

# ANTIGEN-SECRETORY IgA IMMUNE COMPLEXES ARE RETRO-TRANSPORTED INTO MOUSE PEYER'S PATCHES: IMMUNOTARGETING TO DENDRITIC CELLS

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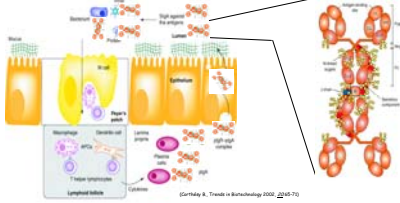
## Introduction

Peyer's patches (PP) represents the primary site for uptake and presentation of ingested antigens in the intestine. Antigens including bacteria and viruses are sampled by M cells, which pass them to underlying antigen-presenting cells including dendritic cells (DC) and macrophages.

This triggers activation of T helper lymphocytes.

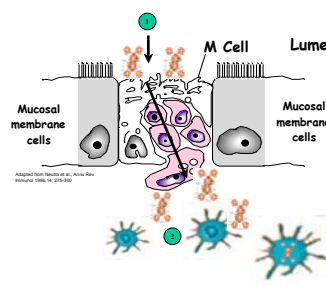
Induction of mucosal T cell response is important for the production of secretory IgA (SIgA), the chief antibody at mucosal surfaces. SIgA consists of two monomeric IgA units, and two additional polypeptides: J chain and secretory component.

Multiple molecular forms of SIgA are obtained by heterologous expression systems developed in our laboratory



## Facts

Previous studies in the laboratory have shown that administration of SIgA into mouse intestinal loop binds specifically to M cells, enter into PP, and are eventually internalized by dendritic cells.



1 - Binding of SIgA to apical membrane of mouse M cell [Mantis N. et al., J. Immunol. 2002, 169:1844-51].

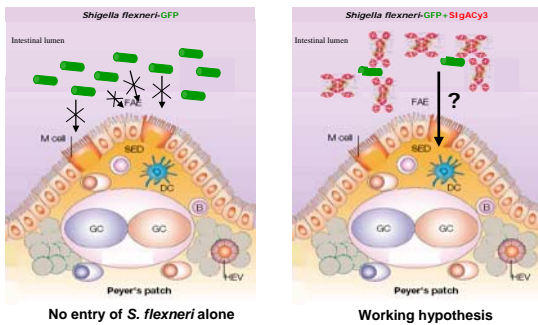
2 - Binding and internalization of SIgA by PP DC both in vivo and in vitro [Rey J. et al., J. Immunol. 2004, 172:3026-33].

The specific internalization of SIgA by PP DC in vivo suggests that this event has a physiological relevance for mucosal homeostasis

## Aim of this work:

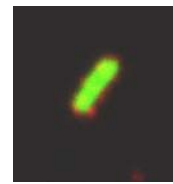
To explore the biological relevance of the uptake of SIgA by Peyer's patch dendritic cells in mucosal homeostasis

The model: Could SIgA serve as a carrier to deliver antigens to Peyer's patch dendritic cells?

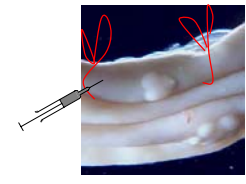


## Tools

In vivo: Intra-intestinal loop injection of immune complexes (SIgAcy3 + S. flexneri-GFP)



SIgA-S. flexneri immune complexes (I.C.)



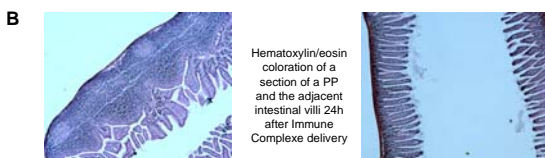
Injection of I.C. or S. flexneri into a mouse intestinal loop containing a PP

Ex vivo: 25-minute incubation of SIgAcy3 with highly enriched DC freshly isolated from mouse PP, followed by surface labeling

## in-vivo



SIgA-*Shigella flexneri*-GFP complexes were found in PP after delivery in intestinal loops in contrast to *Shigella flexneri* alone which do not penetrate the mouse PP. These Immune complexes were captured by Peyer's patch Dendritic Cells



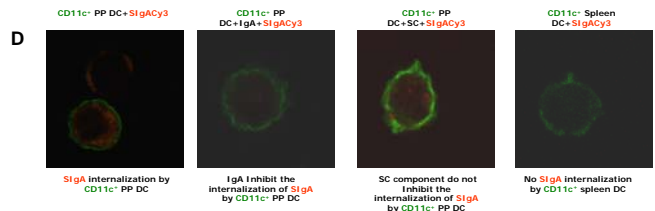
The entry of *S. flexneri* in association with SIgA does not lead to a tissue damage; no artifactual diffusion within the epithelium

## Results

## ex-vivo



The SIgA was internalized by myeloid (CD11c<sup>+</sup>/CD11b<sup>+</sup>) DC and bound to the surface of the new CD11c<sup>+</sup>/CD19<sup>+</sup> DC subtype, but no internalization by or binding to the CD11c<sup>+</sup>/CD8<sup>+</sup> lymphoid DC subtype was observed



The internalization and binding of SIgA by Peyer's patch dendritic cells is mediated by the IgA moiety of the molecule. This putative IgA receptor appears to be specifically expressed by dendritic cells from Peyer's patches

## Conclusions

- In addition to immune exclusion, our results show that SIgA can serve as a carrier to deliver antigens to PP DC
- The SIgA delivers antigens to Peyer's patch dendritic cells in a non-inflammatory manner
- After retro-transport into Peyer's patches, SIgA is internalized by the myeloid dendritic cell subtype and/or binds to the new subtype expressing both CD11c and CD19 markers. This interaction appears to be mediated by an IgA receptor specifically expressed by dendritic cells from Peyer's patches