学位論文審査結果の要旨

所　属	三重大学大学院医学系研究科 甲 生命医科学専攻　基礎医学系講座 分子病態学分野	氏　名	伊藤（いとう）　温志（あつし）
審　査　委　員	主　査　小林　哲 副　査　渡邊　昌俊 副　査　俵　　功		

（学位論文審査結果の要旨）

Possible Metastatic Stage-Dependent ILC2 Activation Induces Differential Functions of MDSCs through IL-13/IL-13Rα1 Signaling during the Progression of Breast Cancer Lung Metastasis

【主論文審査結果の要旨】

筆者らは論文において下記の内容を述べている。

Breast cancer is the most common cancer in women worldwide, and lung metastasis is one of the most frequent distant metastases. When breast cancer metastasizes to the lung, group 2 innate lymphoid cells (ILC2s) are thought to promote tumor growth via the activation of myeloid-derived suppressor cells (MDSCs), which are known to negatively regulate anticancer immune responses. However, it remains to be elucidated exactly how this ILC2–MDSC interaction is involved in tumor growth during metastases formation. Using a 4T1/LM4 breast cancer mouse model, we found that ILC2s were activated in both the micro- and macro-metastatic regions, suggesting sustained activation throughout the metastatic cascades via IL-33/ST2 signaling. Consistent with IL-13 secretion from activated ILC2s, the frequencies of polymorphonuclear (PMN)- and monocytic (M)-MDSCs were also significantly elevated during the progression from micro- to macro-metastatic cancer. However, the effects of ILC2-induced MDSC functionality on the microenvironment differed in a metastatic-stage specific manner. Our findings indicate that ILC2s may induce the immunosuppressive functions of MDSCs during the later stages of metastasis. Concomitantly, ILC2 may instigate extracellular matrix remodeling by PMN-MDSC activation during the early stages of metastasis. These metastatic-stage specific changes may contribute to metastatic tumor growth in the microenvironment of breast cancer lung metastasis.

本研究は乳がん肺転移のMicro-metastasisからMacro-metastasisに進展する過程を通して、２型自然リンパ球が骨髄由来免疫抑制細胞を活性化させ、細胞外マトリックスのリモデリングの促進と抗腫瘍免疫抑制により腫瘍増殖を促進する癌周囲の微小環境を構築している可能性を示した論文であり、学術上極めて有益であり、学位論文として価値あるものと認めた。

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Atsushi Ito, Yuichi Akama, Naoko Satoh-Takayama, Kanako Saito, Takuma Kato, Eiji Kawamoto, Arong Gaowa, Eun Jeong Park, Motoshi Takao and Motomu Shimaoka