OC05 - **ATP released by intestinal bacteria limits the generation of protective IgA against enteropathogens**

Lisa Perruzza[1,†], Michele Proietti[1,†,‡], Daniela Scribano[2,3], Giovanni Pellegrini[4], Rocco D'Antuono[1], Francesco Strati[1], Marco Raffaelli[1], Santiago F. Gonzalez[1], Marcus Thelen[1], Wolf-Dietrich Hardt[5], Emma Slack[5], Mauro Nicoletti[2] and Fabio Grassi[1,6,7,*]

[1]Institute for Research in Biomedicine, Università della Svizzera Italiana, 6500 Bellinzona, Switzerland

[2]Department of Experimental and Clinical Sciences, University "Gabriele D'Annunzio", 66100 Chieti, Italy

[3]Departement of Public Health and Infectious Diseases, University ''La Sapienza'' of Rome, 00185 Rome, Italy

[4]Laboratory for Animal Model Pathology, Institute of Veterinary Pathology, Vetsuisse Faculty, University of Zurich, 8057 Zurich, Switzerland

[5]Institute of Microbiology, ETH Zürich, 8093 Zürich, Switzerland

[6]Istituto Nazionale Genetica Molecolare ''Romeo ed Enrica Invernizzi'', 20122 Milan, Italy

[7]Department of Medical Biotechnology and Translational Medicine (BIOMETRA), Università degli Studi di Milano, 20129 Milan, Italy

**Correspondence to: fabio.grassi@irb.usi.ch*

[†]These authors contributed equally to this work

[‡]Present address: CCI-Center for Chronic Immunodeficiency, Universitätsklinikum Freiburg, 79106 Freiburg, Germany

lisa.perruzza@irb.usi.ch

In the small intestine, T cell dependent secretory IgA originates in PPs within the ileal mucosa. We previously demonstrated that adenosine triphosphate (ATP) released by commensals in the small intestine limits high affinity IgA responses via ionotropic P2X7 receptor expressed in T follicular helper (Tfh) cells of the Peyer's patches (PPs). In the small intestine of mice housed in specific pathogen free (SPF) facility we detected micromolar concentrations of endoluminal ATP that was barely detectable in germ-free mice. ATP releasing bacteria were identified both in humans and mice. Accordingly, we detected extracellular ATP in cultures from different bacterial strains isolated from ilea of our mouse colony. Here we show that abrogation of endoluminal ATP release by bacteria elicits more potent secretory IgA response and can confer enhanced protection to Salmonella infection in vaccination protocol with attenuated *Salmonella thyphimurium*. Therefore, modulation of signalling by bacterial ATP in vaccination protocols can promote effective mucosal protection from enteropathogens.