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BME Researchers Identify Proteins That May Provide Lung Cancer Drug Targets

By Mark Dwortzan

Researchers from the Biomedical Engineering Department and the Boston University School of Medicine have identified a number of proteins which, when activated, allow researchers to distinguish between lung cancer and normal lung tissue cells with almost 97 percent accuracy. In addition, they have developed a new computational strategy to analyze this data and identify key biological pathways, or molecular circuits, that are active in cancer and dormant in normal cells.

Professor Simon Kasif (BME) co-directs the Center for Advanced Genomic Technology

The study, which appeared in the Nov. 25 issue of PLoS ONE, may ultimately lead to the development of drugs specifically aimed to inhibit these proteins. The senior co-authors were Professor Simon Kasif (BME), who co-directs the Center for Advanced Genomic Technology, and Assistant Professor Martin Steffen (BME), who directs the Proteomics Core Facility at BUSM.

According to Kasif and Steffen, there are many features that distinguish cancer cells from normal cells. For instance, they look different histologically, they proliferate and divide at different rates and they're less communicative with their neighbor cells. Cancer cells also do not "commit suicide" (programmed cell death) as normal cells do when their genomes become unstable.

Much of the cellular machinery behind these biological processes is run by a command, control and communication system called signal transduction, which itself is primarily controlled by a process called phosphorylation. When a protein is phosphorylated, it either becomes active or repressed, depending on its special function.

"Therefore, identifying the phosphorylation status of proteins in cancer cells versus normal cells provides us with a unique ability to understand and perhaps intervene with the command and control center of cancer cells," said Kasif. "Drugs are most effective on cancers when they attack the proteins that are activated."

While cancers are highly heterogeneous in their make-up, the BU researchers believe that a drug that would target this collection of proteins would be an effective treatment for most lung cancers.

"This is the first statistically validated phosphopeptide signature to diagnose any disease, much less cancer or lung cancer," noted Steffen.

Other key contributors to the study include Chang-Jiun Wu, a postdoctoral associate at the BU Center for Advanced Genomic Technology, and Tianxi Cai, associate professor of biostatistics at the Harvard School of Public Health.

Funded by the National Human Genome Research Institute and the American Lung Association, this research was performed in collaboration with Cell Signaling Technology, employing their Phosphoscan "test kit." A follow-up study is currently underway at BU to identify which cancers respond or do not respond to existing cancer drugs based on the results of this test.

This article is based on a press release issued by Boston University School of Medicine.