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Study points to potential new lung cancer therapy

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New findings about regulation of PD-L1, a protein that allows cancer to evade the immune system, has shown therapeutic promise for several cancers, including the most common form of lung cancer.

The PD-L1-based therapies inhibit the protein but they don't work for everyone. Now, scientists at The University of Texas MD Anderson Cancer Center have uncovered more detail about how PD-L1 is regulated by the tumor suppressor gene, p53, allowing non-small cell lung cancer to grow.

"We identified a novel mechanism by which p53 regulates PD-L1 and tumor immune evasion through control of miR-34a expression," said James Welsh, M.D., associate professor of Radiation Oncology.

P53 is a tumor suppressor gene that, when mutated, plays a role in many cancers, promoting tumor growth. The microRNA known as miR-34a is a gene commonly found in the lung, and is often missing or under-expressed in tumors.

"Although clinical studies have shown promise for targeting PD-1/PD-L1 signaling in non-small cell lung cancer, little is known about how PD-L1 expression is regulated," said Welsh. "Our study showed that it's regulated by miR-34a that has been activated by p53."

Understanding more about the mechanics behind these crucial signaling pathways may open up new therapy options for patients. Welsh's team,

which included Maria Angelica Cortez, Ph.D., an instructor of Experimental Radiation Oncology, looked further into how these findings can be tied to existing treatments.

"Our results suggest that miR-34a delivery combined with standard therapies, such as radiotherapy, may represent a novel therapeutic approach for lung cancer," said Cortez.

The mouse study found that MRX34, an investigational drug that mimics miR-34's tumor-suppressing abilities, increased the immune system's CD8 cells when combined with radiotherapy. A MRX34 clinical trial is currently underway at MD Anderson.

More information: The data was presented on April 20 at the 2015 American Association for Cancer Research (AACR) Annual Meeting in Philadelphia.

Provided by University of Texas M. D. Anderson Cancer Center