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Title: A decisive role for B cells in priming of allergy and tolerance by preconceptional immunization of the mother

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Body: Antigen challenge in early life, even before birth has been shown to crucially influence an individual's susceptibility to allergy and asthma. In this context, we showed in a murine asthma model that maternal tolerization by mucosal allergen application shortly before pregnancy induces tolerance in the offspring via transfer of immunoglobulins and induction of tolerogenic T cells. We aimed to further decipher the role of B cells in this context. In an ovalbumin-based murine asthma model, we analyzed the effect of preconceptional maternal tolerization on the offspring's asthma risk and compared B cell knock out (µMT) versus wild type mice. As shown before, preconceptional maternal tolerization protected the progeny of wild type mice, which showed reduced airway inflammation, BALF cell count, ova-specific IgG, IgE and Th2 cytokines as compared to the offspring of non tolerized controls. In contrast, in B cell knock out mice preconceptional tolerization led to an aggravation of the offspring's asthmatic phenotype, where higher BALF cell count and stronger lung inflammation, airwayhyper reactivity, and Th2 cytokines occurred. The transfer of B cells into µMT dams before tolerization and mating had a tolerogenic effect in the F1 generation. Furthermore, preconceptional tolerization and cross-mating of µMT and wild-type mice revealed a significant correlation between the offspring's B cells and immunoglobulins on the one hand and regulatory T cells and tolerance induction on the other hand. In summary, our data show a crucial role for B cells in the maternofetal priming towards allergens.