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Protein complex linked to cancer growth may also help fight tumors, researchers say

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Researchers at Moffitt Cancer Center and Tianjin Medical University Cancer Institute and Hospital in China have discovered a gene expression signature that may lead to new immune therapies for lung cancer patients. They found that NF-κB, a protein complex known to promote tumor growth, may also have the ability to boost the immune system to eliminate cancerous cells before they harm, as well as promote antitumor responses.

The study appeared in the June 3 issue of *The Journal of Clinical Investigation*.

NF-?B is a protein complex that controls gene expression. The regulation of NF-?B also plays an important role in regulating the body's immune response to infection. Incorrect regulation of NF-kB has been linked to cancer, inflammatory and autoimmune diseases, septic shock, viral infection, and improper immune development.

"New insight into how tumor pathways regulate the anti-tumor immune response may help us to devise new ways for improving immune therapy ," said study lead author Amer Beg, Ph.D., senior member of Moffitt's Immunology Program. "Studies are now underway to start a clinical trial to determine whether the novel gene expression signature described in this work may help initiate new and better immunotherapy treatments."

According to Beg, NF-?B proteins regulate key genes involved in immune response, inflammation, cell death and cell growth. Work in his

lab is aimed at a better understanding of how NF-?B regulates immune response and how the consequences of impaired regulation of responses are related to disease.

The researchers analyzed the role of NF-?B in lung cancer cells that were used to develop the NF-?B gene signature. Key studies in mice showed that NF-?B can mediate immune rejection of tumors. The studies were then extended to human tumor specimens. "In this study we found that NF-?B activity is strongly associated with immune system T-cell infiltration in lung cancer," explained study co-author Dung-Tsa Chen, Ph.D., member of the Biostatistics Department at Moffitt. "Multiple genes, capable of enhancing T-cell responses, were found in the NF-?B signature. This means that NF-?B, thought of as a tumor promoter, also helps facilitate an immune response."

Their finding—that the presence of high levels of NF-?B in lung cancer tumors can act as a suppressor—provides new insight into how tumor pathways regulate the anti-tumor response.

"T-cell presence in tumors can be associated with immune surveillance and improved patient survival," explained Beg. "The focus of immune therapy, boosting T cell-induced responses against solid tumors, has shown considerable promise. However, tolerance-inducing mechanisms and the presence of suppressive cell types in the tumor microenvironment can dampen the response to immunotherapy. Our findings provide new insights into beneficial pathways that also operate in tumors and can regulate anti-tumor responses."

Provided by H. Lee Moffitt Cancer Center & Research Institute

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