Okayama University Medical Research Updates （OU-MRU） 2021.10 Vol.95

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Okayama University research: Liquid biopsies: A new avenue for detecting cancer in the blood.

(Okayama, 7 October) **In a study reported in the journal *Cancers*, researchers from Okayama University describe the use of MCT1, a molecule found in the blood, for the detection of synovial sarcoma.**

Soft-tissue sarcoma is a cancer that originates in supportive tissues of the body such as muscles, cartilage, and fat. Methods for detecting and monitoring this rare form of cancer are relatively primitive and nonspecific. Now, a research team led by Assistant Professor FUJIWARA Tomohiro (M.D.) at Okayama University has discovered a molecule in the blood which can help predict the degree of synovial sarcoma.

The cells in our body release tiny sacs that contain biomolecules. The sacs, or extracellular vesicles (EVs), released from tumors contain substances specific to cancer cells. Now, EVs are secreted into the blood, making it easy to acquire them for diagnostic tests. To obtain more information about synovial sarcoma, the researchers first isolated and analyzed EVs secreted by various synovial sarcoma cells and circulating in patients with synovial sarcoma. One protein, monocarboxylate transporter 1 (MCT1), was found to be considerably higher in EVs from patients with synovial sarcoma compared to healthy individuals. What's more, MCT1 was found attached to the outer membrane of these EVs, making is easy to track.

To better understand the diagnostic potential of MCT1 expressed on the EVs, mice were transplanted with synovial sarcoma cells and their blood was drawn after tumors started growing. MCT1 levels found in the blood closely correlated with tumor growth in these mice. Additionally, when the tumors were surgically removed from some of the mice, their MCT1 levels went down. These findings were then validated in humans, by assessing the blood from patients with synovial sarcoma before and after treatment.

Cancer patients are typically treated with chemotherapy (which shrinks the tumor) followed by resection of the tumor. When a cohort of such patients was studied, some patients with synovial sarcoma showed lower levels of MCT1 just after chemotherapy, but all showed reduced MCT1 levels after resection. When their tumors were closely analyzed, MCT1 was found located either on the surface of cells, or deep within the cells. However, patients with MCT1 found on the cell surface had the lowest chances of survival. MCT1 was helpful in distinguishing the tumor status of patients and predicting their response to treatment. Lastly, the team investigated the exact role of MCT1 in synovial sarcoma. When MCT1 was blocked in synovial sarcoma cells, the cells showed lower chances of survival, migration, and invasion of neighboring cells. It is thus likely that MCT1 directly contributes to the progression of synovial sarcoma.

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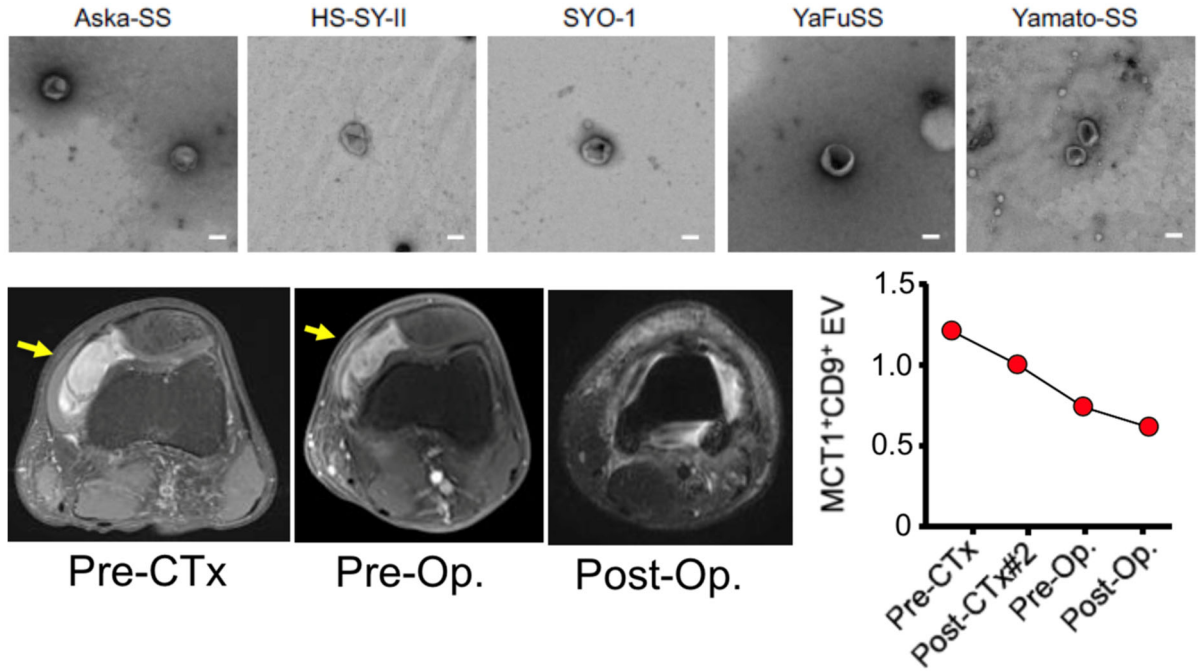
"This work describes a new liquid biopsy technique to sensitively monitor synovial sarcoma using circulating MCT1^{+}CD9^{+} EVs and indicates the therapeutic potential of MCT1 in this tumor," suggest the researchers. Given its role in accurately identifying the status of tumors and its contribution to the progression of tumors, MCT1 could be a promising target for development in the diagnosis and treatment of synovial sarcoma.

Background

Liquid biopsy: Liquid biopsies are tests performed on blood, urine, or saliva that aid in the diagnosis of a disease. In the case of cancer, liquid biopsies are usually preferred as they eliminate the need to extract tumor tissues which often involves invasive procedures. These biopsies aid oncologists with early detection of disease, monitoring tumor growth and predicting a patient's response to treatments. Thus, using liquid biopsy to track markers such as MCT1 can prove to be effective in the timely therapeutic intervention of patients with sarcoma.

Extracellular vesicles (EVs): EVs are tiny sacs released by cells into the surrounding medium. EVs contain proteins, fats, and other biomolecules and ferry them to neighboring and distant cells; this is typically how our cells communicate with each other. Since EVs must often traverse distances, they are found within tissues like blood and lymph that flow throughout the body. Tumor-borne EVs are a new target in cancer research as they are easy to capture and contain specific information about their parent cancer cells.



Caption

Top. An image of the extracellular vesicles secreted from various types of sarcoma cells.
Bottom. Levels of MCT1^{+}CD9^{+} in a 21-year-old male with synovial sarcoma in his left knee.

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Reference

Suguru Yokoo, Tomohiro Fujiwara, Aki Yoshida, Koji Uotani, Takuya Morita, Masahiro Kiyono, Joe Hasei, Eiji Nakata, Toshiyuki Kunisada, Shintaro Iwata, Tsukasa Yonemoto, Koji Ueda, Toshifumi Ozaki. Liquid Biopsy Targeting Monocarboxylate Transporter 1 on the Surface Membrane of Tumor-Derived Extracellular Vesicles from Synovial Sarcoma. *Cancers*, 2021, 13(8), 1823.
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Reference (Okayama Univ. e-Bulletin): Dr. FUJIWARA's team

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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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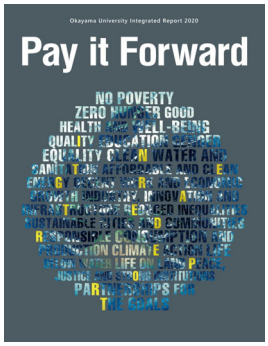

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