Foraging on the host: Uncovering metabolic host-gut microbiota interactions at the single cell level

DAVID BERRY[1]*, BÄRBEL STECHER[2], ARNO SCHINTLMEISTER[3], JOCHEN REICHERT[1], ISABELLA RAUCH[4], THOMAS DECKER[4], BIRGIT WILD[5], WOLFGANG WANEK[3,5], ANDREAS RICHTER[3,5], ALEXANDER LOY[1] AND MICHAEL WAGNER[1,3]

[1]Division of Microbial Ecology, Department of Microbiology and Ecosystem Science, University of Vienna (*correspondence: berry@microbial-ecology.net)
[2]Max von Pettenkofer Institute of Hygiene and Medical Microbiology, Ludwig Maximilian University of Munich
[3]Core Facility for Advanced Isotope Research, Faculty of Life Sciences, University of Vienna
[4]Department of Microbiology, Immunobiology and Genetics, Max F. Perutz Laboratories, University of Vienna
[5]Division of Terrestrial Ecosystem Research, Department of Microbiology and Ecosystem Science, University of Vienna

The mammalian gut secretes insoluble mucus to produce a physical barrier that shields tissue from contact with the luminal microbiota. In this study, we employed a novel *in vivo* stable isotope labeling approach in mouse models to explore microbial utilization of host-derived compounds. Intravenously injected stable isotope-labeled threonine (^{13}C, ^{15}N) was metabolized by the epithelial tissue and appeared in lumen biomass by 8 hours. Individual bacteria enriched in isotope label were identified with single cell-resolution secondary ion mass spectrometry (NanoSIMS) combined with fluorescence *in situ* hybridization (FISH) using specific rRNA-targeted probes. Two species, *Akkermansia muciniphila* and *Bacteroides acidifaciens*, were identified as key degraders, though their activity was dependent on composition of the background microbiota.

This research presents a new approach for shedding light on interactions between host and its intestinal microbiota by tracking compound secretion using stable isotopes and highlights that single cell analysis using high resolution mass spectrometry combined with FISH allows for unprecedented insight into the functioning of this symbiosis *in vivo*.