Synopsis of Original Research Paper

Essential Role of p38 Mitogen-activated Protein Kinase in Contact Hypersensitivity.

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To elucidate the role of p38 mitogen-activated protein kinase (p38) in the pathogenesis of inflammation, a mouse contact hypersensitivity (CHS) model induced by 2,4-dinitro-1-fluorobenzene (DNFB) was used. Ear swelling was induced by challenge with DNFB, accompanied by infiltration of mononuclear cells, neutrophils and eosinophils, and a marked increase in mRNA levels of cytokines such as interleukin (IL)-2, interferon (IFN)-γ, IL-4, IL-5, IL-1β, IL-18 and tumor necrosis factor (TNF)-α in the challenged ear skin. Both ear swelling and the number of infiltrated cells in DNFB-challenged ear skin were significantly inhibited by treatment with SB202190, a p38 inhibitor. Furthermore, the DNFB-induced expression of all cytokines except IL-4 was significantly inhibited by treatment with SB202190. Ribonuclease protection assay revealed that the mRNA levels of chemokines such as IP-10 and MCP-1 in ear skin were markedly increased at 24 h after challenge with DNFB. The induction of these chemokines was significantly inhibited by treatment with SB202190. In p38α +/− mice, both ear swelling and infiltration of cells induced by DNFB were reduced compared with those in wild-type mice. However, induction of cytokines by DNFB was also observed in p38α +/− mice, although the induction of IFN-γ, IL-5 and IL-18 was typically reduced compared with that in wild-type mice. Challenge with DNFB slightly induced IP-10 and MCP-1 mRNA in p38α +/− mice, with weaker signals than those in SB202190-treated wild-type mice. These results suggest that p38 plays a key role in CHS and is an important target for the treatment of CHS.