学 位 論 文 の 要 旨

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主論文の題名

Thioredoxin suppresses airway inflammation independently of systemic Th1/Th2 immune modulation

主論文の要旨

Oxidative-stress plays an important role in the pathogenesis of asthma via the upregulation of local inflammatory mediators and/or promoting Th2-skewing during antigen sensitization. Thioredoxin (TRX), a 12 kDa redox-active protein with antioxidative property, has been recently shown to play a protective role in various inflammatory diseases. Using a mouse model of asthma, we show here that IL-13 and eotaxin production are decreased in TRX-transgenic (TRX-Tg) mice leading to reduced eosinophils recruitment and mucus metaplasia. The reduction in airway inflammation occurs without the attenuation of systemic Th2 immunity in that comparable levels of Th2-type cytokines and immunoglobulins were detected in LN and serum, respectively, from TRX-Tg and WT mice. Likewise, $CD4^+$ T cells from both strains of mice developed similar Th1 and Th2 responses *in vitro*. Asthmatic lungs of TRX-Tg and WT mice contained similar amounts of $GATA\text{-}3^+$ and $Foxp3^+$ T cells. Finally, production of macrophage migration inhibitory factor (MIF), an upstream modulator of airway inflammation, was significantly reduced in the lungs of TRX-Tg mice. Our data suggests that TRX suppresses airway inflammation by inhibiting MIF production thereby limiting the downstream recruitment of eosinophils to the lung independently of modulating systemic Th1/Th2 immunity.

（注）２，０００字以内にまとめて記入すること。