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GUT MICROBIOTA

D-amino acids employed against gut pathogens

The intestinal epithelium can combat pathogenic microbiota by converting D-amino acids (D-aa) released by bacteria into H_2O_2, a potent microbicidal product, according to a new study.

Proteins primarily consist of L-amino acids; however, D-aas can also have important biological functions. Bacteria synthesize a number of D-aas, which are incorporated into their cell walls and can be released into the environment; however, whether gut microbiota emit these molecules and how they might modulate host physiology has not previously been explored.

The investigators found that several D-aas were abundant in the intestines of specific pathogen-free (SPF) mice, but not in germ-free (GF) mice. The team then observed that D-amino acid oxidase (DAO), an enzyme that deaminates neutral D-aas to form H_2O_2, is present on the intestinal epithelium of mice — as well as in human goblet cells — and is secreted into the gut lumen. Furthermore, DAO was upregulated in SPF mice compared with GF mice, suggesting that the microbiota induce intestinal production of DAO.

The team found that treatment of several enteric pathogens with DAO and D-aas *in vitro* resulted in a reduction in colony-forming units. Intriguingly, the cholera-causing pathogen *Vibrio cholerae* was also sensitive to DAO in the absence of added D-aas, and this toxicity was attenuated in a mutant strain with deficient D-aa production. Furthermore, DAO-induced toxicity could be blocked by catalase, an enzyme that breaks down H_2O_2. Importantly, the mutant *V. cholerae* strain was also better able to colonize the mouse intestine than wild-type *V. cholerae*, a difference that was attenuated in DAO mutant mice.

"Overall, our work revealed that microbial D-aas are a new microbe-associated molecular pattern that are recognized by a host enzyme, DAO," explains author Matthew Waldor. "The interplay between D-aas and DAO modifies the composition of the microbiota and modulates mucosal defence."

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