節が可能になっていくことが期待される。

文 献

1) Karl OA, Pocelli SA : The diverse functions of CD1d-restreicted NKT cells and their potential for immunotherapy. Immunol Let 100 : 42-55, 2005
2) Brigl M, Brenner MB : CD1 : antigen presentation and T cell function. Annu Rev Immunol 22 : 827-890, 2004
3) Kawano T, Cui J, Koezuka Y, et al : CDd-restricted and TCR-mediated activation of Va4 NKT cells by glycosylceramides. Science 278 : 1626-1629, 1997
4) Zhou D, Mattner J, Cantu C 3rd, et al : Lysosomal glycosphingolipid recognition by NKT cells. Science 306 : 1786-1789, 2004
5) Miyake S, Yamamura T : Therapeutic potential of gylcolipid ligands for natural killer (NK) T cells in the suppression of autoimmune diseases. Curr Drug Targets Immune Endocr Metabol Disord 5 : 315-322, 2005
6) Araki M, Kondo T, Gumperz JE, et al : Th2 bias of $CD4^+$ T cells derived from multiple sclerosis in remission. Int Immunol 15 : 279-288, 2003
7) Pal E, Tabira T, kawano T, Taniguchi M, et al : Costimulation-dependent modulation of experimental autoimmune encephalomyelitis by ligand stimulation of Vα14 NKT cells. J Immunol 166 : 662-668, 2001
8) Miyamoto K, Miyake S, Yamamura T : A synthetic glycolipid prevents autoimmune encephalomyelitis by inducing Th2 bias of natural killer T cells. Nature 413 : 531-534, 2001
9) Oki S, Chiba A, Yamamura T, et al : The clinical implication and molecular mechanism of preferential IL-4 production by modified glycolipid-stimulated NKT cells. J Clin Inv 113 : 1631-1640, 2004
10) Oki S, Tomi C, Yamamura T, et al : Preferential Th2 polarization by OCH is supported by incompetent NKT cell induction of CD40L and following production of inflammatory cytokineds by bystander cells *in vivo*. Int Immunol 17 : 1619-1629, 2005
11) Baxter AG, Smity MJ : The role of NK cells in autoimmune disease. Autoimmunity 35 : 1-14, 2002
12) Flodstrom M, Shi F-D, Sarvetnick N, Ljunggren H-G : The natural killer cell-friend or foe in autoimmune disease? Scand J Immunol 55 : 432-441, 2002
13) Fench AR, Yokoyama WM : Natural killer cells and autoimmunity. Arthritis Res Therapy 6 : 8-14, 2004
14) Zhang B, Yamamura T, Kondo T, Fujiwara M, Tabira T : Regulation of experimental autoimmune encephalomyelitis by natural killer (NK) cells. J Exp Med 186 : 1677-1687, 1997
15) Matsumoto Y, Kohyama K, Aikawa Y, et al : Role of natural killer cells and TCRγδT cells in acute autoimmune encephalomyelitis. Eur J Immunol 28 : 1681-1688, 1998
16) Shi F-D, Wang H-B, Li H, et al : Natural killer cells determine the outcome of B cell-mediated autoimmnity. Nat Immunol 1 : 245-251, 2000
17) Takahashi K, Miyake S, Kondo T, et al : Natural killer type 2 bias in remission of multiple sclerosis. J Clin Inv 107 : R23-R29, 2001
18) Takahashi T, Miyake S, Endoh M, Yamamura T : The regulatory role for natural killer cells in the "smoldering" state of multiple sclerosis. Brain 127 : 1917-1927, 2004
19) Bielekova B, Catalfamo M, Reichert-Scrivner S, et al : Regulatory $CD56^{bright}$ natural killer cells mediate immunomodulatory effects of IL-2Ra-targeted therapy (daclizumab) in multiple sclerosis. Proc Natl Acad Sci U S A 103 : 5941-5946, 2006
20) Sakaguchi S : Naturally arising $CD4^+$regulatory T cells for immunologic self-tolerance and negative control of immune responses. Annu Rev Immunol 22 : 531-562, 2004
21) Sakaguchi S, Sakaguchi N, Asano M, et al : Immunologic self-tolerance maintained by activated T cells expressing IL-2 receptor alpha-chains (CD25). Breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. J Immunol 155 : 1151-1164, 1995
22) von Herrath MG, Harrison LC : Antigen-induced regulatory T cells in autoimmunity. Nat Rev Immunol 3 : 223-232, 2003
23) Kohm AP, Carpentier PA, Anger HA, et al : $CD4^+$ $CD25^+$regulatory T cells suppress antigen-specific autoreactive immune responses and central nervous system inflammation during active experimental autoimmune encephalomyelitis. J Immunol 169 : 4712-4716, 2002
24) Hu D, Ikizawa K, Lu L, et al : Analysis of regulatory CD8 T cells in Qa-1-deficinet mice. Nat Immunol 5 : 516-523, 2004
25) Rifa'I M, Kawamoto Y, Nakashima I : Essential roles of $CD8^+CD122^+$regulatory T cells in the maintenance of T cell homeostasis. J Exp Med 9 : 1123-1134, 2004
26) Viglietta V, Baecher-Allen C, Weiner HL, et al : Loss of functional suppression by $CD4^+CD25^+$regulatory T cells in patients with multiple sclerosis. J Exp Med 7 : 971-979, 2004
27) Haas J, Hug A, Viehover A, et al : Reduced suppressive effect of $CD4^+CD25^{high}$ regulatory T cells on the T cell immune response against myelin oligodendrocyte glycoprotein in patients with multiple sclerosis. Eur J Immunol 35 : 3343-3352, 2005

Abstract

Therapeutic potential for targeting regulatory cells for the treatment of multiple sclerosis

Sachiko Miyake

from

Section Chief, Department of Immunology, National Institute of Neuroscience, NCNP, 4-1-1 Ogawahigashi, Kodaira, Tokyo 187-8502, Japan.

Multiple sclerosis (MS) is a chronic demyelinating disease of presumed autoimmune pathogenesis. Regarding the pathogenesis of MS, studies have indicated that autoimmune T cells targeting myelin components play a crucial role in mediating the inflammatory process. It is now widely accepted that regulatory cells are involved in the prevention of or recovery from autoimmune diseases. The present review will focus on the potential role of three different types of regulatory cells including $CD4^+CD25^+$T cells, NK cell and NKT cells in the control of pathogenesis of MS. The recent advances in glycolipid therapy targeting NKT cells for autoimmune disease models will also be discussed.

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