

STUDY POINTS TOWARD POSSIBLE IMMUNOTHERAPY FOR SUBSET OF NON-SMALL CELL LUNG CANCER

A new study led by researchers at the OSUCCC – James bridges preclinical and human data to identify a subset of non-small cell lung cancer (NSCLC) characterized by a specific genetic deficiency that shows poor response to immune checkpoint blockade (ICB) therapy.

Published in the [Journal of Clinical Investigation](#), the study was supported in part by a Pelotonia Idea Grant and resources from the OSUCCC – James Pelotonia Institute for Immuno-Oncology (PIIO). Corresponding authors were **Junran Zhang, MD, PhD**, professor of Radiation Oncology, and **Zihai Li, MD, PhD**, founding director of the PIIO and deputy director for translational research at the OSUCCC – James. **Zhaojun Qiu, PhD**, **No-Joon Song, PhD**, and **Anqi Li, PhD**, were co first-authors.

Immune checkpoint proteins are biological regulators that keep the immune system from rampantly and indiscriminately attacking cells. ICB is a form of immunotherapy that blocks or inhibits these proteins, enhancing the immune system's ability to attack cancer cells.

This study focused on a gene called *PPP2R2A*, which produces protein phosphatase 2 (PP2A). The study authors state that, in over 40% of NSCLC cases, a regulatory subunit of PP2A is underexpressed, or too inactive.

Because low *PPP2R2A* expression correlates with poor prognosis for lung cancer patients, treating *PPP2R2A*-deficient NSCLC “represents an unmet medical need,” they write.

Their study found that *PPP2R2A*+/- cancer cells were very sensitive to ICB of an immune checkpoint protein called PD-L1 in a mouse model of lung cancer, indicating that low expression of *PPP2R2A* and its encoded protein could enhance the immune system's anticancer efficacy.

“These findings underscore the therapeutic potential of ICB in treating *PPP2R2A*-deficient NSCLC while suggesting that *PPP2R2A* deficiency, together with PD-L1 expression, could serve as a biomarker for guiding ICB-based therapies,” they write, noting that this could be beneficial to many patients with NSCLC, which represents about 80% of lung cancer cases.

The scientists point out that current FDA-approved ICB therapies for NSCLC can be used alone or in combination with other therapies; however, “Only a subset of patients respond, highlighting the need for biomarker-guided approaches to improve outcomes.”

“This study identifies a new subset of NSCLC patients who are more likely to respond to immune checkpoint therapy,” Dr. Zhang says. “By showing how low levels of *PPP2R2A* expression in tumor cells influence the immune system's ability to fight cancer, we define a more reliable biomarker to help guide immunotherapy decisions for a subset of NSCLC.”

“This work represents a long-term interest of Dr. Zhang's laboratory to study the interplay between cancer biology and the host immune defense mechanism,” says Dr. Li. “We are pleased to collaborate with Dr. Zhang to uncover the potential use of *PPP2R2A* deficiency, together with PD-L1 expression, to guide immunotherapy for lung cancer patients.”

Besides the aforementioned authors, other scientists from Ohio State who co-authored this study were: **Deepika Singh, PhD**; **Chandra Prasad, PhD**; **David Carbone, MD, PhD**; and **Qi-en-Wang, PhD**. Scientists from the Georgia Cancer Center at Augusta University Medical College and USF Health at the University of South Florida also were co-authors.