EXPERIMENTAL ARTHRITIS

Lipid presentation suppresses inflammation

Regulatory B (B_{reg}) cells can interact with and induce the suppressive activity of invariant natural killer T (iNKT) cells to restrain excessive inflammation, according to new findings. “For the first time we show that in addition to protein antigen, B_{reg} cells can present lipid antigen and activate iNKT cells that suppress excessive immune responses and control arthritis,” reports Kristine Oleinika, lead author of the study published in *Nature Communications*.

CD1d, an MHC class I-like molecule that presents lipid antigens to iNKT cells, is expressed by the majority of reported B_{reg} cell subsets. However, the relevance of CD1d expression for the suppressive

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functions of B_{reg} cells, and the effects of iNKT cell– B_{reg} cell interactions on iNKT cell function, were previously unknown. Oleinika and colleagues sought to investigate the role of iNKT cell– B_{reg} cell interactions in suppressing autoimmune responses.

Administration of α -galactosylceramide (α -GalCer), an iNKT cell agonist, is known to inhibit the development of autoimmunity in mice. In a mouse model of antigen-induced arthritis, the group found that the suppressive effects of α -GalCer on disease development were impaired in both B cell-deficient mice and B cell-depleted mice. “We generated mixed bone marrow chimeric mice that lacked CD1d expression exclusively on B cells, allowing us to investigate the contribution of this cell population to arthritic inflammation,” remarks corresponding author Claudia Mauri. “We found that not only did these mice develop exacerbated

disease compared with control animals, but also that α -GalCer lost its potent disease-ameliorating effect, if B cells are unable to present lipids.”

The expression of CD1d by B cells was required for an α -GalCer-induced increase in expression of IFN γ and promyelocytic leukaemia zinc finger (PLZF, also known as ZBTB16) in iNKT cells, the latter of which is a transcription factor responsible for the rapid production of cytokines by iNKT cells. “We report [an unexpected] new phenotype of PLZF⁺IFN γ ⁺ iNKT cells that are able to suppress inflammation partially via IFN γ ,” says Oleinika. “The latter [finding] is particularly important as IFN γ has often been associated with a pathogenic response in arthritis.”

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