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Title: Role of basophils in immunological memory responses to pneumococcal protein antigens and S. pneumoniae infections in mice

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Body: Basophils have been shown to play an important role in memory immune responses to vaccination with pneumococcal protein antigens. We here examined whether increased basophil counts would provide increased humoral immune responses and thus protection against S. pneumoniae. Mice underwent primary and secondary immunization with pneumococcal surface protein A (PspA). Prior to secondary immunization, mice were treated with IL-3 or IL-3 complexed with α-IL-3 antibody (IL-3 complex) to increase basophil pool sizes. Subsequently, mice were challenged with invasive S. pneumoniae and developing bacteremia and survival were monitored over time. Treatment of mice with IL-3 and even more so IL-3 complex resulted in strongly expanded basophil pool sizes and significantly increased PspA-specific antibody titers that protected mice from pneumococcal sepsis but unexpectedly did not improve their survival. However, passive immunization of mice with antiserum of IL-3 complex-treated, PspA-immunized mice significantly improved their survival after challenge with invasive S. pneumoniae. These data show that although IL-3 complex treatment of mice boosts their basophil counts and protects mice from pneumococcal sepsis, it still exerts severe side-effects in mice after intratracheal challenge with S. pneumoniae, and as such does not offer as adjuvant-independent approach to improve lung protective immunity against lung-tropic pathogens.