Seminar's informations Anya Jones and Kyle Mincham

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Biopolymères Interactions Assemblages

Reduced susceptibility to allergic airways disease in BALB/c offspring following maternal therapeutic immunomodulator (OM85) treatment during gestation

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Abstract

Seminal studies of traditional farming families across Europe indicate that maternal exposure to benign environmental microbial stimuli whilst pregnant can potentially play a key role in mitigation of asthma risk in their offspring. The potential to harness this environmental phenomenon by therapeutically mimicking farm microbial exposure in pregnant women therefore presents a novel strategy in preventing the development of allergic disease in children.

We aimed to investigate the therapeutic potential of an immune modulating agent (OM85) in protecting against development of allergic asthma in offspring via treatment of the pregnant mother, and to elucidate the cellular and molecular mechanisms that promote protection.

We employed a pregnant BALB/c mouse model. OM85 was given orally to pregnant BALB/c mice selected at random for the last half of gestation; controls were left untreated. All offspring were experimentally sensitized to ovalbumin and exposed to aerosol challenge. We determined bronchoalveolar lavage cellular and molecular profiles, airways tissue cellular responses and profiles via multi-colour flow cytometry, IgE titres and airways hyperresponsiveness to methacholine.

Sensitized and allergen aerosol challenged offspring from OM85 treated mothers had attenuated airways eosinophil infiltration and diminished methacholine responsiveness compared to equivalent offspring from non-treated mothers. Flow cytometric analysis identified a significant increase in $CD103^+$ conventional dendritic cells within peripheral lung tissue of sensitized and aerosol challenged offspring from OM85 treated mothers, but reduced expression of the activation marker MHC II. Furthermore, these offspring displayed increased $Foxp3^+$ regulatory T cells (Treg) within the tracheal mucosa, and their mucosal Tregs exhibited increased CD69 and CD152 expression.

The susceptibility to allergic airways disease in mice sensitized and aerosol challenged during the early post-weanling period is thus markedly attenuated by previous maternal OM85 treatment during gestation, and this effect appears associated with an increase in the frequency and functional capacity of regulatory cell populations within the airways mucosa. Our findings suggest that therapeutic treatment of mothers during gestation with immune modulating agents may be a viable strategy to promote fetal immune training in utero and improve the outcomes of allergic disease onset in later life.