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Okayama University research: A protein found on the surface of cells plays an integral role in tumor growth and sustenance

(Okayama, 27 March) **Researchers at Okayama University describe in the journal *Scientific Reports* the role of an extracellular protein, versican, in regulating tumor growth and providing a newly formed network of blood vessels to further nourish the tumor.**

Angiogenesis is the creation of new blood vessels from the branching of pre-existing ones. This phenomenon is especially important in the context of cancer, because it supplies the tumors with additional oxygen and nutrients to keep them growing. An effective strategy in treating cancer would therefore be to prevent angiogenesis. However, factors in the tumor microenvironment that may boost angiogenesis are still poorly understood. The tumor microenvironment, is a mix of host tissue (stroma) and tumor cells.

A recent study in *Scientific Reports* by Professor Satoshi Hirohata *et al*. has found a link between angiogenesis and the tumor microenvironment, in the form of an extracellular matrix protein called versican. Versican is involved in several vascular processes, but its role regarding tumor angiogenesis isn't well understood. Professor Hirohata and his team members at Okayama University looked at different cancer cells lines, and found that although initially they all had varying amounts of versican, tumors derived from all the cell lines had amplified quantities of the protein. Using a technique called western blotting, they showed that a melanoma producing cell line B16F10, had very low levels of versican which increased drastically after tumor initiation, while a lung cancer cell line (LLC) had high levels of versican before tumor induction, which were even more pronounced after. Interestingly, it was found that all the tumors had versican which was at least partly derived from the stromal microenvironment.

After establishing the origins of tumor versican, the researchers noticed that versican was located in the vicinity of blood vessels, within tumors. It was also stationed specifically with macrophages (safe-guarding cells in the blood), suggesting that stromal macrophages might be producing it. Versican present in tumors was not only in its complete form, but also a smaller cleaved form, which is easily distinguishable from normal versican. Interestingly, distribution of cleaved versican was considerably different from that of intact form, indicating that cleaved versican in the tumor vessel may play a unique role for tumor angiogenesis. Finally, to see the direct effects of versican on tumor angiogenesis, the

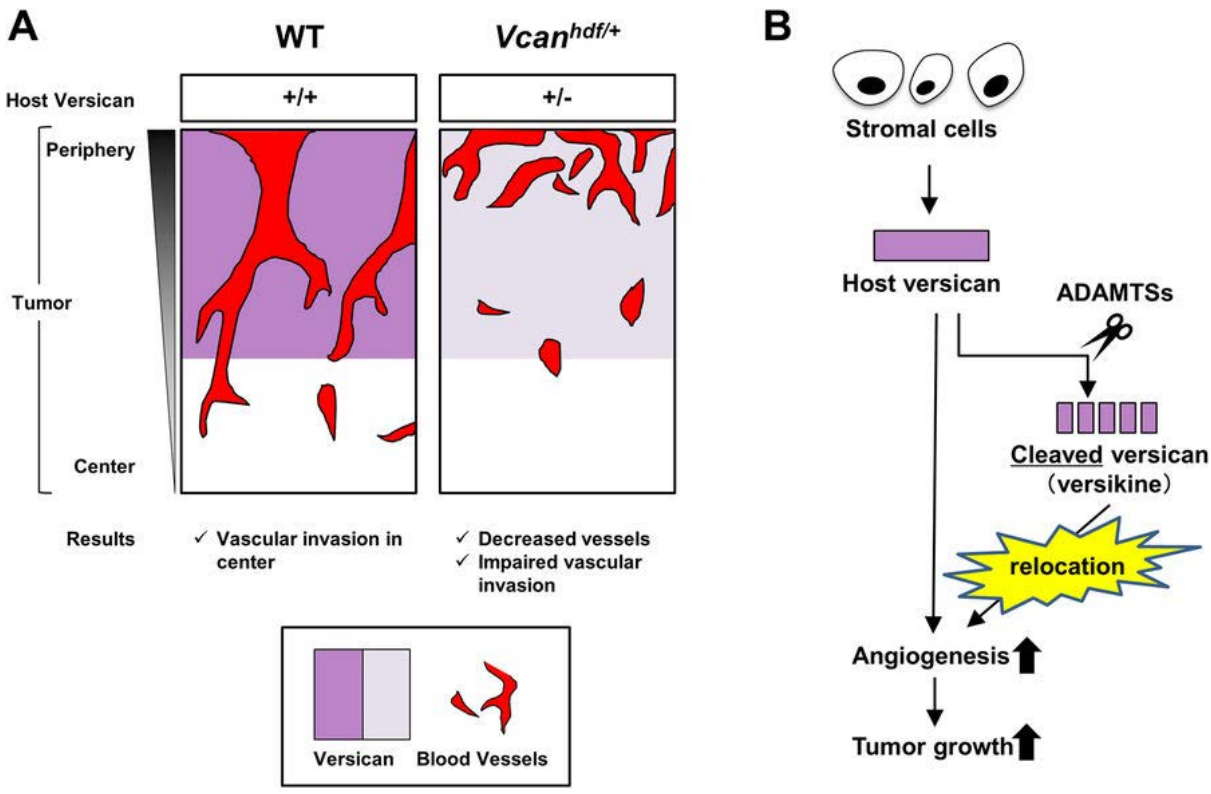
researchers compared two B16F10 genetic variants of mice: one that inherently produced versican, and one that could not. The latter had smaller tumor size and fewer blood vessels, strongly suggesting a firsthand involvement of versican with tumor angiogenesis.

