Determining the mechanism by which the bacterium *Oxalobacter formigenes* stimulates the gut epithelium to excrete oxalate and prevent kidney stones

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Oxalobacter formigenes (*Of*) is a commensal intestinal bacterium whose only growth substrate is oxalate, the component of most kidney stones. *Of* stimulates enterocytes to excrete oxalate, lower plasma and urine oxalate, and thereby prevent kidney stones. The aim of this project is to elucidate how *Of* induces intestinal oxalate excretion with the goal of developing probiotic/pharmacological therapies for prevention of kidney stones. We are using a molecular genetic/animal model approach.

Mutant *Of* that cannot stimulate oxalate excretion should not be able to colonize mice fed a normal diet lacking oxalate. We will isolate transposon insertions in *Of* genes whose products are exported, which would be the target population for genes that interact with the host. *Of* mutants will be inoculated into mice fed an oxalate-free diet, and we will screen for *Of* colonization by its presence in feces and/or intestinal homogenates. Colonization mutants will then be inoculated into mice fed an oxalate-containing diet. Oxalate transport-stimulating mutants will now be able to colonize since oxalate will be provided in the diet.

We will identify the mutated gene by DNA sequencing, construct a deletion of the gene, and confirm the mutant phenotype. The mutant *Of* will be examined for defective oxalate transport by my colleague, Marguerite Hatch, in an ex vivo intestinal tissue model.

The long term goal is to purify the oxalate transport-stimulating factor or to clone the genes into *E. coli* and determine if the factor and/or recombinant bacteria can stimulate oxalate transport when fed to mice.