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Lupus serum IgG induces skin inflammation through TNFR1 signalling

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Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by high autoantibody levels and multi-organ tissue damage including kidney and skin. Cutaneous manifestations are frequent in patients with SLE, yet the etiology and pathogenesis of skin injury in SLE remains unclear. We reasoned that lupus serum containing high levels of autoreactive immunoglobulin (Ig) contributes to skin injury. Here we report that serum from SLE patients and lupus-prone mice induces skin inflammation following intradermal injection into normal mice. Lupus serum depleted of IgG failed to cause skin inflammation. Monocytes, but not lymphocytes, were found crucial in the development of lupus serum-induced skin inflammation, and lupus serum IgG was found to induce monocyte differentiation into dendritic cells (DCs). Tumor necrosis factor (TNF)-_ and TNF receptor (TNFR) 1, but not TNFR2, were required for the development of lupus serum-induced skin inflammation. TNFR1, not TNFR2, represented the main molecule expressed in the skin lesions caused by injected lupus serum. Our studies demonstrate that lupus serum IgG causes skin injury by involving the TNFR1 signaling pathway and monocyte differentiation to DCs. Furthermore, The treatment of TNFR1 inhibitor can reduce skin injury on lupus MRL/lpr mice. Accordingly, disruption of TNFR1-mediated signaling pathway and blockade of DC generation may prove of therapeutic value in patients with cutaneous lupus erythematosus.

Biography

Guo-Min Deng has completed his Ph.D in 2001 from Gothenburg University, Sweden and postdoctoral studies in 2006 from National Institutes of Health (NIH), Bethesda, MD, USA. He is a research leader in lupus animal study in Division of Rheumatology of Beth Israel Deaconess Medical Center and instructor in Medicine in Harvard Medical School. He has published more than 20 papers in reputed journals including two first-author papers in Nature Medicine in Rheumatology field and serving as an reviewer in several reputed journals.