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Intranasal instillation of antigen loaded DC induces rapid and long lasting antigen specific immune response and non responsiveness to aerosol challenge

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We evaluate the impact of a single intranasal sensitization with antigen loaded DC subsets on humoral immune responses, T cell cytokine production and allergen induced broncho-alveolar lavage (BAL) cellular infiltrate. BALB/c bone marrow derived DC were generated under the agis of Flt-3 ligand (FL-DC) or GM-CSF (GM-DC) containing plasmacytoid DC and myeloid DC, respectively. DC were loaded with OVA (1mg/ml) for the final 12 hrs in presence or absence of CpG-ODN (1μM). OVA loaded DC (10^6/25μl) were administered by single intranasal installation and OVA specific humoral response was determined. BAL analysis was performed 24hrs after 2xOVA aerosol challenge (d166/167). IL-4, IL-5 and IFN-γ release of MACS sorted CD4 splenocytes (d168) was analyzed by ELISA. Mice sensitized with OVA loaded DC developed a rapid (earliest time point d14) and long lasting (>130d) Ab response. CpG activated FL-DC induced a solid IgG2a response (Th1 dominated) but failed to induce IgE or IgG1. In contrast, GM-DC induced a mixed profile (IgG2a, IgG1 and IgE). CpG activation led to a shift with increased IgG2a and decreased IgG1 and IgE. Despite elevated OVA-specific IgE/IgG1 levels, mice sensitized by OVA loaded DC when challenged with OVA aerosol did not develop allergic inflammation of the lung (while control mice sensitized i.p. with OVA/alum did). Splenic CD4 T cells obtained from DC-sensitized mice 24 hrs after aerosol challenge demonstrated high level of spontaneous cytokine production, suggesting a long lasting memory effect also on the cellular level. Consistent with the humoral response, CD4 cells from GM-DC sensitized mice produced significantly more IL-4 and IL-5 spontaneously and upon OVA restimulation as cells obtained from FL-DC sensitized mice. In conclusion, a single intranasal administration of antigen loaded DC induces a rapid and long lasting humoral and cellular immune response. Despite high levels of antigen specific IgE and IgG1, animals are non responsive to aerosolized antigen challenge, suggesting that intranasal administration of antigen loaded DC may convey protection against inflammatory responses to harmless airborne allergen.