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# Moffitt Cancer Center researchers design small molecule to disrupt cancer-causing protein

STAT3 protein's ability to cause malignancy is suppressed when neutralized by S31-1757

Peer-Reviewed Publication

H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE

Researchers at Moffitt Cancer Center and colleagues at the University of South Florida have developed a small molecule that inhibits STAT3, a protein that causes cancer. This development could impact the treatment of several tumor types, including breast, lung, prostate and others that depend on STAT3 for survival.

The study appeared in the Jan. 15 online issue of *Cancer Research*, a publication of the American Association for Cancer Research.

"STAT3 has been associated with poor prognosis and resistance to chemotherapy in patients with cancer," explained Said M. Sebti, Ph.D., chair of the Drug Discovery Department at Moffitt. "Two STAT3 molecules need to bind to each other, a process called dimerization, to cause malignancy. We developed a small molecule called S31-1757 to prevent dimerization by disrupting STAT3-STAT3 binding. Once disrupted, STAT3's ability to help cancer cells survive, grow and invade is neutralized."

"Activated STAT3 contributes to cancer at several levels," said study co-author Nicholas J. Lawrence, Ph.D., senior member of Moffitt's Drug Discovery Department. "It triggers the uncontrolled proliferation, invasion and spread of cancer cells. That makes STAT3 an attractive target for drug discovery and therapy."

STAT3 was first found to be involved in malignant transformation in 1995, but researchers have been unable to develop an inhibitor for the protein. In part, the challenge stemmed from the fact that STAT3-STAT3 binding is a protein-protein interaction involving a large surface area, difficult to target with drug-like small molecules.

The researchers, who had been working on finding an inhibitor for STAT3-STAT3 dimerization for some time, recently overcame that challenge and demonstrated in laboratory studies that S31-1757 was effective in neutralizing STAT3's activity.

"We used several approaches to demonstrate that S31-1757 is able to inhibit malignant transformation by its ability to inhibit the STAT3 function," Sebti said. "These included targeting the ability of STAT3 to bind itself."

Their findings will be presented at the annual AACR meeting in April in Washington, D.C.

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This study was partially supported by a National Cancer Institute grant (R01CA140681).

**About Moffitt Cancer Center**

Located in Tampa, Moffitt is one of only 41 National Cancer Institute-designated Comprehensive Cancer Centers, a distinction that recognizes Moffitt's excellence in research, its contributions to clinical trials, prevention and cancer control. Since 1999, Moffitt has been listed in *U.S. News & World Report* as one of "America's Best Hospitals" for cancer. With more than 4,200 employees, Moffitt has an economic impact on the state of nearly \$2 billion. For more information, visit [MOFFITT.org](http://MOFFITT.org), and follow the Moffitt momentum on Facebook, twitter and YouTube.

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