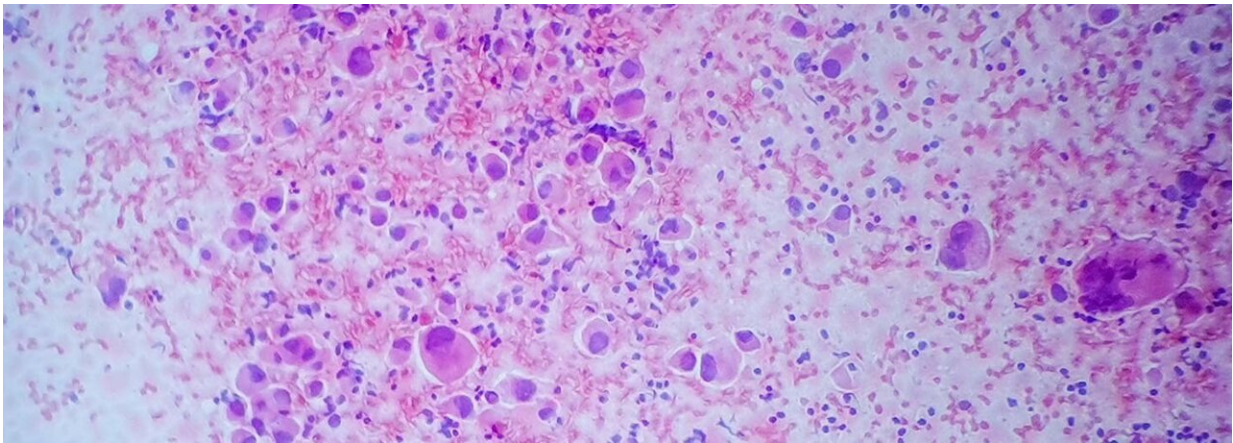


# Specific cancer driving protein plays important role in lung cancer development

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Credit: H. Lee Moffitt Cancer Center & Research Institute

Lung cancer is the second most common cancer in the U.S. and the No. 1 cause of cancer related death. Despite considerable progress in treatment options, most lung cancer patients have extremely poor outcomes with an average five-year survival rate of 21.7%. To help identify new drug targets for this patient population, Moffitt Cancer Center researchers are working to improve their understanding of the molecular mechanisms behind lung cancer. In a new article published in *Nature Communications*, the laboratory of Elsa R. Flores, Ph.D., in collaboration with the Baylor College of Medicine and MD Anderson Cancer Center, shows how the protein  $\Delta Np63$  contributes to disease

development through the regulation of stem cells and crucial elements known as enhancers, which regulate genes that control cell identity.

One of the prevailing theories of cancer development suggests that alterations in signaling pathways in stem cells may lead to disease development. Stem cells are present throughout all tissues and have the capacity to self-renew and the potential to differentiate into multiple types of cells. The protein  $\Delta Np63$  plays an important role in the regulation of stem cells and skin cancers. It is also expressed within the [lung](#); however, little is understood about how it may play a role in lung cancer development.

Given its role in the skin, Moffitt researchers hypothesized that  $\Delta Np63$  may have similar functions in the lung. They performed a series of laboratory experiments using preclinical mouse models of lung adenocarcinoma and squamous cell carcinoma, and human cancer cell lines to define the role of  $\Delta Np63$  in lung cancer development. They created mice that were deficient for  $\Delta Np63$  in the lung and discovered that the mice without  $\Delta Np63$  developed fewer lung tumors and had fewer stem cells compared to control mice. These observations suggest that  $\Delta Np63$  may function as a tumor promoter and regulate the self-renewal and differentiation process of stem [cells](#) in the lung, as it does in the skin.

Next, the Flores lab further investigated the molecular mechanisms controlled by  $\Delta Np63$  and discovered the protein regulates the enhancer region of genes involved in cell differentiation and cell identity, with one of the key genes being BCL9L.

Additional studies found that BCL9L mediates the tumor promoting effects of  $\Delta Np63$  in the lung cancer subtypes adenocarcinoma and squamous cell carcinoma. Importantly, they also discovered that lung adenocarcinoma patients who have high levels of BCL9L have a poorer

prognosis.

"Our findings demonstrate a unifying oncogenic role for  $\Delta$ Np63 that modulates the enhancer landscape in lung [cancer stem cells](#) in both lung adenocarcinoma and squamous cell [lung cancer](#). We will use these findings to develop novel therapeutic approaches to inhibit development of these highly deadly tumor types," said Flores, associate center director of Basic Science and senior member of the Department of Molecular Oncology at Moffitt.

**More information:** Marco Napoli et al,  $\Delta$ Np63 regulates a common landscape of enhancer associated genes in non-small cell lung cancer, *Nature Communications* (2022). [DOI: 10.1038/s41467-022-28202-1](https://doi.org/10.1038/s41467-022-28202-1)

Provided by H. Lee Moffitt Cancer Center & Research Institute

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