Animal gut is colonized with a huge number of commensal bacteria, collectively called gut microbiota; for example, the adult human colon hosts some 40 trillion microbes classified into several hundred species. These microbes closely interact with each other and further with the host to establish the unique and complicated gut ecosystem, which deeply impacts our physiology and pathology including host defense and immunity. However, the underlying mechanisms of how gut ecosystem influences host defense and immune system have poorly understood.

We have proposed an integrated omics approach, where different levels of exhaustive analyses such as (meta)genomics, (meta)transcriptomics and metabolomics are combined. By applying this approach, we have shown that Bifidobacterium-derived acetate can modify gene expression of the colonic epithelium to confer resistance against enterohemorrhagic Escherichia coli 0157, which ultimately protects mice from O157-infectious death.

We have also found that butyrate produced by the gut microbiota can enhance differentiation of colonic regulatory T (Treg) cells from naïve T cells, via epigenetic modification through its histone deacetylase inhibitory ability.

Multiple sclerosis (MS) is a demyelinating disease. While its precise pathogenesis is not clear, it is thought to be an autoimmune disorder including the host genetic factors and environmental factors; among the latter is the gut microbiota. We are studying experimental autoimmune encephalomyelitis (EAE), an animal model for MS with the integrated omics approach, and the results will also be discussed.

**ABSTRACT**

INTEGRATED OMICS APPROACH FOR UNDERSTANDING THE GUT ECOSYSTEM AND DEMENTIA

**SPEAKER**
Dr. HIROSHI OHNO  
Group Director, Laboratory for Intestinal Ecosystem  
RIKEN Center for Integrative Medical Sciences

**HOST:**  
Department of Infection and Immunity

**RESPONSIBLE LIH SCIENTIST:**  
Dr. Mahesh DESAI  
(mahesh.desai@lih.lu)

www.lih.lu

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* Opposite Luxembourg Institute of Health, House of BioHealth, 29, rue Henri Koch, L-4354 Esch/Alzette