“Dissecting the roles of innate cells in the skin and intractable skin diseases”

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The skin is not merely a physical barrier but also an active immunological interface, exposed to various external stimuli including microbes. Over the recent years, our laboratory has defined hair follicles as control towers that regulates immune cells residing in the skin. Hair follicles produce chemokines and cytokines that are crucial for the localization and tissue-residency of immune cells including the Langerhans cells, resident memory T cells, and innate lymphoid cells. We also discovered that disruption of the ADAM17-EGF receptor axis and ADAM10-Notch signaling axis leads to dysbiosis on the skin surface and in the hair follicles, respectively. The former leads to microbiome predominance of Staphylococcus aureus and results in atopic skin inflammation, whereas the latter leads to Corynebacterium species predominance that trigger irreversible hair follicle destruction. These findings highlight the distinct mechanisms that regulate the microbiome in different compartments of the skin. In this talk, I will focus on the deeper layers of the skin-the hypodermis (a.k.a subcutaneous tissue), a common site for cellulitis, which we found to be enriched with macrophages. We enabled layer-specific depletion of macrophages, which had prominent effects on the organization of the extracellular matrix, counterintuitively rendering mice highly protected against S. aureus-mediated cellulitis. I will also introduce our ongoing efforts to understand the histology and pathophysiology of Degos disease, an extremely rare and highly fatal disease of unknown etiology.