The healthy gut microbiome provides many benefits to the host organism, one of which is establishing and maintaining an environment of colonization resistance to enteric pathogens such as members of the Enterobacteriaceae. This colonization resistant environment is established partly due to the fermentative metabolism of strict anaerobes such as species within the Lachnospiraceae family that produce short-chain fatty-acids (SCFA) and acidification in the colonic lumen. The stress-response mechanisms by which the Lachnospiraceae tolerate this acidic environment are unknown. Using a random forest model to predict relations between whole-genome sequence (WGS) and SCFA production of 325 isolates, genes of urease and Ni²⁺ uptake were identified as predictors of high SCFA production. Interestingly, there is a heterogenous presence of urease genes within the Lachnospiraceae, particularly within the genus Blautia, and the role and regulation of this operon in Lachnospiraceae is unknown. Preliminary data from genomic analysis and models of metabolic flux have suggested that the Lachnospiraceae may use urease to resist the intracellular acidification of the low pH high SCFA environment, as well as to compete with ureolytic Enterobacteriaceae for urea as a nitrogen source. The goal of this research is to understand the role and regulation of the urease operon within the Lachnospiraceae, and to understand the influence of urease on production of SCFA and acidification. Improved understanding of genes that contribute to colonization resistance will lead to improved isolate selection for defined therapeutic consortia designed to restore colonization resistance.