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POSTER PRESENTATION Open Access

A bacterial immune-prophylactic approach against asthma for infants and children

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Objective/purpose

The prevalence of asthma in Canada (and worldwide) has been increasing over the last 20 years with currently over 3 million Canadians suffering from it. Asthma appears to result from environmental influences directing a genetically predisposed host towards a pro-allergic, Th2-dominated immune response. Studies in humans and animals identify the time around birth and early infancy as a period during which the decision of pro-allergic versus non-allergic immune responses to environmental stimuli appears to be made. Presumably this is the reason why the incidence of first diagnosis is highest in infants and children, although asthma can occur at any age. The very fact that all three components (environmental, genetic and developmental) are necessary for asthma to occur also offers the opportunity to intervene early in life through *e.g.* vaccination against allergies. Vaccination as a strategy to prevent or cure asthma is a tremendous opportunity. An ideal vaccine would be one that prevents or cures asthma after only one dose and protects for life. It is well established that the whole heat-killed bacterium *Listeria monocytogenes* (*Lm*) given as an adjuvant along with model allergens effectively prevent allergic sensitization and/or allergic inflammation in adult animals following local allergen challenge. We have successfully developed a novel, live, but highly attenuated neonatal vaccine platform based on the bacterium *Listeria monocytogenes* (*Lm*). Our published data suggest that our *Lm*-based vaccine platform is capable of inducing strong anti-allergic immune responses for an entire life only after one dose given to newborn mice. Now we have investigated whether our *Lm*-based vaccine platform will provide protection from allergic reactions upon challenge with the allergen, after only one immunization given around birth. Our specific aim addressed the following objective: **Do our *Listeria monocytogenes* vaccine strains producing model allergen ovalbumin (OVA) and inducing a strong Th1 response, prevent allergic reactions upon challenge with the allergen in a neonatal mouse model?**

Methods

We focused on assessing protection against OVA-allergic reactions in mice that were immunized *i.p.* as newborns with heat-killed *Lm* vs. those vaccinated with our live-attenuated *Lm*-OVA or *Lm* or NaCl alone. We have coupled immune-focused analysis (total and differential counts of broncho-alveolar lavages, OVA-stimulation assays on lung cells and splenocytes, measurement of IgG1, IgE and IgG2a levels in serum) with the histopathological examination of lungs. Furthermore, we started to delineate the molecular mechanisms (Realtime PCR of immunological-relevant genes) underlying the surprisingly high efficacy of the live-attenuated *Lm*-based vaccine approach.

Findings

Our novel *Lm*-based vaccine platform was particularly safe and very-well tolerated in newborns. Using this live-attenuated platform in comparison to the already established heat-killed *Lm* approach in adult mice, we determined that mice immunized as newborns with our live *Lm* vaccine platform producing ovalbumin were indeed entirely protected from allergic OVA-sensitization after just one immunization given around birth. Furthermore, our live *Lm*-based approach was far superior to heat-killed *Lm*-based approaches, as it resulted in an almost complete inhibition of the recruitment of inflammatory cells into lungs of immunized mice after OVA-challenge. Interestingly, mice immunized with our live attenuated *Lm* strain not expressing OVA but sensitized and challenged with OVA showed inhibition of the

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recruitment of only eosinophils, but not inhibition of any of the other inflammatory cells into the lungs upon challenge.

Deliverables

The analysis of our single dose *Lm*-vaccination strategy in mice represents the first attempt to truly test the ability of a neonatal vaccine to prevent allergic reactions in early in life, but for the entire life. We furthermore expect to be able to optimize this approach to apply our *Lm*-based vaccines against food allergies or other clinically relevant forms of allergic disease as an immune-modulatory based therapeutic intervention in previously sensitized individuals.

Relevance

It offers immediate translation into human vaccine design and current immunization policies against asthma, as *Listeria monocytogenes* has already been approved for human applications.

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