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Title: Pulmonary immunostimulation with macrophage-activating lipopeptide-2 in influenza-A-virus infected mice increased survival of subsequent pneumococcal pneumonia

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Body: Rationale: Secondary bacterial infections in the course of seasonal influenza virus epidemics are associated with high morbidity and mortality, and Streptococcus pneumoniae is the most prevalent causal pathogen. Local immunosuppression due to pulmonary influenza virus infection has been discussed as major cause in the pathogenesis of secondary bacterial lung infection. Thus, specific local stimulation of the pulmonary innate immune system might improve host defense against secondary bacterial pathogens. Methods: Influenza-A/H1N1/PR/8/34-virus infected female C57BL/6 mice received the TLR-2 ligand macrophage-activating lipopeptide-2 (MALP-2) intratracheally 24h prior to transnasal infection with S. pneumoniae. Results: Intratracheal application of MALP-2 increased pro-inflammatory cytokine and chemokine release and enhanced recruitment of leukocytes, mainly neutrophils in the alveolar space of influenza virus infected mice. After secondary pneumococcal infection, Influenza-A-virus infected mice pretreated with MALP-2 showed increased survival rates compared with untreated influenza infected mice. Notably, levels of pro-inflammatory cytokines and leukocytes were comparable in bronchoalveolar lavages of virus infected mice treated with MALP-2 and untreated infected controls. Further, MALP-2 significantly reduced bacterial numbers in the lung tissue without changing pulmonary viral load. Conclusion: Local immunostimulation with MALP-2 in influenza virus infected mice improved pulmonary bacterial elimination and increased survival in secondary pneumococcal pneumonia.