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Okayama University research: A berry vine found in Asia proves useful in combating lung cancer.

(Okayama, 11 August) **In a study reported in *Food and Chemical Toxicology*, researchers from Okayama University describe the effects of Yamabudo, a garden vine, in mitigating lung cancer in the lab.**

Lung cancer is known to be the most fatal form of cancer. Chemicals like 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) found in tobacco are usually the main culprits behind smoking-related lung cancer causing cancer biologists to actively explore targeted treatments. Now, a research group led by Associate Professor ARIMOTO-KOBAYASHI Sakae at Okayama University has reported the potential of a berry-producing vine, Vitis coignetiae Pulliat (colloquially known as Yamabudo in Japan), against lung cancer in mice.

The team has previously shown that juice extracted from the Yamabudo fruit and 2,6-dimethoxy-1,4-benzoquinone (DBQ), a chemical found within it, have protective effects against skin cancer. Thus, in this study the potential of both these chemicals was investigated. Mice were first treated with NNK to establish lung cancer models and tumors that subsequently developed within their lungs were assessed. After 30 weeks, mice given Yamabudo juice or DBQ showed greatly reduced tumor size. To understand the mechanism of Yamabudo further, human lung cancer cells were employed. NNK induces cancer by facilitating a chemical change in the DNA structure, known as DNA methylation. To mimic this process, cells were exposed to MNNG (a chemical that artificially induces DNA methylation) and the effects of Yamabudo were studied. Indeed, cells that were treated with Yamabudo juice or DBQ showed lower levels of DNA methylation.

The DNA methylation induced by NNK also plays a role in mutating the DNA, making all exposed cells susceptible to cancer. The methylated forms of DNA tend to form large complexes which can undergo damage more easily. Therefore, NNK-induced mutations were analyzed next to see if Yamabudo also plays a protective role in this regard. The number of NNK-induced mutations was, in fact, found to be considerably reduced by Yamabudo juice or DBQ. Yamabudo thus mitigated lung cancer by repairing the DNA damage caused by toxins. Lastly, the team also assessed biological pathways which typically help cancer cells proliferate. While all such pathways were active in the lung cancer cells, treatment with Yamabudo showed a dampening of these cancer-facilitating signals.

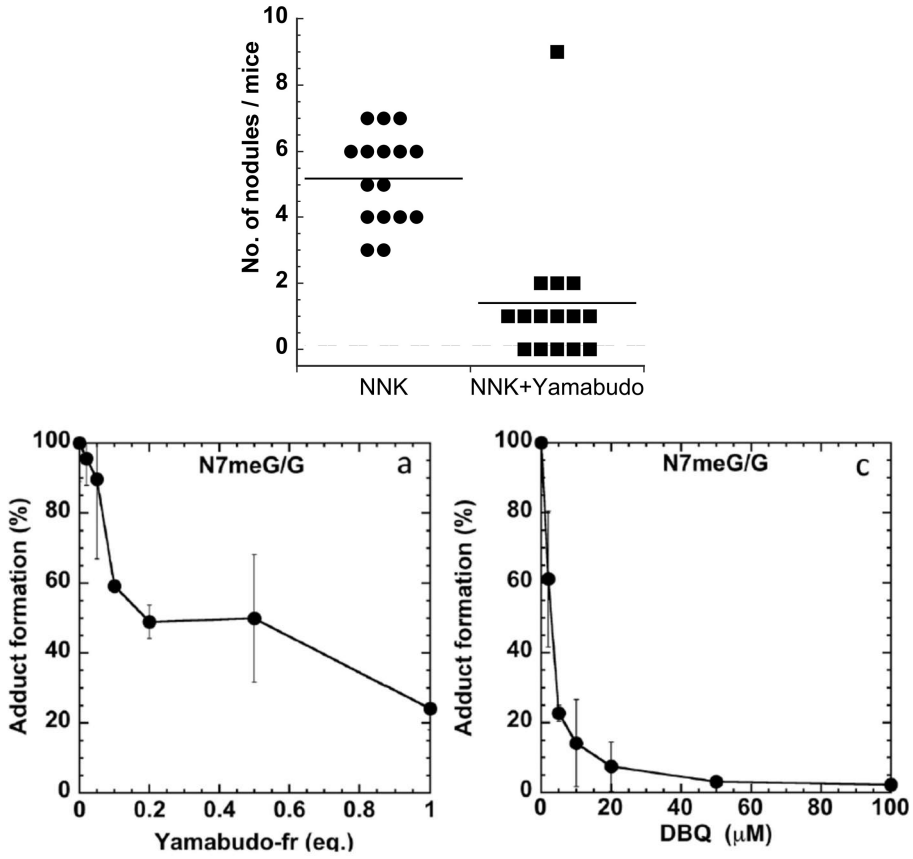
“Stimulation of repair of alkyl DNA adducts and suppressed growth signaling pathways are potential anti-tumorigenic targets of Yamabudo juice and DBQ in NNK-induced lung tumorigenesis,” conclude the researchers. Given the broad range of tumor-suppressing

properties Yamabudo displays, it is one herbal medicine that should be explored further in lung cancer research.

Background

Yamabudo: *Vitis coignetiae* Pulliat, also known as crimson glory vine or "Yamabudo" in Japan, is a berry-producing vine that grows primarily in East Asia. The juice extracted from Yamabudo berries comprises several chemical compounds that have medicinal properties. While its protective properties against skin cancer have briefly been shown before, this is the first study that explores the potential of Yamabudo in lung cancer.

DNA methylation: DNA methylation is a natural chemical process intended to regulate proper functioning of our genes. A chemical group known as the "methyl" group is usually bound onto specific regions of the DNA as a mechanism to prevent genes from being turned on when not in use. However, certain toxins and other external factors can also induce DNA methylation which sometimes prevents important genes (such as those that suppress cancer) from being active. Unfortunately, the methylated forms of DNA are passed on when cells replicate. DNA methylation thereby also abets the spread of cancer. Controlling DNA methylation is an important strategy in keeping certain cancers in check.



Caption

***Top*.** Incidence of lung nodules of the left lung lobe in NNK-treated mice without any drug (left) and with Yamabudo juice (right)

***Bottom*.** Effects of increasing doses of yamabudo juice and DBQ on the complex formation (adducts) of methylated DNA in lung cancer cells.

Reference

Sakae Arimoto-Kobayashi, Kensuke Sasaki, Ryoko Hida, Naoko Miyake, Nana Fujii, Yusuke Saiki, Kyohei Daimaru, Hirono Nakashima, Toshio Kubo, Katsuyuki Kiura. Chemopreventive effects and anti-tumorigenic mechanisms of 2,6-dimethoxy-1,4-benzoquinone, a constituent of Vitis coignetiae Pulliat (crimson glory vine, known as yamabudo in Japan), toward 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumorigenesis in A/J mice. *Food and Chemical Toxicology*, Volume 154, August 2021, 112319.
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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

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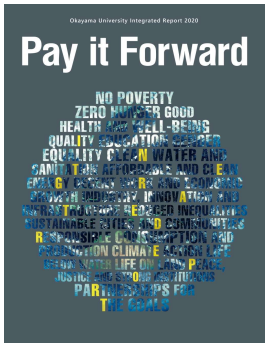

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