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CD226 ligation protects against EAE by promoting IL-10 expression via regulation of CD4+ T cells differentiation

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IL-10 is an important anti-inflammatory cytokine that has been implicated in a variety of autoimmune conditions, including multiple sclerosis (MS). It has been shown that anti-CD226 treatment ameliorates experimental autoimmune encephalomyelitis (EAE), the widely accepted model of MS. However, the mechanism still needs to be elucidated. Here we show that CD226 ligation by anti-CD226 mAb LeoA1 efficiently promoted IL-10 production in human peripheral blood monocytes (PBMC) or in mixed lymphocyte culture (MLC) system. Meanwhile, LeoA1 treatment significantly induced the CD4+IL-10+ T cell differentiation while suppressing the generation of Th1 and Th17 through modulating IL-10R1 dependent STAT signaling pathway. Furthermore, CD226 pAb administration *in vivo* effectively reduced the onset of EAE in mice by promoting IL-10 production and regulating T cell differentiation. More importantly, the onset and severity of EAE in CD226 knockout mice was reduced and the serum IL-10 expression levels in CD226 knockout mice with EAE were higher than that in control mice. These findings establish that CD226 plays an important role in mediating autoimmune diseases and IL-10 is an important factor that mediates the inhibitory effects of CD226 ligation on EAE. Our findings thus provide hitherto unrecognized mechanism of CD226 targeted therapy of EAE. In conclusion, our data suggest manipulating IL-10 and its relative signaling pathway could be a feasible therapeutic strategy to improve the efficacy of CD226 associated treatment of human autoimmune diseases and disorders.

Biography

Rong Zhang is currently a Doctoral candidate at the Fourth Military Medical University and is also performing research as a joint PhD in Department of Anatomy and Cell Biology, University of Pennsylvania, School of Dental Medicine. He has done some work concerning the genotype and treatment of genetic diseases and is now doing research mainly on immunoregulatory properties of mesenchymal stem cells on immune cells. He has published 2 papers in reputed journals.

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