Medical & healthcare, Drug discovery

Novel medical development for early-stage lung cancer focusing on macrophages

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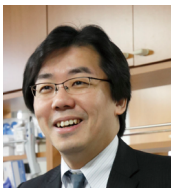


Abstract

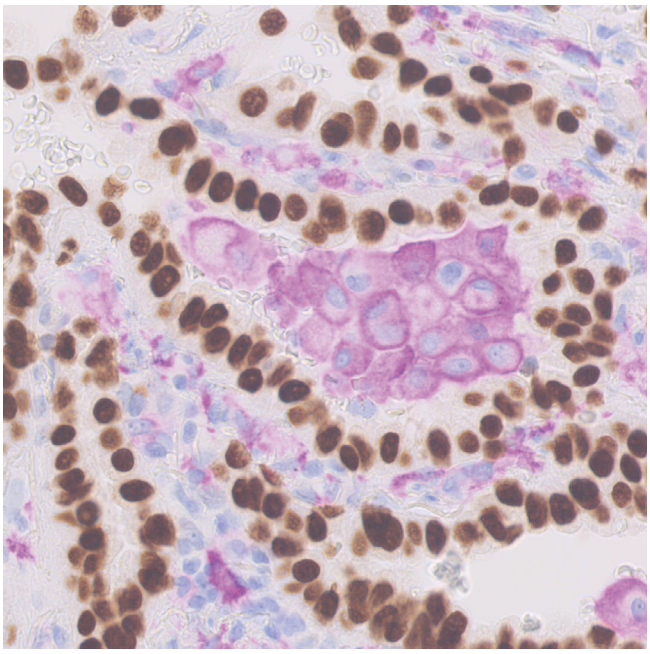
We conducted research using lung cancer model mice and RNA sequencing, which comprehensively quantifies gene expression in the cells. We therefore revealed that alveolar macrophages, immune cells that reside abundantly only in lungs, produce the protein named activin A in lung cancer environment, compared to those in normal lungs. Moreover, we also revealed that lung cancer cells skillfully utilize the protein to form a vicious cycle that promotes the cancer cell proliferation.

Background & Results

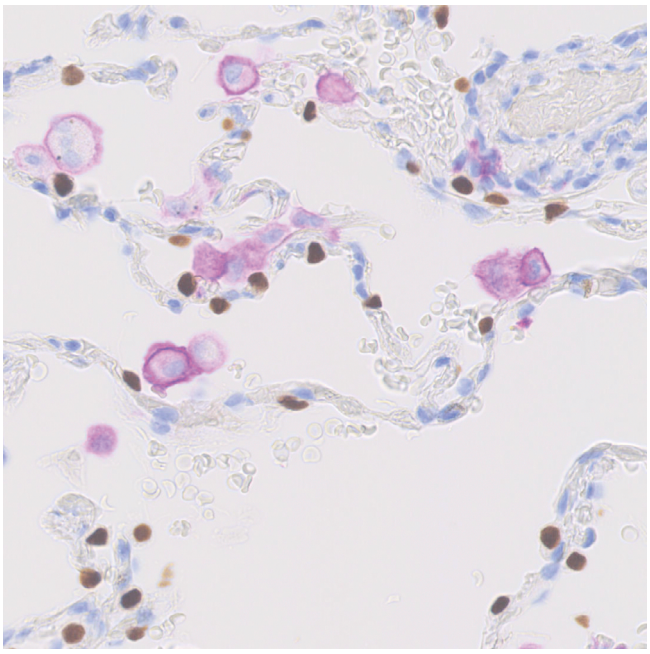
Our research indicates that inhibition of activin A produced by alveolar macrophages is considered to be one of the potential targets for lung cancer treatment that medical applications including drug development are expected. In addition, this mechanism of alveolar macrophages discovered in our study has been confirmed from the early stage of lung cancer. Therefore, focusing on alveolar macrophages and activin A is sure to contribute to the early diagnosis of lung cancer. Furthermore, the inhibition of activin A is considered to be useful in suppressing the progression of early cancer to advanced ones. The intervention toward this mechanism is therefore expected to contribute to increased opportunities for lung cancer cure through surgery at an early stage.

Significance of the research and Future perspective

Humans utilize the immune system to eliminate foreign substances such as pathogens, and similar immune systems also work to eliminate cancer cells. In addition to cancer cells, various immune cells such as lymphocytes, macrophages, and neutrophils exist in the cancer microenvironment to form the characteristic immune system against cancer. Alveolar macrophages (AMs) are the most abundant immune cell in normal lungs, and it was thought that these cells also have some effect on lung cancer cells in the lung cancer microenvironment. However, AMs are only found in the lungs, and it was difficult to create an experimental system that could study the lung cancer microenvironment in detail. Therefore, how AMs interact with lung cancer cells had not been rarely elucidated. In this study, we conducted research using lung cancer model mice in which lung cancer tissue was set in vivo. We found that when AMs were depleted from the mice, the size of lung cancer tumor became smaller than when AMs were maintained. Next, we performed RNA sequence to analyze the gene expression profiles of AMs. We clarified that AMs produce activin A in lung cancer tissue, which promotes the growth of lung cancer, and that the inhibition of activin A leads to the growth suppression of lung cancer. Furthermore, we analyzed human lung cancer tissues and confirmed that AMs express activin A, especially in cases of early-stage lung cancer.



Alveolar macrophages in lung carcinoma tissue (purple cells). Brown dots indicate the nuclei of lung cancer cells.



Alveolar macrophages in normal lung tissue (purple cells). Brown dots indicate the nuclei of epithelial cells.

Patent

Treatise Taniguchi, Seiji; Matsui, Takahiro; Kimura, Kenji et al. In vivo induction of activin A-producing alveolar macrophages supports the progression of lung cell carcinoma. Nature Communications. 2023, 14, 143. doi: 10.1038/s41467-022-35701-8

URL

Keyword lung cancer, macrophage, early detection, early treat