This study has found yet another remarkable way in which cancer cells exploit host tissues to proliferate. “Our findings suggest that versican is an intriguing target to consider in combating tumor growth and angiogenesis”, conclude the authors conclude optimistically.

Background

Stroma: Stroma refers to layers of cells which have a connective or supporting role in tissues. Stromal cells are generally make up the extracellular matrix and provide anchoring of blood vessels and nerves to nearby tissues.

Versican: Versican is a type of protein known as glycol-protein, found in the extracellular matrix. Structurally, it has five different forms and plays a role in cellular process of adhesion, helping cells make contact with other cell types.



Caption

High levels of versican are located with tumor blood vessels in normal B16F10 mice (WT), while the genetic variant unable to produce versican ($Vcan^{hdf/+}$) had much fewer blood vessels in the tumor (A). A diagrammatic representation of how the host versican is modified and relocated to promote angiogenesis and tumor growth (B).

Reference
Keiichi Asano, Courtney M. Nelson, Sumeda Nandadasa, Noriko Aramaki-Hattori, Daniel J. Lindner, Tyler Alban, Junko Inagaki, Takashi Ohtsuki, Toshitaka Oohashi, Suneel S. Apte & Satoshi Hirohata. Stromal Versican Regulates Tumor Growth by Promoting Angiogenesis. *Scientific Reports*, volume 7;17225, 2017.
DOI: 10.1038/s41598-017-17613-6
http://www.nature.com/articles/s41598-017-17613-6

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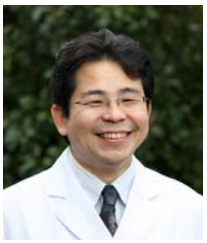

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◆About Okayama University

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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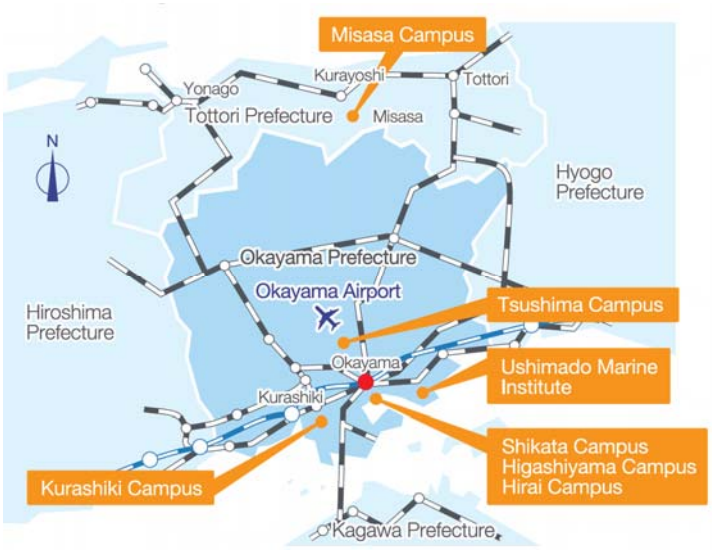

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