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Okayama University research: Disrupting blood supply to tumors as a new strategy to treat oral cancer

(Okayama, 17 March) **Researchers at Okayama University have recently published a study in *Cells* in which they reduced the size of oral cancer tumors by damaging the blood vessels surrounding the tumor cells.**

Cancer cells have ingenious mechanisms of survival within the body. One strategy they adopt is developing a network of blood vessels around themselves as a source of blood supply. Scientists have long been investigating ways to prevent this blood flow to cancer cells. CXCR4 is a protein known to be closely involved with tumor growth. However, its exact role in tumor progression is unclear. A research team led by Assistant Professor KAWAI Hotaka and YOSHIDA Saori(graduate student, D.D.S.), Assistant Professor EGUCHI Takanori at Okayama University has now shown that CXCR4 is the main culprit maintaining the arrangement of tumor blood vessels.

Firstly they found, immunohistochemistry on human clinical specimens revealed that tumor vessels expressed CXCR4 in human oral cancer specimens. The next question to arise was whether the CXCR4-rich blood vessels were promoting tumor growth. In order to investigate this further, the oral cancer cells were transplanted into mice. Once the tumor growed in mice body, they were given AMD3100—a drug that antagonises CXCR4. When the tumors were subsequently observed under a microscope, several areas were found to necrotic. A characteristic pattern of necrosis was observed in which the tumor tissue that were at a distance away from the blood vessel was necrotic, leaving the tumor tissue close to the periphery of the blood vessel.. This randomized pattern of tumor cell death was termed ‘tumor angiogenic inhibition triggered necrosis’ (TAITN) by the researchers. The wide area of tumor tissue also showed a severe lack of oxygen which was accompanied by an impairment of angiogenesis. CXCR4 inhibition thus seemed to induce tumor necrosis by damaging the blood vessels and preventing the cells of a healthy oxygen supply.

This study is the first to show the role of CXCR4 in promoting tumor growth by supplying cancer cells with a healthy, organized network of blood vessels. Strategies that can disrupt this network can be explored further as anti-cancer therapies. “CXCR4 plays a crucial role in tumor angiogenesis required for OSCC progression, whereas TAITN induced by CXCR4 antagonism could be an effective anti-angiogenic therapeutic strategy in OSCC treatment”, concludes the team.

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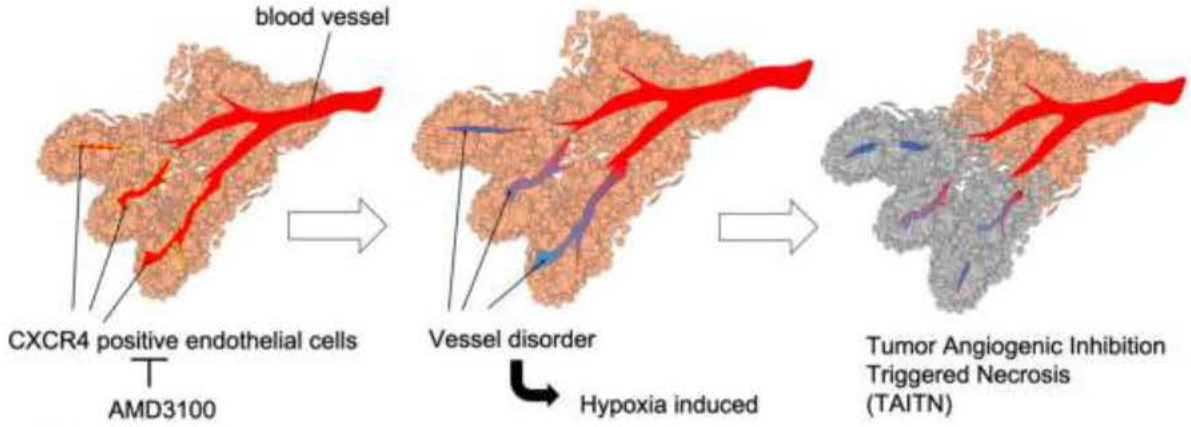
Background

CXCR4: CXCR4 is a protein vital in maintaining and growing the cells that produce blood within our body. In fetuses, CXCR4 is also responsible for the formation of certain blood vessels. Incidentally, CXCR4 is also present in various forms of cancers such as breast, liver, and oral cancer. Often, tumors which show the presence of CXCR4 tend to grow faster that those without. Given its link with blood vessels and cancer progression, the research team from Okayama University sought out to investigate whether CXCR4 directly promotes cancer growth by supplying tumors with blood.



Caption

CXCR4 antagonism induced tumor necrosis through vessel disorder. Left, a CXCR4 antagonist AMD3100 inhibited CXCR4-positive endothelial cells of tumor vessels. Middle, inhibition of CXCR4-positive endothelial cells induced vessel disorder and caused hypoxia in surrounding tumor cells. Right, necrosis was caused in the surrounding tumor cells through vessel disorder. Taken together, we propose a novel mechanistic concept of "Tumor Angiogenic Inhibition Triggered Necrosis (TAITN)".

Reference

Saori Yoshida, Hotaka Kawai*, Takanori Eguchi*, Shintaro Sukegawa, May Wathone Oo, Chang Anqi, Kiyofumi Takabatake, Keisuke Nakano, Kuniaki Okamoto, Hitoshi Nagatsuka. Tumor Angiogenic Inhibition Triggered Necrosis (TAITN) in Oral Cancer. *Cell*, 2019, 8(7), 761.
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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

Japan（日本）

Hirofumi Makino, M.D., Ph.D.
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