

## Title: Novel synthetic analogue of microbial metabolite, UroA mitigates inflammatory bowel diseases.

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Inflammatory Bowel Diseases (IBDs), which consists of ulcerative colitis, Crohn's disease, affects as many as 1.4 million people in the USA. Chronic inflammation and microbial dysbiosis are major features of IBDs. Beneficial effects rendered by healthy dietary practices are not uniform among individuals and are attributed to variations in gut microbiota and their active metabolites. To overcome the challenge of inter-individual differences in gut microbiota, their metabolites and poor bioavailability, here we propose direct usage of microbial metabolites to maintain gut immune homeostasis to mitigate IBDs.

Urolithin A (UroA) is one of such beneficial microbial metabolite derived from ellagic acid and ellagitannins, major polyphenolic components of berries and pomegranate. Based on UroA structure, we developed novel potent structural analogue, UAS03, which exhibited increased anti-inflammatory and gut barrier functional activities compared to parent UroA compound. In this proposal we will test the hypothesis that **'treatment with UroA/UAS03, protects from developing IBDs by reducing barrier dysfunction and inflammation'**. The pilot project investigates the molecular and cellular mechanisms of UroA and UAS03 and their therapeutic efficacies in IBD pre-clinical models. The successful completion of proposed studies will allow obtaining UAS03 and UroA mechanisms of actions and establishes the basis for therapeutic usage in IBDs.

### Diet-Microbiota interactions

