Discovery of a new gene critical in the development of lung and pancreatic cancers

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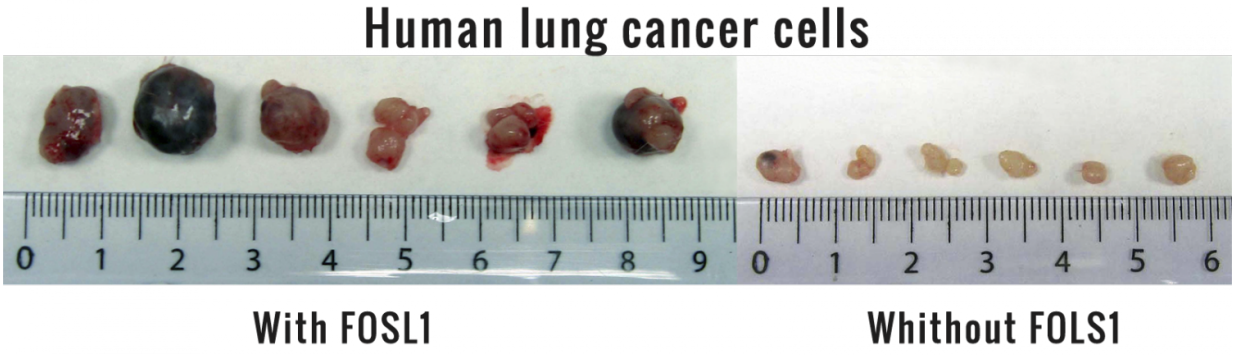

Human lung cancer cells WITH & WITHOUT FOSL1. Credit: CIMA researchers

Researchers at the Center for Applied Medical Research (CIMA) of the University of Navarra have identified a critical gene, FOSL1, in the development of lung and pancreatic cancer. The results of the work, a collaboration with researchers in the U.S., U.K. Germany and Denmark, have been published in the latest issue of the scientific journal *Nature Communications*.

Approximately 25 percent of patients with lung cancer and 90 percent of those with pancreatic cancer show mutations in the KRAS gene, the most commonly mutated oncogene in cancer, and, at present, there are no effective therapies for these patients.

Using an innovative bioinformatic application that analyzes samples from patients with different types of cancer, the CIMA researchers have identified a core of eight genes regulated by the KRAS oncogene. From these genes, the researchers focused on FOSL1, because they found that in lung and pancreatic cancer, "patients with high-level mutations of the gene had the worst survival prognosis," according to Dr. Silve Vicent, a researcher on the CIMA Solid Tumors and Biomarkers Program and head of this study. "What is most important is that inhibition of FOSL1 brings about a great reduction in the size of the tumors in the lungs and pancreas. Thus, the results present this gene as a new molecular target to which new drugs should be directed," the researcher added.

The work, which began three years ago, used a total of 2000 samples from patients with lung cancer, pancreatic cancer, cholangiocarcinoma, colorectal cancer and multiple myeloma, together with cell lines from human and mouse tumors and genetically modified models.

A combined strategy of drugs and clinical trials

The CIMA researchers have also shown that FOSL1 affects another gene, AURKA, which, to date, had been thought to be regulated independently of the KRAS oncogene; clinical trials with a drug inhibitor are currently ongoing.

For the first time, the CIMA researchers have tested the combination of drugs against AURKA with drugs against another important gene for tumors with the KRAS mutation, MEK, and have observed greater elimination of tumor cells. "This combined strategy promotes reduction of the size of tumors with mutated KRAS," Dr. Vicent stressed. "The fact that both drugs are already being used clinically is heartening, as the benefits of this new treatment may reach patients within a relatively short time."

"The next step will be the identification of biomarkers which respond to the combined treatment we have described. This step is critical, as not all patients with mutated KRAS are identical; therefore, the type of molecular changes that characterize patients who may finally benefit from this treatment must be better defined," he said.

More information: Adrian Vallejo et al, An integrative approach unveils FOSL1 as an oncogene vulnerability in KRAS-driven lung and pancreatic cancer, *Nature Communications* (2017). DOI: 10.1038/ncomms14294

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