

Integrated understanding of disease pathogenesis based on interstitial cell diversity (Interstitial literacy)



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Purpose and Background of the Research

● Outline of the Research

To achieve healthy longevity, it is necessary to establish individualized treatment and prevention methods for various diseases such as infectious diseases, autoimmune diseases, cancer and fibrosis. However, the mechanisms of disease onset and exacerbation for these diseases have not yet been fully elucidated. In the process of disease onset and progression, research has so far focused mainly on the parenchyma of organs and the cells that reside in the space. Therefore, our research will shift the focus from the parenchyma-driven perspective and focus on the interstitium. Traditionally, in diseases with "interstitial" attached (e.g., interstitial pneumonia, tubulointerstitial nephritis, interstitial cystitis, etc.), "interstitial" has indicated the "location" where pathologies originate from various causes and has not reflected the cause or condition. As a results, an integrated understanding of the interstitium as a discipline has not progressed. Interstitial pneumonia, for example, is a disease in which the ventilatory and diffusion capacity of the lung parenchyma is significantly reduced due to thickening of the lung interstitium. It is not yet clear what kind of intercellular crosstalk occurs between interstitial cell populations (fibroblasts, immune cells, blood vessels, and nerves) during the actual pathogenesis of the disease, nor what the functional significance of this crosstalk is for the parenchyma (see Fig. 1). For other diseases as well, research in the parenchymal space has progressed, but little research has been done in the interstitial space. Therefore, clarifying the dynamism and crosstalk of various cell populations that emerge in the interstitium during the onset and exacerbation of pathological conditions is an urgent issue in fully understanding of the pathogenesis of various diseases. In this project, we focus on crosstalk between multiple cell types in the interstitium, which has rarely been focused on in the process of disease onset and progression, and comprehensively clarify the cellular dynamism and molecular characteristics that enter and exit the interstitium, and untangle the relationships between them to

comprehensively understand the mechanisms of disease onset. This area of research, known as 'interstitial literacy,' focuses on understanding the complex interactions and characteristics of these cells, shedding light on how diseases start. By redefining our understanding of the interstitium based on these studies, we hope to uncover new insights into how diseases begin, which has not been clear before.

Along with the progression of the disease, the interstitium thickens, and the types of cells in the area change.

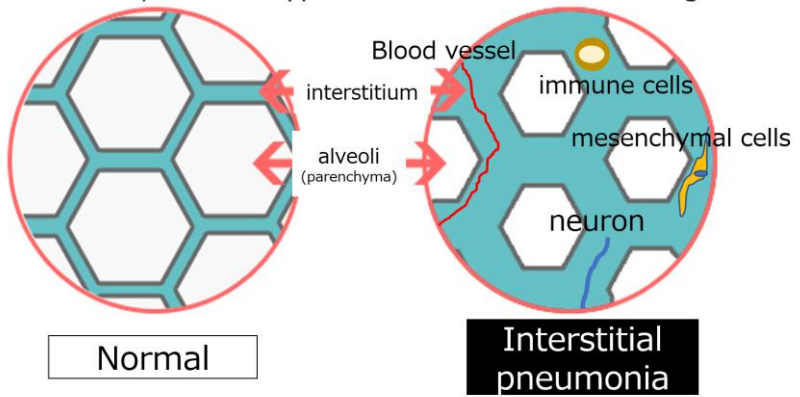


Fig. 1: Pathogenesis of interstitial pneumonia

# Expected Research Achievements

## ● What we aim to clarify in this research.

We want to understand complex cell interactions, called intercellular crosstalk, among interstitial cells and how these interactions influence disease progression (see Fig. 2).

## Our goals are:

1. To understand how different cell populations within the interstitium communicate with each other.
2. To figure out how the immune, nervous, vascular/lymphatic, and mesenchymal systems interact simultaneously, which we define as complex cellular crosstalk.
3. To understand how changes in intercellular crosstalk among interstitial cell populations affect the substrate.

