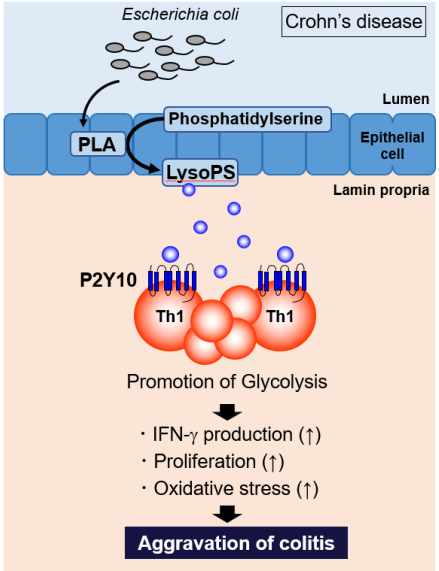
Lysophosphatidylserines derived from microbiota in Crohn's disease elicit pathological Th1 response

Crohn's disease (CD), the main inflammatory bowel disease (IBD) clinical phenotype, is a chronic gastrointestinal tract disorder with transmural inflammation with unknown etiology.

Hideki Iijima (Graduate School of Medicine, Osaka University), Hisako Kayama (Graduate School of Medicine, Osaka University/IFReC), Kiyoshi Takeda (IFReC/Graduate School of Medicine, Osaka University), and the research group identified key metabolites derived from dysbiotic microbiota, which induce enhanced Th1 responses and exaggerate colitis in mouse models.

Patients with CD showed elevated lysophosphatidylserine (LysoPS) concentration in their feces, accompanied with a higher relative abundance of microbiota possessing a gene encoding the phospholipid-hydrolyzing enzyme phospholipase A. LysoPS induced metabolic reprograming, thereby eliciting aberrant effector responses in both human and mouse IFN-γ-producing CD4+ T cells. Administration of LysoPS into two mouse colitis models deteriorated large intestinal inflammation. LysoPS-induced aggravation of colitis was impaired in mice lacking P2ry10 and P2ry10b, and their CD4+ T cells were hypo-responsive to LysoPS. Their findings elaborate on the mechanism by which metabolites elevated in patients with CD harboring dysbiotic microbiota promote Th1-mediated intestinal pathology.

Elevation of intestinal lysophosphatidylserine (LysoPS) concentration due to microbial phospholipase A (PLA)-mediated hydrolysis of phosphatidylserine in the host cell membrane in patients with Crohn's disease causes progression of intestinal inflammation by eliciting immunopathological Th1 responses through promotion of glycolysis via P2Y10 receptor.



Article

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Authors: Yuriko Otake-Kasamoto[#], Hisako Kayama[#], Toshihiro Kishikawa, Shinichiro Shinzaki, Taku Tashiro, Takahiro Amano, Mizuki Tani, Takeo Yoshihara, Bo Li, Haruka Tani, Li Liu, Akio Hayashi, Daisuke Okuzaki, Daisuke Motooka, Shota Nakamura, Yukinori Okada, Hideki Iijima[*], Kiyoshi Takeda[*], and Tetsuo Takehara ([#]; equal contribution, *; equal correspondence)