Clostridium difficile Infection and Approaches for Therapeutic Discovery

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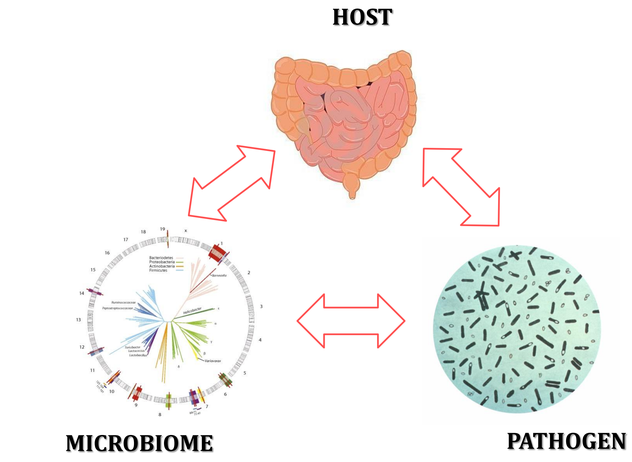
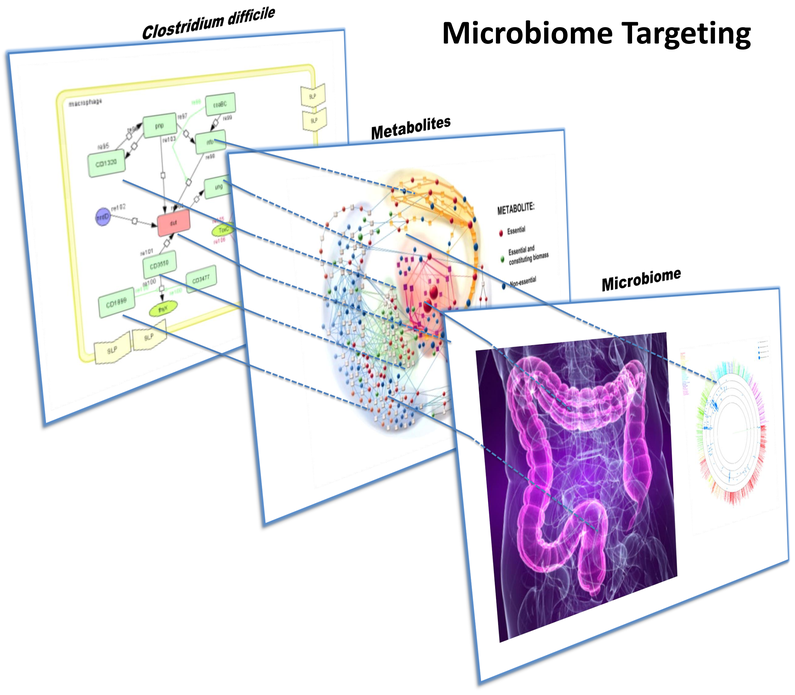
Introduction and Aims

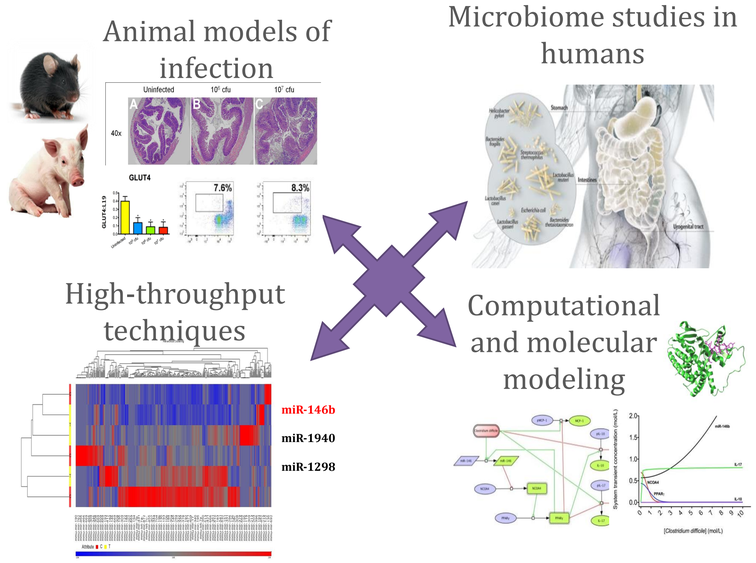
The number of *Clostridium difficile* infections has risen in the past several years, averaging around 14,000 deaths in the U.S. each year. Normally a harmless member of the gastrointestinal flora, the bacteria cause trouble when the normal microbial populations are disrupted, such as when antibiotics are taken. *C. difficile*-associated disease (CDAD) is an inflammation of the colon due to the tissue damage cause by the toxins it produces as well as disrupting the PPARγ pathway. More antibiotics can be taken to clear out the *C. difficile*, but the normal flora is not restored, leaving the patient susceptible to recurrent infections. Between 10-20% of patients have relapses, calling for a need to clear the infection and prevent another from taking place. New therapeutics for treating these infections. It is a goal of NIMML to better understand the mechanisms to how *C. difficile*, the microbiota, and the host interact with one another in order to gain better insight to manage and treat the disease.