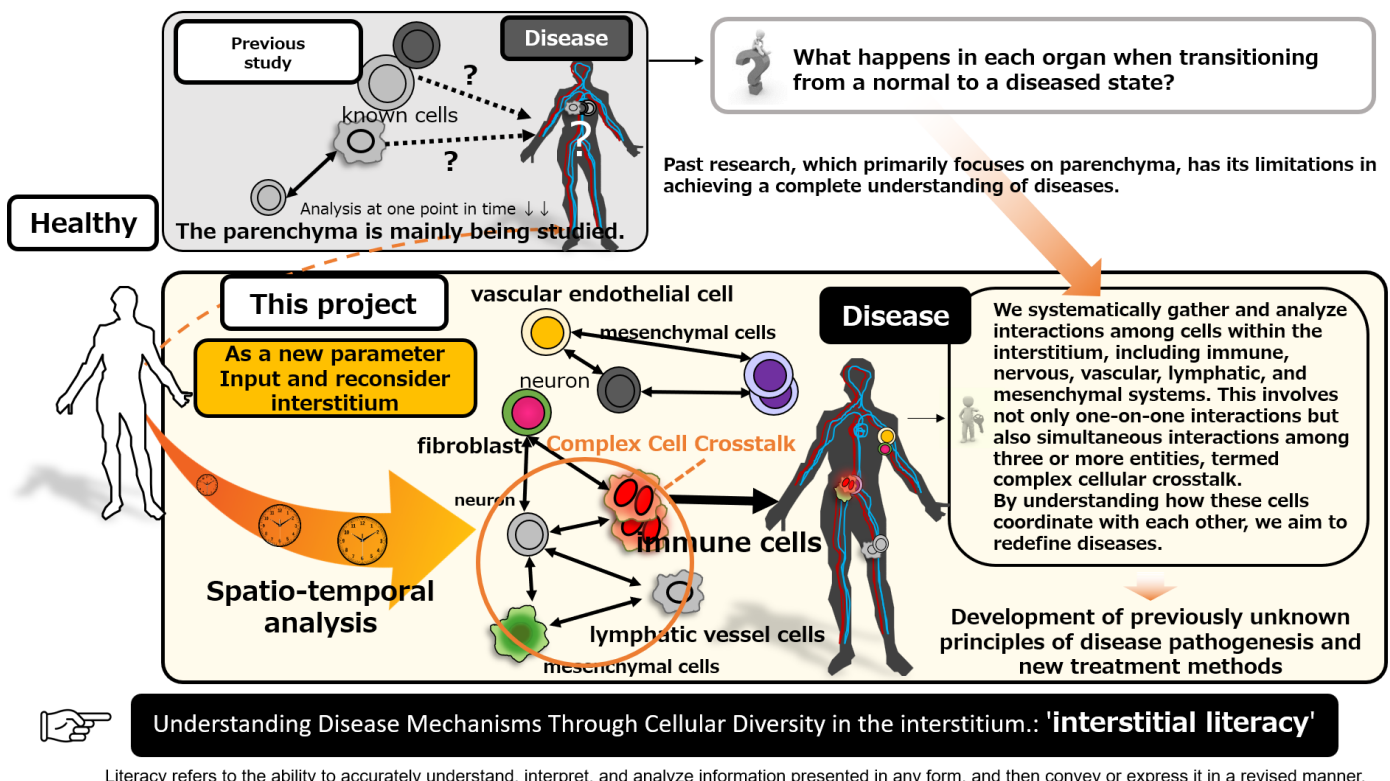


Fig. 2: Outline and Goals of the Research

## ● The Influence of Academic Progress on Society and Furthering Research

This research focuses on understanding how diseases develop by examining the cells within the interstitium, the structural tissue of organs. We aim to reveal how these cells interact in the interstitium across four integrated research areas. By studying the various cells that appear in interstitial spaces as diseases progress and examining their complex communication, we hope to redefine how interstitial functions contribute to disease development and worsening. Our findings could open up new approaches to developing interventions and treatments for diseases, which would be highly beneficial to society. Although we primarily study diseases affecting organs like the brain, lungs, liver, intestines, and bone marrow, our approach could also shed light on diseases and organs not directly targeted here. By applying our insights to other organs, we could improve our understanding of a wide range of diseases. This research aims to establish a new field of 'interstitial literacy' that transcends current academic boundaries and promises to bring about significant advancements.

Homepage Address, etc.

<https://interstitial-literacy.org/>