

Interleukin-1 Signaling and CD4⁺T Cells Control B Cell Recruitment To The Lungs In Chronic Beryllium Disease

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Chronic beryllium disease (CBD) is a debilitating pulmonary disorder that occurs due to persistent exposure to beryllium (Be) particles in the workplace. Be-exposure causes activation of the innate immune system, resulting in the secretion of interleukins and chemokines that drive the accumulation of B and T cells in the lungs. However, the mechanisms by which innate molecules influence the recruitment of B cells and B cell-mediated protection in CBD are poorly understood. In this study, we employed multiple approaches to examine the role of innate immune signaling and CD4⁺ T cells in B cell recruitment and function in the lungs. We show that the absence or blocking of IL-1R1 signaling prevents the recruitment of B cells to the lungs of BeO-exposed mice. Additionally, we show that B cell recruitment to the lungs depends on the chemokine receptor, CXCR5, and CD4⁺ T cells. In BeO exposed mice, lung B cells down-regulate IgM but showed an increased IgD and CD44 surface expression. Further, RNA sequencing of pulmonary tissue-specific B cells in CBD revealed distinct gene signatures compared to splenic B cells, with increased expression of pathways involved in antigen presentation, tight junction interactions, and interferon signaling. Overall, our study shows that B cell recruitment and aggregate formation during CBD depend on sequential activation of innate and adaptive immune responses.