

The role of TNFR pre-ligand assembly domain in autoimmune diseases

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TNF alpha is an important proinflammatory cytokine and exerts its effect by binding to TNF receptor (R)1 and 2. The first cysteine rich domain was named pre-ligand assembly domain (PLAD). PLAD is responsible for assembly of TNFR chain and TNF alpha binding. PLAD protein was found to block TNF alpha-mediated effects in vitro. TNFR1 not TNFR2 PLAD protein can inhibit arthritis-induced by TNE, LPS and bacterial DNA. TNFR1 not TNFR2 PLAD protein can significantly prevent collagen-induced arthritis and established collagen-induced arthritis. TNFR1 PLAD binds to TNFR1 and inhibit TNF alpha binding to TNFR and then block the downstream signal transduction. TNFR1 and TNFR2 PLAD protein specifically block signal transduction of TNFR1 or TNFR2, respectively. TNFR1 PLAD can inhibit TNF-mediated NF-kB activation, osteoclast activation. TNFR1 PLAD can reduce expression of iNOS. Furthermore, TNFR1 not TNFR2 PLAD can reduce skin injury but does not have benefit for kidney damage in lupus MRL/lpr mice. This data demonstrate that TNFR1 PLAD protein can inhibit inflammatory arthritis and lupus skin injury. It indicates that TNFR1 PLAD is an important therapeutic target in future.

Biography

Guo-Min Deng has completed his Ph.D from Gothenburg University in Sweden and postdoctoral studies from National Institutes of Health (NIH), MD. He was assistant professor of Medicine in Harvard Medical School, Harvard University. He has published more than 20 papers in reputed journals including two first author's papers in Nature Medicine and serving as an editorial board member of repute. At present he accepted a new position in China, professor and Chairman, Department of Microbiology and Immunology, Nanjing Medical University, Nanjing, China.

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