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TGen presents lung cancer studies at Amsterdam conference

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The Translational Genomics Research Institute (TGen) is presenting two key studies, including one today, at the 14th World Conference on Lung Cancer, July 3-7 in Amsterdam.

One study, presented July 4, involved a gene called GLI1, which may limit the effectiveness of the most common combination chemotherapy given to patients with small cell lung cancer (SCLC).

Another study, presented today, July 7, suggests that combination drug therapy may be needed to combat non-small cell lung cancer (NSCLC) — the more common type of lung cancer — when patients have elevated levels of a protein called JAK2.

Both studies will be presented at the Amsterdam conference, which is sponsored by the International Association for the Study of Lung Cancer (IASLC). The association hosts an international lung cancer meeting every two years. Both studies also will be published in a special supplement of the *Journal of Thoracic Oncology.*

GLI1 may compromise chemotherapy

In the study involving GLI1, laboratory tests of six SCLC cell lines showed that GLI1 can play an important role in resistance to the drugs cisplatin and etoposide, which given together are the standard first-line chemotherapy for SCLC.

"Resistance to chemotherapeutic drugs is particularly crippling in SCLC," said Dr. Glen Weiss, Co-Unit Head of TGen's Lung Cancer Research Laboratory, who led the research in both studies presented at the conference. "We are optimistic that this GLI1 study will lead to more detailed examinations that will provide a better way of treating patients."

Next steps include using RNA interference tests to validate the role of GLI1 and several related genes along the Hedgehog Signaling Pathway — a series of chemical reactions within a cell. The Hedgehog pathway contains genes that lead to GLI1, a known tumor-promoting gene. Weiss' team also plans to conduct tests on actual tumors from SCLC patients.

VARI joins TGen in JAK2 study

The Van Andel Research Institute (VARI), TGen's affiliate in Grand Rapids, Mich., joined TGen in conducting the JAK2 study.

The JAK2 protein can activate the gene called STAT3, part of a family of genes that provide instructions for making proteins that are part of the essential chemical signaling pathways that control growth and development in cells. STAT3 has been found to be overactive in cases of several types of cancer, including breast, prostate, pancreas, leukemia and lymphoma.

In laboratory tests involving seven NSCLC cell lines, the TGen-VARI study found that STAT3 was activated in some cell lines by JAK2, independent of key oncogenic, or cancer-causing mutations.

"JAK2-STAT3 signaling plays crucial roles in tumor-cell behavior that may not be effectively inhibited by drugs that selectively target these mutations," Dr. Weiss said. "This suggests that there may be a potential role for combination therapy, so you have a better chance of knocking out a NSCLC tumor, or keeping it at bay."

Dr. Jeff MacKeigan, Head of VARI's Laboratory of Systems Biology, said this yearlong study, funded by a TGen-VARI integration grant, should benefit future lung cancer research because of the study's clinically annotated tissue microarray.

"Our human tumor samples may be used for meaningful exploratory research on other key signaling pathways in NSCLC," MacKeigan said.

Provided by The Translational Genomics Research Institute