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The Role of Endoplasmic Reticulum Stress in Allergic Asthma

Abstract:

Chronic asthma has the ability to restructure the airways of the lung however the exact mechanism for this restructuring is unknown. The unfolded protein response (UPR) is known to play a critical role in many chronic inflammatory and autoimmune diseases. Therefore we analyzed the expression of UPR pathways in allergic airway inflammation and remodeling which are known to play an important role in the pathogenesis of asthma. Specifically we investigated the role of proteins ERp57 and ATF6 in the UPR by knocking down those genes in mice using small interfering RNA (siRNA). Mice exposed to the allergen house dust mite (HDM) demonstrated a robust activation of UPR markers (IRE1α, GRp78, ATF6, ERp57 and Chop) and caspase-3 (an indicator of programmed cell death) compared to the allergen ovalbumin. The mice treated with siRNA and challenged with HDM showed a decrease in UPR induction and active caspase-3 expression. Furthermore, siRNA mediated knock down of ATF6 and ERp57 led to decreased inflammation and fibrosis. Collectively our work suggests that HDM-induced UPR transducers ATF6 and ERp57 regulate two major components of asthma, airway inflammation and fibrosis. Therefore, the knockdown or inhibition of ER stress-transducers may provide a potential therapeutic avenue in chronic allergen induced asthma.