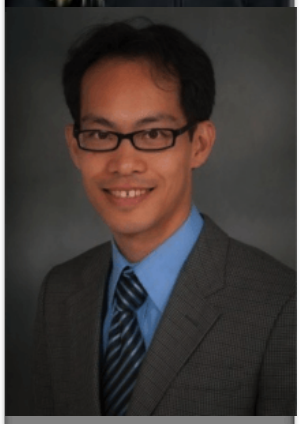

USE OF STOOL IMMUNE TRANSCRIPTOME TO PREDICT RECURRENT CLOSTRIDIUM DIFFICILE INFECTION.

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Background: *Clostridium difficile* is a gram positive, anaerobic, spore forming bacterium capable of producing exotoxins that bind to receptors on intestinal epithelial cells. *Clostridium difficile* infection (CDI) is responsible for antibiotic associated colitis and is a common hospital pathogen, causing 12.1% of health-care associated infections. CDI was responsible for about half- million infections in 2011, 29,000 of which died within thirty days of diagnosis. Despite the high morbidity and mortality related to the disease, little is known about CDI and the human immune response.

Purpose: The purpose of this study was to determine the host transcriptomic predictors for patients with recurrent Clostridium difficile infection (CDI) compared to patients who are cured after a single course of treatment.
We used a newly-developed method of isolating the host immune transcriptome from stool to test the hypothesis that at time of CDI diagnosis, prior to treatment, there are differences in host markers that can predict recurrent disease.

Methods: We analyzed the host immune transcriptome from patients with CDI in a non-invasive way using stool samples. We extracted total RNA using the PureLink RNA mini kit (LifeTechnologies), then isolated host poly-(A)+ mRNA with the NucleoTrap mRNA mini kit (Clonetech). We converted mRNA into cDNA and used RNA sequencing to give us the read counts of the human genes expressed in the stool. With these read counts I performed a differential analysis using DESeq2 to compare Hospital vs. Community Acquired cases of CDI.

Results: In our preliminary comparison of Hospital (n=2) versus Community Acquired (n=2) *Clostridium difficile*, only one gene, ARPC2, showed a statistically significant (p value ≤.05) difference. ARPC2 is an actin protein that interacts with cortactin to promote the conformational change of the actin cytoskeleton through the entirety of the cell. The expression of actin is noteworthy because the toxin of *Clostridium difficile* interacts directly with the cytoskeleton of the host cells. The toxins act to target epithelium of the colon and disturb the tight junctions present by breaking down the actin filaments present. Thus, overexpression of actin by the host may be a biologically plausible response to CDI and toxin expression, making this gene a good candidate for host-based diagnostics. To achieve our initial objectives, we are in the process of comparing recurrent vs. non-recurrent cases of CDI using this same methodology.

Implications: The potential use of host transcriptomics through the use of stool samples would be revolutionary for any medical diagnosis, not just for *C. difficile*. If we can understand what genes the host differentially expresses during a disease, it can aid in predicting whether an individual is more susceptible and the degree of resulting severity of infection.