OC09 - **Defective purinergic control of T follicular helper cells alters the IgA-targeted gut microbiota and host metabolism**

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Abstract: The secretory immunoglobulin A in mammalian gut contributes to host physiology and immune homeostasis by shaping microbiota composition. Deletion of P2rx7, encoding for the ATP-gated ionotropic P2X7 receptor, leads to T follicular helper (Tfh) cells expansion in the Peyer's patches of the small intestine, dysregulated germinal center (GC) reactions and enhanced secretion of intestinal IgA; the resulting alterations of the gut microbiota in turn affects host metabolism.

Through amplicon-based 16S rRNA gene sequencing of fecal IgA-coated bacteria (IgA-SEQ), this study defines bacteria normally residing in the small intestine that are selectively targeted by IgA and correlate with immunologic and metabolic alterations in P2rx7$^{-/-}$ mice.

Different members within the IgA coated and uncoated microbiota correlate with the obese - like phenotype of P2rx7$^{-/-}$ mice. Accordingly, we observed a dramatic increase in the abundance of IgA-coated *Lactobacillus* in P2rx7$^{-/-}$ mice. Oral administration of intestinal *Lactobacillus* isolates from P2rx7$^{-/-}$ mice in wild-type animals resulted in altered glucose homeostasis. Thus, P2X7 mediated control of Tfh cells activity plays a crucial role in shaping a beneficial intestinal microbial community for host metabolism by regulating T-dependent IgA response towards selected members of the gut microbiota.