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Discovery of small molecule enzyme inhibitors from gut microbes as potential anti-inflammatory and anticancer agents

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Abstract

Symbiotic bacteria have been associated with a *healthy gut enterotype*, but the biochemical basis of any benefits derived from these microbes has not been well-defined. We are examining the secondary metabolome of a symbiotic gut bacterium grown in liquid culture to assess its ability to protect gut mucosa from molecular events that lead to the development of colorectal cancer. Compound isolation and purification will be guided by bioassays that target specific mechanisms associated with the development and progression of colorectal cancer. Three key mechanisms are an *epigenetic model* that involves the **c**ytosine-guanine **i**sland **m**ethylation **p**henotype (CIMP+), an *inflammation-associated* model, and an epithelial-mesenchymal transition model, which will be described. Although the use of *live* probiotic bacteria to benefit a host organism by improving the balance of intestinal microorganisms dates back to the early twentieth century, the idea of mining these gut microbes for potential small molecule therapeutic agents is new. The structures of pure compounds are determined using the standard tool box of the natural products chemist: 1D and 2D NMR experiments, mass spectrometry, UV and IR spectroscopy, and x-ray crystallography. This project initiates a new venture in drug discovery from the secondary metabolome of the Human Microbiome. As University of Chicago Martin Boyer Professor E.B. Chang noted "Its potential in terms of drug and reagent discovery is the equivalent of an Amazon rain forest. There exists enormous untapped biological opportunity for discovery."

Biography

Andrea Stierle completed her Ph.D. studies in Organic Chemistry and Biochemistry at Montana State University and postdoctoral studies at the Scripps Institution of Oceanography and Montana State University, Department of Plant Pathology. She is a Research Professor at the University of Montana in the Department of Biomedical and Pharmaceutical Sciences.