Microbiota-mediated shaping of gut secretory IgA in systemic metabolism

Lisa Perruzza[1]*, Francesco Strati[1#], Tanja Rezzonico-Jost[1], Ivo Kwee[1], Diego Morone[1], Hai Li[2], Paolo Sonego[3], Claudio Donati[3], Pietro Franceschi[3], Victor Greiff[4], Andrew Macpherson[2] and Fabio Grassi[1]

*lead presenter: lisa.perruzza@irb.usi.ch

[1]Institute for Research in Biomedicine, Faculty of Biomedical Sciences, Università della Svizzera italiana (USI), Bellinzona, Switzerland
[2]Maurice Müller Laboratories (Department of Biomedical Research), Universitätsklinik für Viszerale Chirurgie und Medizin Inselspital, University of Bern, Bern, Switzerland
[3]Computational Biology Research Unit, Research and Innovation Centre, Fondazione Edmund Mach, San Michele all'Adige (TN), Italy
[4]Department of Immunology, University of Oslo, Oslo, Norway
#present address: Mucosal Immunology lab, Department of Experimental Oncology, European Institute of Oncology (IEO), Milan, Italy

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The human gastrointestinal (GI) tract is a complex ecosystem, in which all the three domains of life (Archaea, Bacteria and Eukarya) and Viruses co-exist in close association with the host. This microbial community, referred to as the gut microbiota, has co-evolved with the host in a mutualistic relationship that influences many physiological functions such as energy harvesting, development and function of the immune system.

The equilibrium between the gut microbiota and the host is a key element in human health. In fact, alterations in the composition of the microbial community, termed dysbiosis, have been associated to an increasing number of medical conditions. Central in the homeostatic relationship between immune system and gut microbiota is the local production of secretory immunoglobulin A (SIgA).

Adenosine triphosphate (ATP) is a ubiquitous extracellular messenger, which activates purinergic receptors in the plasma membrane termed P2 receptors. The P2X7 receptor subtype is a widely expressed ATP-gated nonselective cationic channel; in the Peyer's patches of the small intestine, it regulates T follicular helper (Tfh) cell abundance and thereby T dependent SIgA.

Depletion of bacteria-derived eATP in the small intestine results in enhanced SIgA response, altered enterocyte transcriptional regulation and dysregulated systemic metabolism. We hypothesize eATP constitutes an inter-kingdom signalling molecule with an important function in shaping a beneficial gut ecosystem for host metabolism via modulation of the SIgA response.