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Team discovers protein pathway involved in lung cancer metastasis

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Smoking is the leading cause of lung cancer, and it is estimated that more than 159,000 people in the United States died from the disease last year. Most of these deaths were because the cancer had spread to other organ sites. Following their recent discovery of a protein pathway, Moffitt Cancer Center researchers are one step closer to understanding how lung cancer cells metastasize.

Nicotine from cigarettes is a highly addictive drug that can stimulate cell growth and block cell death - two hallmark characteristics of cancer. Recent evidence also shows that nicotine can cause cancer cells to change their shape, increase their motility and become metastatic.

Scientists from Moffitt reported in the Jan. 19 online edition of *Cancer Research* that nicotine induces the metastatic spread of lung cancer cells by stimulating a protein called beta-arrestin-1. Activation of beta-arrestin-1 causes lung cancer cells to produce proteins associated with increased motility and invasion. These proteins cause the cells to change their shape and become more motile, allowing them to move to different sites.

The researchers wanted to further investigate the mechanisms of how beta-arrestin-1 causes cell invasion. They discovered that beta-arrestin-1 associates with another protein called E2F1 in the nucleus to promote the development of metastasis. E2F1 is known to contribute to the development of cancer by promoting cancer cell proliferation; however, this is the first time that E2F1 has been shown to contribute to metastasis

of lung cancer.

The scientists confirmed these observations in mice and in human lung cancer samples. They found that human lung cancer samples with high levels of beta-arrestin-1 also had high levels of proteins associated with cell adhesion and motility. Additionally, blocking beta-arrestin-1 in lung cancer cells prevented their growth and metastasis in mice. These observations suggest that blocking beta-arrestin-1 may be an effective therapeutic strategy for metastatic disease.

According to Srikumar Chellappan, Ph.D., chair of the Department of Tumor Biology at Moffitt, "we expect that this study will lead to new therapeutic strategies to combat cancer metastasis. For example, inhibiting the binding of beta-arrestin-1 to E2F1 would be a potential avenue to prevent metastasis. Identification and development of novel drugs that can target beta-arrestin-1 can be an important step in this direction."

More information: *Cancer Research*, cancerres.aacrjournals.org/con… CAN-14-0681.full.pdf

Provided by H. Lee Moffitt Cancer Center & Research Institute