The Journal of Immunology

Comment on "B Cell Depletion Enhances T Regulatory Cell Activity Essential in the Suppression of Arthritis"

Ting-Yu Wang, Fei-Hua Wu and Zhi-Gui Jin

J Immunol 2012; 188:519; ;
doi: 10.4049/jimmunol.1190084
http://www.jimmunol.org/content/188/2/519

The Journal of Immunology is published twice each month by
The American Association of Immunologists, Inc.,
1451 Rockville Pike, Suite 650, Rockville, MD 20852

Print ISSN: 0022-1767 Online ISSN: 1550-6606.

Letters to the Editor

THE JOURNAL OF IMMUNOLOGY

Comment on "B Cell Depletion Enhances T Regulatory Cell Activity Essential in the Suppression of Arthritis"

We read the interesting article by Hamel et al. (1), which provides encouraging data on the role of B cells in arthritis. We suggest that increasing T regulatory cells (Tregs) reveals a novel mechanism of B cell depletion in rheumatoid arthritis (RA) therapy.

B cells play a pivotal role in the pathogenesis of RA through autoantibody production, chemokine/cytokine secretion, and inhibiting autoreactive T cell responses (2). Although a series of treatment regimens that affect B cells was developed (3), the exact mechanism for the efficacy of B cell-depletion therapy remains unclear. The depletion of B cells with a decrease in autoantibodies in RA does not necessarily correlate with the clinical outcome, indicating that mechanisms other than producing Abs are in operation. Recently, Yeo et al. (4) identified B cells as the main source of receptor activator of NF-κB ligand, which contributes to osteoclast activation and bone destruction. Interestingly, Hamel et al. (1) first correlated B cell depletion with the improvement of Tregs, which can inhibit osteoclast formation and activation (5), and with other regulatory mechanisms. The authors found that during proteoglycan-induced arthritis (PGIA), B cell depletion strikingly increased Tregs and decreased the severity of arthritis. In addition, both Tregs and B cell depletion restored proteoglycan-induced arthritis, although the resurgent autoantibody response was absent.

Collectively, B cell depletion could be used for controlling arthritis by improving Tregs. Better insights into the role of B cell depletion in Treg-mediated osteoclast suppression could result in innovative therapies for RA and other bone-destructive diseases.

Ting-Yu Wang, Fei-Hua Wu, and Zhi-Gui Jin

Department of Pharmacy, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200011, The People's Republic of China

Address correspondence and reprint requests to Dr. Ting-Yu Wang, Department of Pharmacy, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, 639 Zhizaoju Road, HuangPu District, Shanghai 200011, The People's Republic of China. E-mail address: wangty1982@gmail.com

References

1. Hamel, K. M., Y. Cao, S. Ashaye, Y. Wang, R. Dunn, M. R. Kehry, T. T. Glant, and A. Finnegan. 2011. B cell depletion enhances T regulatory cell activity essential in the suppression of arthritis. *J. Immunol.* 187: 4900–4906.
2. Hamel, K., P. Doodes, Y. Cao, Y. Wang, J. Martinson, R. Dunn, M. R. Kehry, B. Farkas, and A. Finnegan. 2008. Suppression of proteoglycan-induced arthritis by anti-CD20 B Cell depletion therapy is mediated by reduction in autoantibodies and CD4+ T cell reactivity. *J. Immunol.* 180: 4994–5003.
3. Nakken, B., L. A. Munthe, Y. T. Konttinen, A. K. Sandberg, Z. Szekanecz, P. Alex, and P. Szodoray. 2011. B-cells and their targeting in rheumatoid arthritis - Current concepts and future perspectives. *Autoimmun. Rev.* 11: 28–34.
4. Yeo, L., K. M. Toellner, M. Salmon, A. Filer, C. D. Buckley, K. Raza, and D. Scheel-Toellner. 2011. Cytokine mRNA profiling identifies B cells as a major source of RANKL in rheumatoid arthritis. *Ann. Rheum. Dis.* 70: 2022–2028.
5. Zaiss, M. M., B. Frey, A. Hess, J. Zwerina, J. Luther, F. Nimmerjahn, K. Engelke, G. Kollias, T. Hünig, G. Schett, et al. 2010. Regulatory T cells protect from local and systemic bone destruction in arthritis. *J. Immunol.* 184: 7238–7246.

www.jimmunol.org/cgi/doi/10.4049/jimmunol.1190084