

Scientists discover link between nicotine and breast cancer metastasis

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Breast cancer is the second most common cancer among women in the United States, and cigarette smoking is associated with a higher incidence of breast cancer spread, or metastasis, lowering the survival

rate by 33% at diagnosis.

While cigarette smoking's link to [cancer](#) is well-known, the role of nicotine, a non-carcinogenic chemical found in tobacco, in breast-to-lung metastasis is an area where more research is needed.

Now, scientists at Wake Forest School of Medicine have found that nicotine promotes the spread of [breast cancer](#) cells into the lungs.

The study is published in the January 20 online edition of *Nature Communications*.

"Our data shows that nicotine exposure creates an environment in the lungs that is ripe for metastatic growth," said Kounosuke Watabe, Ph.D., lead author of the study and professor of cancer biology at Wake Forest School of Medicine, part of Wake Forest Baptist Health.

This environment is called a pre-metastatic niche, which attracts pro-tumor neutrophils, a type of immune cells. The pre-metastatic niche releases a protein called STAT3-activated lipocalin 2 (LCN2) from the neutrophils to induce metastatic growth.

For the study, Watabe's team first studied 1,077 [breast cancer patients](#) and found that current smokers or former smokers have a higher incidence of lung metastasis compared to patients who never smoked.

Then, using a mouse model of breast cancer metastasis, the researchers discovered that persistent exposure to nicotine generates an inflammatory microenvironment in the lungs characterized by an influx of activated neutrophils to create a pre-metastatic niche.

Even after quitting nicotine for 30 days, the incidence of distant metastasis was not reduced, suggesting an ongoing risk for breast cancer

patients who are former smokers.

Watabe and colleagues also looked for a drug that might block this accumulation of neutrophils and identified salidroside, a natural compound found in the plant *Rhodiola rosea*. This compound, which has anti-inflammatory, anti-cancer and anti-viral properties, significantly decreased the number of pro-tumor neutrophils and subsequently reduced the incidence of lung metastases in mice.

"Based on these findings, breast cancer patients should opt for smoking cessation programs that do not use nicotine replacement products," Watabe said. "Furthermore, our findings show that salidroside may be a promising therapeutic drug to help prevent smoking-induced [breast cancer lung metastasis](#), although more research is needed."

More information: Abhishek Tyagi et al, Nicotine promotes breast cancer metastasis by stimulating N2 neutrophils and generating pre-metastatic niche in lung, *Nature Communications* (2021). [DOI: 10.1038/s41467-020-20733-9](https://doi.org/10.1038/s41467-020-20733-9)

Provided by Wake Forest University Baptist Medical Center

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