OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Clinical & Cellular Immunology
October 15-17, 2013 Hampton Inn Tropicana, Las Vegas, NV, USA

Lactobacillus rhamnosus GG down regulates autophagy in intestinal mononuclear cells to enhance effector T cell responses induced by rotavirus vaccine

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Autophagy has been reported to attenuate adaptive immune responses by destabilizing the immunologic synapse between dendritic cells and T cells, leading to reduced effector T cell activation. Our previous studies showed that probiotic *Lactobacillus rhamnosus* GG (LGG) suppresses virulent rotavirus-induced autophagy in ileal epithelial cells of gnotobiotic pigs. In addition, LGG as mucosal adjuvant significantly enhanced the virus specific IFN-γ producing T cell responses to an attenuated rotavirus (AttHRV) vaccine. Our hypothesis is that LGG promotes effector T cell responses by down-regulating autophagy to stabilize immunologic synapse. In the present study, we investigated the effect of LGG on autophagy in ileal mononuclear cells (MNC) of human gut microflora associated gnotobiotic pigs vaccinated with the AttHRV2x vaccine and fed with or without LGG. MNC from ileum of Gn pigs euthanized on post-AttHRV inoculation day 28 were cultured with lysosomal inhibitor bafilomycin A1 for 0, 2 or 4 hrs to measure the autophagy flux. MNC were lysed and analyzed by immunobloting using anti-LC3 and p62 antibodies. We demonstrated that total cellular LC3-I and LC3-II levels were reduced in LGG fed pigs compared to non-LGG groups. The LC3 turnover (difference in LC3-II level between inhibitor treated and non-treated cells) was also reduced in the LGG fed group. There is a slight increase in p62 level. These data showed that LGG down-regulated autophagy flux in intestinal MNC. Further studies are underway to identify cell types involved and the mechanisms. This study will improve our understandings of the mechanisms for the immunostimulating effects of probiotic adjuvants.

Biography

Lijuan Yuan completed her Ph.D. at The Ohio State University and post-doctoral training at Laboratory of Infectious Diseases, NIAID, NIH. She is an Assistant Professor at the Department of Biomedical Sciences and Pathobiology at Virginia Polytechnic Institute and State University. She has published 62 peer-reviewed papers, reviews and book chapters, serves as *ad-hoc* reviewer for 23 different journals and as editorial board member of six journals. She serves on special review panels for NIH, NSF and as *ad-hoc* reviewer for Wellcome Trust and several other international funding agencies. She is the recipient of Pfizer Award for Research Excellence 2011.

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