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Intestinal IgA as a modulator of gut microbiota

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Recently dysbiosis (gut commensal microbial imbalance) is frequently reported to be associated with illnesses such as inflammatory bowel disease (IBD), obesity, cancer, etc. Immunoglobulin A (IgA) is the main antibody isotype secreted into the intestinal lumen. IgA plays a critical role in the defense against pathogens and in the maintenance of intestinal homeostasis through gut microbial control. However, how secreted IgA regulates gut microbiota is not completely understood. In the previous study, we found that the high-affinity intestinal IgA produced by somatic hypermutation process is important to control non-pathogenic gut bacteria as well as pathogens. Our main question is what kind of bacterial molecule intestinal high-affinity IgA recognizes and targets.

To address this question, we generated hybridomas from IgA-producing cells in the small intestine of wild type mice. As a candidate of efficient gut microbiota modulator, we selected W27 IgA that binds to multiple bacteria but not beneficial ones such as *Lactobacillus casei*. Via specific recognition of an epitope in serine hydroxymethyltransferase (SHMT), a bacterial metabolic enzyme, W27 IgA selectively inhibited the *in vitro* growth of bound bacteria, including *Escherichia coli*, while having no effect on unbound beneficial bacteria such as *L. casei*. It indicates that W27 IgA has an ability to improve the intestinal environment. Indeed, W27 oral treatment could modulate gut microbiota composition and have therapeutic effect on both lymphoproliferative disease and colitis models in mice. Thus, W27 IgA oral treatment is a potential remedy for a variety of diseases associated with dysbiosis, acting through restoration of the host-microbial symbiosis.