The immune-stromal-bone interaction in arthritis

Immune system closely interacts with stromal cells in health and diseases. Rheumatoid arthritis (RA) is one of the most common autoimmune diseases worldwide. In RA, the activated immune system co-operates with synovial fibroblasts to enhance inflammation and destruction of bone and cartilage in joints. The crucial role of osteoclasts in bone destruction has been demonstrated by basic studies and the clinical efficacy of antibodies targeting RANKL, an important mediator of osteoclastogenesis. New technologies, such as single-cell RNA sequencing, have revealed the heterogeneity of synovial fibroblasts and immune cells. To understand the mechanisms of bone damage in RA, it is important to clarify how the immune system promotes the tissue-destructive properties of synovial fibroblasts and influences bone cells. The interaction between immune cells and fibroblasts underlies the imbalance between regulatory T (Treg) cells and T helper 17 (Th17) cells. We recently clarified the key transcription factor ETS1, which governs the pathological tissue-destructive programs in synovial fibroblasts. An improved understanding of the interplay among the immune system, synovial fibroblasts and bone based on the combination of in silico analysis and biological studies will contribute to the identification of novel therapeutic targets in RA.

Lipid as a building material for biotechnologies

The long-term goal of my research is to understand and control the self-assembly of biological molecules such as lipids and peptides for identifying their supramolecular structures, functions, their physiological roles in human health, and applying this expertise for developing biotechnologies.

There are still many types of forces that cannot be measured with existing technologies, such as molecular forces at nanoscale or the detection of curved or anisotropic forces. Mechanochromic materials are expected to play a pivotal role in these niches. In my talk, I will introduce the mechanism and applications of a mechanochromic lipid polymer called polydiacetylene towards biosensing.1

We report a unique cooperative function between two well-known antimicrobial peptides (LL-37/HNP1) that kills bacteria more efficiently, whereas minimizing the host damage by suppressing mammalian cell membrane lysis.2 Such a “double cooperativity” may be used in our immune system and may help with developing efficient and safe antimicrobial agents in future. In this presentation, we will report our recent efforts in understanding its molecular mechanism by biophysical assays.

References

1. *Nano Letters* **2021**, *21* (1), 543-549.
2. *Biophysical Journal* **2020**, *119* (12), 2440-2450.

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