

BASICS AND APPLICATIONS OF GUT BACTERIAL LIPID-METABOLIZING ENZYMES - A TRIBUTE TO THE LATE PROFESSOR HIDEAKI YAMADA-

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Dietary lipids are one of the three major nutrients for human. In these days, dietary lipids are found to be also important for human health. It is known that the lipids we ingest are broken down to free fatty acids and mono-acyl glycerol by pancreatic lipase and absorbed from the small intestine, and the unabsorbed free fatty acids are excreted through the large intestine. However free unsaturated fatty acids are generally known to be growth inhibitors for gut microbiota. Therefore, we were interested in how the unabsorbed free unsaturated fatty acids are metabolized by the gut microbiota. After investigation of linoleic acid metabolism, we revealed two polyunsaturated fatty acid metabolisms in gut microbiota. One of them is saturation metabolism in *Lactobacillus plantarum*¹⁾ and *Clostridium bifermentans*, and the other is hydration metabolism in *Lactobacillus acidophilus*²⁾ and *Pediococcus* sp.³⁾. As to saturation metabolism in *Lactobacillus plantarum*, the enzyme system was found to consist of four enzymes (hydratase, dehydrogenase, isomerase, enone reductase) and generate hydroxy fatty acids, oxo fatty acids, and conjugated fatty acids as intermediates (Fig.1). The homologous genes encoding these four enzymes were found in genome sequences of many gut microorganisms. Therefore, acting in concert, gut microbiota may mediate the unsaturated fatty acid saturation metabolism in gastrointestinal tract. Furthermore, we confirmed the existence of these fatty acids in host tissues depending on the existence of gut microbes using specific pathogen free (SPF) mouse and germ free mouse. Successive analysis revealed health promoting activity of these hydroxy and oxo fatty acids, i.e., intestinal epithelial barrier protection³⁾, anti-obesity⁴⁾, and anti-inflammatory activity⁴⁾, etc. Especially, HYA (10-hydroxy-*cis*-12-octadecenoic acid), which is converted from linoleic acid using CLA-HY, suppresses an increase in postprandial blood glucose concentration in human^{5,6)}. Therefore, we developed novel production system for HYA using lactic acid bacteria toward commercialization. These studies could open a new application of gut microbial fatty acid metabolisms and their metabolites for health promotions.

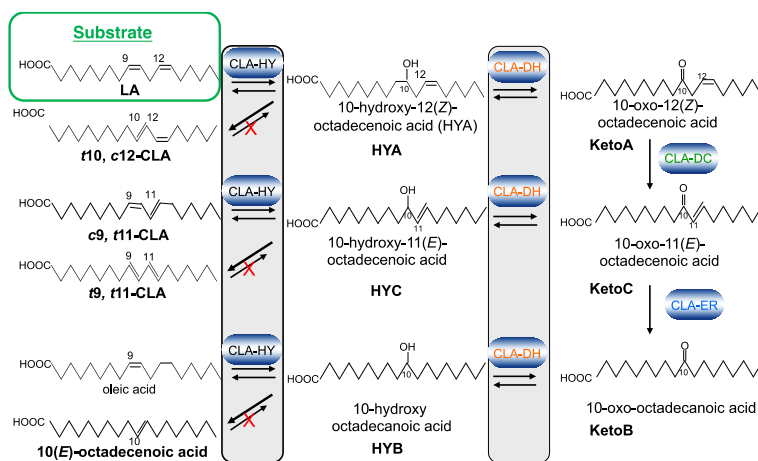


Fig. 1 Linoleic acid-saturation metabolism in *Lactobacillus plantarum*

Reference

- 1) S. Kishino et al., PNAS, **110**, 17808 (2013).
- 2) A. Hirata et al., J. Lipid Res., **56**, 1340 (2015).
- 3) J. Miyamoto et al., J. Biol. Chem., **290**, 2902 (2015).
- 4) T. Nagatake et al., Mucosal Immunol., **15**, 289 (2022).
- 5) Y. Yonejima et al., Prog. Med., **37**, 1105 (2017). 6) Y. Yonejima et al., Prog. Med., **39**, 1147 (2019).