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Title: "Lipoprotein-induced Th17 Responses Mediate *Mycoplasma pneumoniae* Vaccine Enhanced Disease in a Murine Model "

Abstract:
Mycoplasma pneumoniae is a significant human respiratory pathogen that causes over 2 million cases of community-acquired pneumonia and approximately 100,000 adult hospitalizations annually in the United States alone. Disease exacerbation caused by infection with *M. pneumoniae* after inoculation with different vaccine candidates has hampered the development of an efficacious vaccine against this significant pathogen. *M. pneumoniae* vaccine enhanced disease (VED) was first reported in human volunteers in the late 1960s and has been recently recapitulated in a murine model utilizing a live attenuated *M. pneumoniae* mutant, or crude antigenic extracts of *M. pneumoniae* as vaccine candidates. We hypothesized that *M. pneumoniae* lipoproteins play a role of in the induction of *M. pneumoniae* VED. We found that vaccination of BALB/c mice with *M. pneumoniae* lipid-associated membrane proteins (LAMPs) followed by challenge with *M. pneumoniae* resulted in VED associated with elevated IL-17A levels and elevated neutrophilia. Treatment of the LAMP fraction with lipoprotein lipase prior to vaccination eliminated disease exacerbation and reduced bacterial loads after infection indicating that the lipid moieties of *M. pneumoniae* lipoproteins are the factors responsible for *M. pneumoniae* VED. *M. pneumoniae* VED is associated with high levels of serum IL-17A. We neutralized IL-17A *in vivo* and found reduced lung lesions, and decreased neutrophilia, thereby indicating that lipid moieties of *M. pneumoniae* lipoproteins induce VED in an IL-17A dependent manner, potentially through exuberant neutrophil recruitment. We are in the process of further investigating the mechanism of IL-17A-mediated VED. Given our data to date, we believe that future *M. pneumoniae* vaccine constructs should not include native *M. pneumoniae* lipoproteins in their formulations.