Okayama University Medical Research Updates （OU-MRU） 2022.03 Vol.101

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Okayama University research: Oral tumor progression mechanism identified

(Okayama, 25 March) **Researchers at Okayama University report in *JCI Insight* the biomolecular mechanism underlying the progression of oral squamous cell carcinoma, a common tumor of the head and neck. The finding is likely to be relevant for developing oral cancer treatment strategies.**

Oral squamous cell carcinoma (OSCC), a common type of tumor in the head and the neck, consists of, among other components, stroma — a heterogeneous group of cells that provides structure to a tissue. Recent research has revealed that OSCC patients with a high proportion of stroma in the tumor have a worse prognosis. Intending to develop potential treatment, understanding the role of stroma in driving OSCC progression is crucial. Now, Assistant Professor KAWAI Hotaka (D.D.S., Ph.D.) and May Wathone Oo (graduate student) at Okayama University has identified the mechanism responsible for OSCC growth: the tumor 'recruits' a particular kind of bone marrow-derived cells, a process facilitated by the presence of a specific compound expressed in cancer stroma.

First, the researchers isolated patient-derived cancer stroma cells for in vitro investigations. Assistant Professor KAWAI and colleagues then transplanted a tumor/stroma complex into green fluorescent protein-positive bone marrow cells transplanted mouse. The fluorescent protein is relatively easy to localize with imaging methods. So the migration of the bone-marrow cells could be followed over several weeks, during which the tumor evolved. These in vivo experiments confirmed that bone marrow-derived cells were recruited into the tumor microenvironment.

The scientists then checked which particular kinds of bone marrow-derived cells are recruited into the tumor. By marking the various candidate types by different marker molecules, they found that a type known as myeloid-derived suppressor cells (MDSCs) are recruited; these are cells that have immunosuppressive functions.

In a last set of experiments, Assistant Professor KAWAI and colleagues were able to identify the main factor in the recruitment mechanism of MDSCs into the tumor microenvironment. They established that patient-derived stroma produces high amounts of a protein called CCL2. Then, when artificially inhibiting the synthesis of CCL2, it was seen that the number of MDSCs decreased — an indication that CCL2 is indeed an enabler for MDSC recruitment.

Background

Myeloid-derived suppressor cells (MDSCs) are a group of immune cells originating from bone marrow stem cells. MDSCs are implicated in pathological situations, including chronic

infections and cancer. They have strong immunosuppressive activities (as opposed to immunostimulatory properties associated with other myeloid cell types) that play a role in regulating the functions of other immune cells.

The action mechanisms of MDSCs are not completely clear, but it has been established from clinical evidence that cancer tissues with a high content of MDSCs are linked with poor patient prognosis and resistance to therapies.

Assistant Professor KAWAI Hotaka and May Wathone Oo at Okayama University have now studied the link between MDSCs and oral squamous cell carcinoma progression and identified the critical resident stromal factor for the recruitment of MDSCs in OSCC.

