnosis, and you discover evidence that a small percentage of people may have actionable mutations, that means that you could reduce mortality," said Bueno. "Even for a mutation that happens one to two percent of the time, it could mean the difference between life and death for a patient. We plan to continue this important research through investigator-sponsored trials evaluating the potential use of cancer immunotherapies for the treatment of [mesothelioma](#)."

More information: "Comprehensive genomic analysis of malignant pleural mesothelioma identifies recurrent mutations, gene fusions and splicing alterations," *Nature Genetics* (2016). [DOI: 10.1038/ng.3520](https://doi.org/10.1038/ng.3520)

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