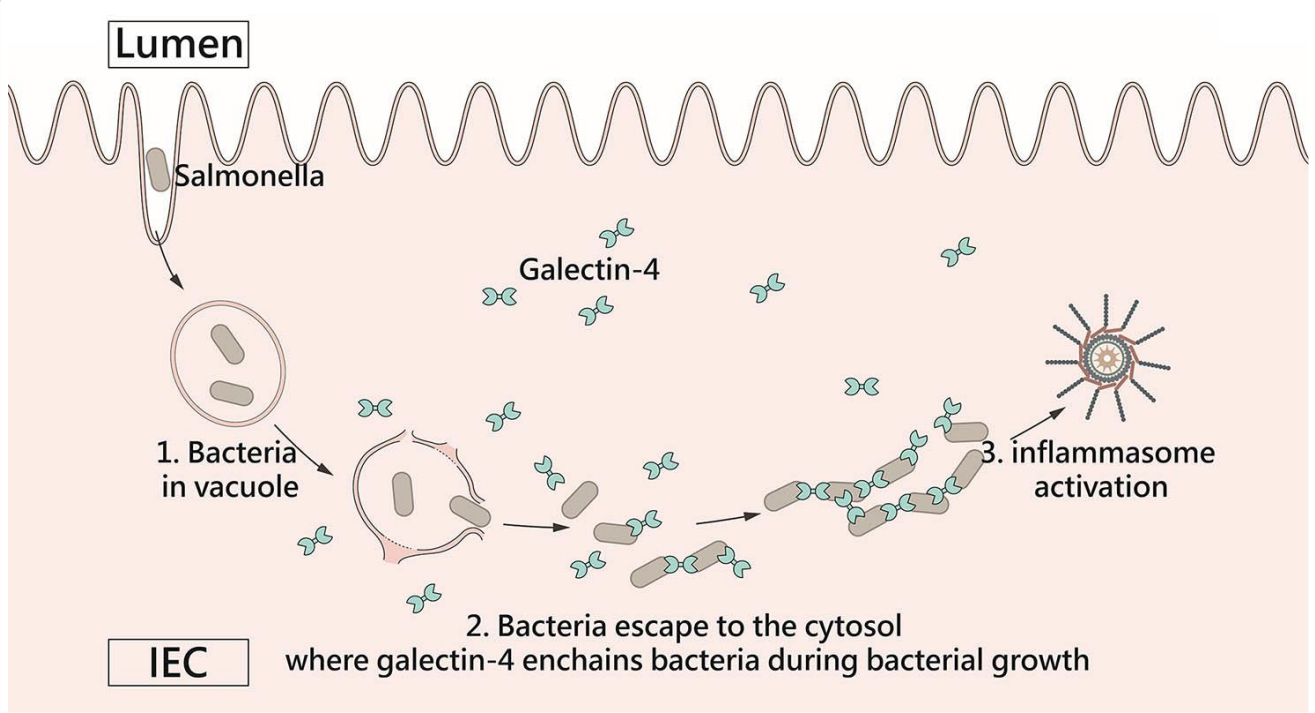
A critical molecule for suppressing gastrointestinal infections through intracellular binding to microbial glycans

Intestinal epithelial cells (IECs) are constantly exposed to many commensal microbes and are the primary sites of contact with invading and non-invading enteric pathogens. Galectins are a major type of glycan-binding protein (GBP) that differ from other GBPs by being located mainly intracellularly. These proteins can decode host-derived complex glycans and are involved in various biological responses. Dr. Fu-Tong Liu (Academician, Academia Sinica) is a pioneer and leader in galectin research. Here, we show that galectin-4, a member of the galectin family of animal GBPs, is specifically expressed in gastrointestinal epithelial cells and known to be able to bind microbes to regulate the host innate immune system.



Our study unravels that intracellular galectin-4 in IECs can readily recognize microbes that invade the cells through binding to glycans on their surfaces. In this way, galectin-4 in IECs coats cytosolic bacteria, induces their chaining and aggregation to restrict bacterial motility. It also potentiates inflammasome activation to strengthen the host innate immune system. Moreover, when mice were challenged orally with *Salmonella* bacteria, fewer bacterial cells were noted to translocate from the intestinal lumen to the mesenteric lymph nodes in the existence of galectin-4.

Our work uses *Salmonella* bacteria, human Intestinal epithelial cells, and animal models to discover a critical mechanism of host response against bacterial infection in the gut mucosal immune system. Galectin-4, through intracellular binding to microbial glycans, may confine bacterial infection and strengthen host innate immune responses, and this provides opportunities for new therapeutic interventions in infected patients from gastrointestinal infections. The results were published in the Proceedings of the National Academy of Sciences of the United States of America (PNAS) on January 23, 2023.

The research team is led by Dr. Fu-Tong Liu (Institute of Biomedical Sciences, Academia Sinica), and the work is completed by Dr. Chi-Shan Li, Dr. Tzu-Han Lo, Mr. Ting-Jui Tu, Mr. Di-Yen Chueh, Dr. Peilin Chen (Research Center for Applied Sciences, Academia Sinica), Cheng-I Yao, and Dr. Chun-Hung Lin (Institute of Biological Chemistry, Academia Sinica). The study is funded by Academia Sinica and the Ministry of Science and Technology.

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