

***Streptococcus pneumoniae* respiratory infection in mice genetically selected for exacerbated and low acute inflammatory responses**

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Streptococcus pneumoniae is the main cause of respiratory infections, leading to the death of 1 million children under the age of 5, per year, worldwide. Acute inflammation is an important innate response against pneumococci that may play a role in the resolution of infection. Here, an invasive respiratory challenge with a serotype 3 pneumococcal strain was studied in two outbred mice lineages, genetically selected for exacerbated (AIRmax) and low (AIRmin) acute inflammatory responses. Susceptibility to pneumococcal infection was evaluated by the intranasal inoculation of the ATCC6303 pneumococcal strain and the evolution of infection was analyzed by CFU counting in the lungs and bronchoalveolar lavage fluids (BALF). Infiltration of cells after the challenge was evaluated in BALF by flow cytometry. The levels of cytokines were evaluated by LUMINEX. After the respiratory challenge, 100% of AIRmin mice died. Conversely, only 36,4% of AIRmax mice succumbed the infection. Lower levels of bacteria were observed in the respiratory tract of AIRmax mice at different time points post-challenge when compared to AIRmin mice. Infiltration of neutrophils (F4/80⁻CD11b⁺Ly6G⁺) was observed at 12h post-challenge in the respiratory tract of AIRmax mice, but these numbers were reduced at 48h-post challenge. AIRmin mice showed moderate infiltration of neutrophils, but the numbers increased progressively after the challenge. The levels of alveolar macrophages (AM, F4/80⁻CD11c⁺CD11b⁻) decreased after the challenge in AIRmax mice, whereas these cells remained unaltered in AIRmin mice. Characterization of the AM showed that cells expressing the CD206 mannose receptor were higher in AIRmin mice at 48h after the challenge, when compared to AIRmax mice. A marked reduction in CD80⁺ AM in AIRmax mice and an increase in CD86⁺ AM in AIRmin mice at 48h post-challenge was observed. Pro-inflammatory cytokines (IFN- γ , IL-6 and TNF- α) increased in the BALF of AIRmax mice after the challenge, but the levels returned to the basal at 48h. Conversely, these cytokines remained high at 48h post-challenge in AIRmin mice. The levels of the anti-inflammatory cytokine IL-10 increased at 12h post-challenge in all AIRmin mice, whereas a variability of IL-10 secretion was observed in AIRmax mice. Our data suggest that a different balance in cytokines together with different populations of AM may be related to the susceptibility to pneumococcal infection in this model.

Keywords: *Streptococcus pneumoniae*; inflammation; immune response.

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