Antigen-specific immune therapy in autoimmune disease and allergic asthma

Brief project description:
We have earlier shown that mucosal administration, e.g. by the sublingual route, can efficiently induce so-called oral tolerance and thereby suppress inflammatory reactions and tissue damage in models of autoimmune disease, such as autoimmune arthritis, encephalitis and diabetes (1-4), and defined the mechanisms for the effects (5-8). We recently further described the importance of B lymphocytes in induction of antigen (Ag)-specific oral tolerance and the associated increase in CD4+Foxp3+ regulatory T cells (Tregs) after mucosal administration of Ag conjugated to cholera toxin B subunit (CTB) (8,9). We are now further assessing the effects of B cells pulsed \textit{in vitro} with Ag/CTB conjugate on the induction of Ag-specific Tregs both \textit{in vitro} and after adoptive transfer \textit{in vivo}. We find a strong increase in Tregs when naive T cells are co-cultured \textit{in vitro} with B cells pulsed with OVA/CTB, and the generated Tregs can effectively suppress CD25-CD4+ effector T cells (Teffs) in secondary \textit{in vitro} cultures. A strong increase in Tregs is also seen \textit{in vivo} in recipients after adoptive transfer of Ag/CTB pulsed B cells. Further, adoptive transfer of B cells pulsed with myelin oligodendrocyte glycoprotein (MOG) peptide35-55 conjugated to CTB efficiently (i) suppresses MOG-specific T cell proliferation and IL-17 and IFN-gamma production, (ii) increases Foxp3+CD4+ Tregs in draining lymph nodes and (iii) protects against the development of experimental autoimmune encephalomyelitis (EAE); similar effects are seen also when the B cell treatment was given “therapeutically” to mice with already on-going EAE. Our results show that B cells pulsed \textit{in vitro} with relevant Ag/CTB conjugates followed by reinfusion of the treated B cells can be used to induce Ag-specific suppression of autoimmune disease.

We are also addressing similar questions in allergic asthma, where we postulate that effective immunotherapy can be achieved by mucosal administration of allergen-CTB fusion proteins that can effectively induce allergen-specific oral tolerance together with blocking secretory IgA antibodies in the respiratory mucosa.

Research group and collaborations:
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Selected references:


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Harbin Medical University, China Master Science 1984 Neuro-ImmunoLgy
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Positions and Honors

1977-1981 Physician (Neurologist), Department of Neurology, Harbin Medical University,

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1988 Excellent student for overseas study approved by National Intellectual-Import
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1989-1992 Fellow, Department of Neurology, Huddinge University Hospital (Karolinska
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1993-1995 Postdoctor, Department of Microbiology & Immunology, University of
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1995-1998 Scientist, Department of Microbiology & Immunology, University of Gothenburg
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Additional recent publications of importance to the field

Intranasal administration of a schistosoma mansoni glutathione S-transferase-cholera toxoid
experimental autoimmune arthritis by nasal administration of a type II collagen-cholera toxoid
Fujiyoshi K, Mestecky JF, Pierreffite-Carle V, Rask C, Sun J-B. Mucosal immunity and
administration of cholera toxin B subunit conjugated to myelin basic protein protects against


