The role of CD169 macrophages in the regulation of inflammation

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CD169+ macrophages, localizing at the border region of secondary lymphoid organ, monitor the entry of particulate matters via blood stream or lymphatic flow, and regulate immune reaction against these antigens. In order to explore the distribution of CD169+ cells outside secondary lymphoid organs, we generated mice that harbor the Cre recombinase gene in the CD169 loci (CD169-Cre mice), and crossed these mice with ROSA26-yellow fluorescent protein reporter mice. Using the CD169-Cre-YFP mice, we detected YFP not only in macrophages located in lymphoid organs, but also in some tissue resident macrophages in several organs such as intestine and kidney. Among them, we focused on CD169+ intestine-resident macrophages, and examined the roles of these macrophages in the experimental colitis. We found that CD169+ macrophages reside not at the villus tip, but at the bottom-end of the lamina propria microenvironment. Following mucosal injury, the CD169+ macrophages recruit inflammatory monocytes by secreting CCL8. Selective depletion of CD169+ macrophages or administration of neutralizing anti-CCL8 antibody ameliorates the symptoms of experimental colitis in mouse. These findings suggest that CD169+ macrophage-derived CCL8 serves as an emergency alert for the collapse of barrier defense, and is a promising target for the suppression of deteriorating mucosal injury.

The character of tissue resident macrophages seems to be determined by a transcription factor specifically expressed in each macrophage. In this context, unique localization and function of CD169+ macrophages prompt us to speculate that these macrophages would be also regulated by specific transcription factors. We are trying to identify such transcription factors, and will discuss about these factors in the presentation.