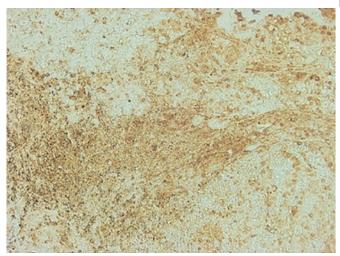


## Continued nicotine use promotes brain tumors in lung cancer patients, study suggests

4 June 2020



Wu et al. demonstrate that nicotine promotes brain metastasis by stimulating the formation of immune cells called M2 microglia. Large numbers of M2 microglia (brown) can be observed in a metastatic brain tumor from a lung cancer patient who continued to smoke. Credit: Wu et al., 2020

Researchers at Wake Forest School of Medicine have discovered that nicotine promotes the spread of lung cancer cells into the brain, where they can form deadly metastatic tumors. The study, which will be published June 4 in the Journal of Experimental Medicine (JEM), suggests that nicotine replacement therapies may not be suitable. The tumors in patients' brains contained large strategies for lung cancer patients attempting to guit smoking. In addition, the researchers show that the naturally occurring drug parthenolide blocks nicotine-induced brain metastasis in mice, suggesting a potential therapeutic option in humans.

Up to 40% of <u>lung cancer patients</u> develop brain metastasis, and the average survival time for these Watabe and colleagues then looked for drugs that

patients is less than six months. "There is an urgent need to understand the mechanisms that drive brain metastasis so that more effective therapies can be developed," says Dr. Kounosuke Watabe, a professor of cancer biology at Wake Forest School of Medicine in Winston-Salem, NC.

Cigarette smoking is a major risk factor for lung cancer, but how it affects the development of brain metastasis is unclear. Watabe and colleagues studied 281 patients with advanced lung cancer and found that brain metastasis was much more common in patients who continued to smoke compared with patients who had never smoked or had successfully quit.

Watabe and colleagues found that, in mice, the spread of lung cancer cells to the brain is driven by nicotine, a major component of tobacco smoke that isn't, in and of itself, carcinogenic. "Many cancer patients find it difficult to guit smoking even after their diagnosis due to nicotine addiction," Watabe says. "E-cigarette, nicotine patch, and nicotine gum are commonly used as nicotine replacement therapies to help these patients cease smoking. However, our results clearly show that nicotine has profound and long-term effects on brain metastasis progression, suggesting that cancer patients should be cautious in their use of nicotine for smoking cessation."

numbers of M2 microglia, a type of immune cell that secretes several molecules capable of enhancing tumor growth. The researchers found that nicotine stimulates the formation of M2 microglia in mice. Removing microglia from mouse brains prevented nicotine from inducing brain metastasis and enhanced the survival of mice with lung cancer.

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might reverse the effects of nicotine and identified parthenolide, a compound present at high levels in the medicinal herb Feverfew (*Tanacetum parthenium*), which has been used for centuries to treat headaches and inflammation. Treating mice with parthenolide prevented nicotine from stimulating the formation of M2 microglia and inhibited the spread of lung cancer cells to the <a href="mailto:brain">brain</a>, thereby improving the animals' survival.

"We therefore think that parthenolide could be useful for the prevention and treatment of <u>brain</u> <u>metastasis</u>, particularly for patients with past and current smoking history," Watabe says.

**More information:** Wu et al., 2020. *J. Exp. Med.* rupress.org/jem/article-lookup ... 10.1084/jem.20191131

Provided by Rockefeller University Press APA citation: Continued nicotine use promotes brain tumors in lung cancer patients, study suggests (2020, June 4) retrieved 25 November 2022 from <a href="https://medicalxpress.com/news/2020-06-nicotine-brain-tumors-lung-cancer.html">https://medicalxpress.com/news/2020-06-nicotine-brain-tumors-lung-cancer.html</a>

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