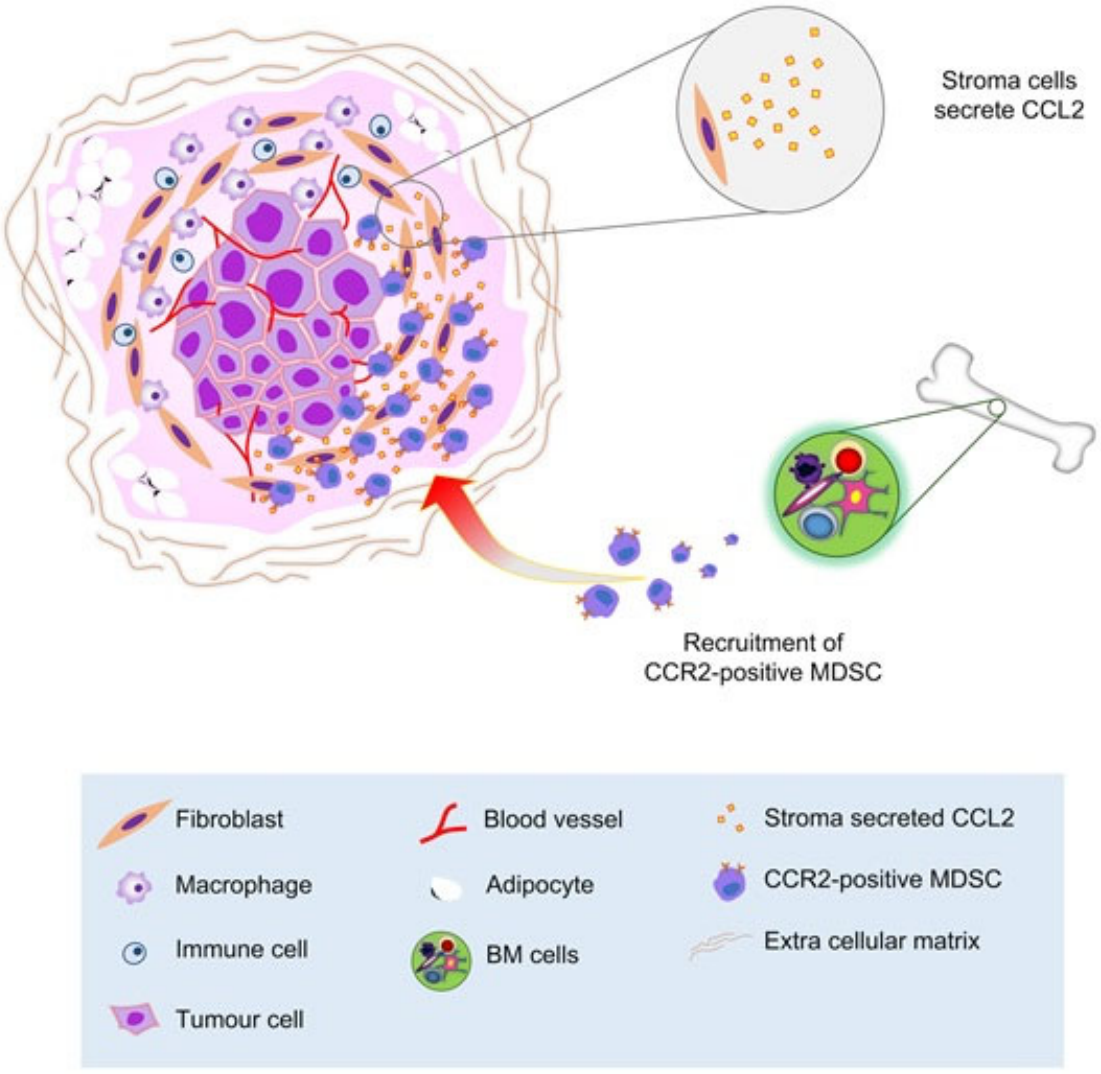

Figure
Schematic showing the biomolecular mechanism underlying oral squamous cell carcinoma growth.

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Reference

May Wathone Oo, Hotaka Kawai, Kiyofumi Takabatake, Shuta Tomida, Takanori Eguchi, Kisho Ono, Qiusheng Shan, Toshiaki Ohara, Saori Yoshida, Haruka Omori, Shintaro Sukegawa, Keisuke Nakano, Kuniaki Okamoto, Akira Sasaki, and Hitoshi Nagatsuka. Resident stroma-secreted chemokine CCL2 governs myeloid-derived suppressor cells in the tumor microenvironment. JCI insight. 2022;7(1):e148960.
DOI：10.1172/jci.insight.148960
https://insight.jci.org/articles/view/148960

Reference (Okayama University e-Bulletin & OU-MRU) : Assistant Professor KAWAI's team

OU-MRU Vol.78：Disrupting blood supply to tumors as a new strategy to treat oral cancer

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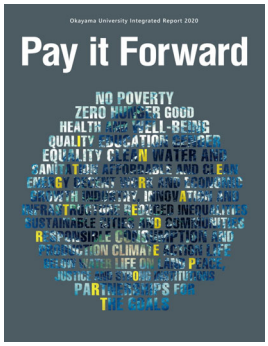

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