Protein boosts lung cancer in smokers, non-smokers; Potential anti-oncogenic target

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Lung cancer is strongly correlated with smoking, and most lung cancer patients are current or former smokers. But it is not rare in nonsmokers. Now, a team of researchers from the H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, shows that a protein called ID1 is a key player in lung cancer in both smokers and nonsmokers. The research is published in the July issue of the journal *Molecular and Cellular Biology*.

The investigators were aware that while nicotine does not cause cancer, earlier studies, including their own, had suggested that it might promote growth and metastasis of cancers that had already formed. They exposed cultured cells to nicotine, after which these cells expressed increased levels of a protein called ID1.

"That protein was the first link between lung cancer in smokers and nonsmokers. In non-smokers, who are not exposed to copious nicotine, its expression is induced by a growth promoting protein called epidermal growth factor, which is known to be involved in cancers in non-smokers," says corresponding author Srikumar Chellappan.

The researchers then connected all this to another protein, Src, which was known to be altered in cancers, and in this altered form to promote tumor growth. "Our studies showed that inhibiting Src prevented the induction of ID1," says Chellappan. "Further, removing ID1 protein from cancer cells prevented their growth, as well as their ability to migrate or invade, which are the early steps of metastasis." They

removed ID1 from the cancer cells through the use of small-interfering RNAs, which can be designed to block expression of particular proteins.

"Our studies thus show that ID1 might mediate the tumor promoting properties of nicotine, and also facilitate the growth of tumors in response to epidermal growth factor," says Chellappan. "These observations raise the possibility that targeting ID1 might be a viable strategy for combating lung cancer."

More information: S. Pillai, et al., 2011. ID1 facilitates the growth and metastasis of non-small cell lung cancer in response to nicotinic acetylcholine receptor and epidermal growth factor receptor signaling. *Mol. Cell. Bio.* 31:3052-3067

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