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NLRP3 inflammasome plays an important role in the innate immune response to *Acinetobacter Baumannii* infection

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The opportunistic Gram-negative bacterium *Acinetobacter Baumannii* (AB) is a leading cause of life-threatening nosocomial pneumonia. Outbreaks of multidrug resistant (MDR)-AB belonging to International Clones (ICs) I and II with limited treatment options are major global health threats. However, the pathogenesis mechanisms of various AB clonal groups are understudied. Although inflammation-associated interleukin-1 β (IL-1 β) levels and IL-1 receptor antagonist polymorphisms were previously implicated in MDR-AB-related pneumonia in patients, whether inflammasomes has any role in the host defense and/or pathogenesis of clinically relevant *Acinetobacter Baumannii* infection is unknown. Using a sub-lethal mouse pneumonia model, we demonstrate that an extensively drug-resistant clinical isolate (ICII) of *Acinetobacter Baumannii* exhibits reduced/delayed early pulmonary neutrophil recruitment, higher lung persistence and most importantly, elicits enhanced IL-1 β /IL-18 production and lung damage through NLRP3 inflammasome, in comparison with *Acinetobacter Baumannii* type strain. *Acinetobacter Baumannii* infection-induced IL-1 β /IL-18 production is entirely dependent on NLRP3-ASC-caspase-1/caspase-11 pathway. Using Nlrp3 $^{-/-}$ mice infection models, we further show that while NLRP3 inflammasome pathway contributes to host defense against *Acinetobacter Baumannii* clinical isolate, it is dispensable for protection against *Acinetobacter Baumannii* type strain. Our study reveals a novel differential role for NLRP3 inflammasome pathway in the immunity against clinically relevant *Acinetobacter Baumannii* infections and highlights inflammasome pathway as a potential immune-modulatory target.

Biography

Neha Dikshit a Post-doctoral Researcher with extensive experience in deciphering host pathogen interactions during infectious diseases such as urinary tract infections and pneumonia. She has been published in high impact journals and has attracted commentaries in journals such as *Nature Urology*. She has presented her research in various national/international conferences and received several awards.

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