Actinobacillus pleuropneumoniae serotype 10 derived ApxI induces apoptosis in porcine alveolar macrophages

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摘要

Abstract

Actinobacillus pleuropneumoniae (AP) is the causative agent of swine pleuropneumonia, a fibrinous, exudative, hemorrhagic, necrotizing pleuropneumonia affecting all ages of pigs. Actinobacillus pleuropneumoniae exotoxins (Apx) are one of the major virulence factors of AP. Due to the complex nature of Apx toxins produced by AP, little is known regarding the interactions of individual species of Apx toxin with target cells. The objective of this study was to examine whether AP serotype 10-derived exotoxin, ApxI, caused apoptosis in porcine alveolar macrophages (PAMs) and to delineate the underlying signaling pathways. Isolated PAMs were stimulated with different concentrations of native ApxI and monitored for apoptosis using Hoechst staining, TUNEL, and DNA laddering assays. The ApxI-stimulated PAMs exhibited typical morphological features of apoptosis, including condensation of chromatin, formation of apoptotic bodies and DNA laddering. ApxI-induced apoptosis in a concentration- and time-dependent manner. Furthermore, to delineate the signaling events involved in ApxI-induced apoptosis, it was observed that caspase 3 was activated in ApxI-stimulated PAMs. Ablation of caspase 3 activity via specific inhibitors protected PAMs from apoptosis by ApxI. This study is the first to demonstrate that native ApxI causes apoptosis in PAMs at low concentrations and that these apoptotic events are mediated via a caspase 3-dependent pathway. These findings suggest a role of ApxI in AP infection as it might impair the host defense system through the induction of apoptosis in PAMs