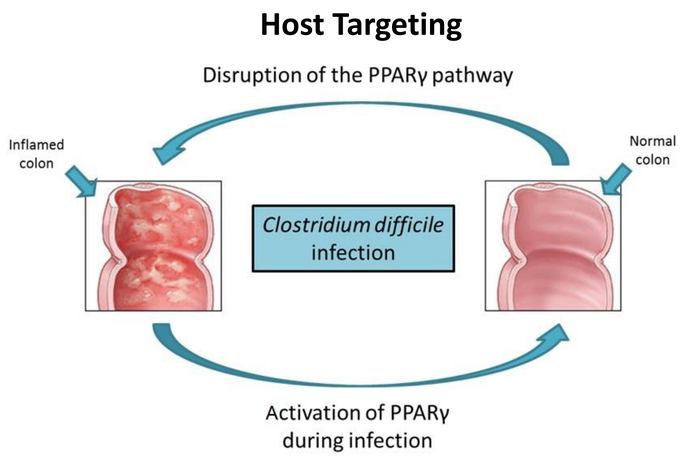
Uncovering the interactions between the host, the microbiota, and *C. difficile*. By studying these interactions, certain pathways can be uncovered and targeted to alleviate the CDAD.



Modulating the microbiome and its metabolites. Manipulating the abundance of certain populations in the microbiome can change metabolmic profile of the gut. Several of these metabolites can have therapeutic effects during a *C. difficile* infection.

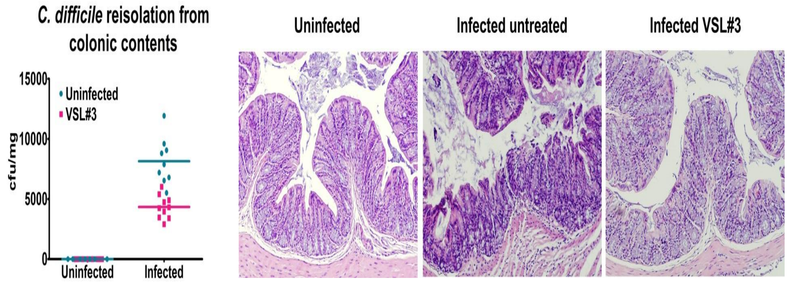


A transdisiplinary approach to therapeutics discovery. NIMML utilizes people from various scientific backgrounds to have a combined comprehensive knowledge of the subject and allow for the use of novel approaches to solve complex problems.

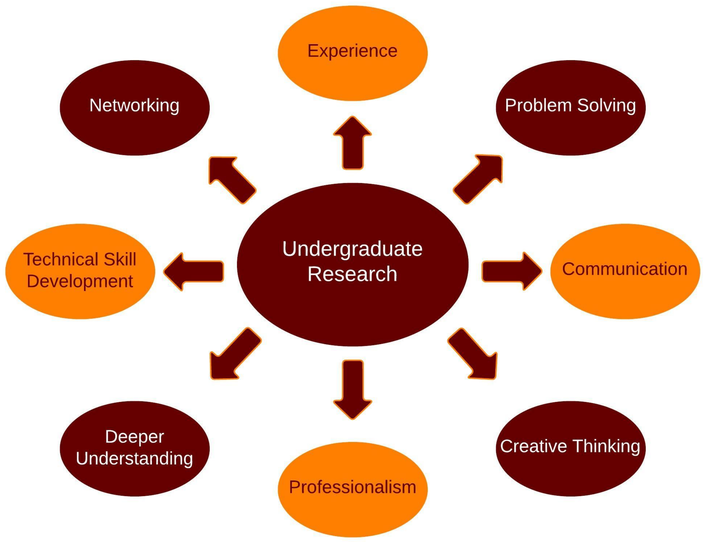


The role of PPARγ during a *C. difficile* infection. The pathway is disrupted by the infection, leading to unnecessary inflammation. The colon can return to a normal state by pharmacological activation of PPARγ. This presents itself as a therapeutic target.

Probiotics studies



The probiotic VSL#3 has been tested in our mouse studies and has been shown to be effective in relieving the inflammation associated with CDAD. We hypothesize that the probiotic bacteria secrete metabolites in the gut which activate anti-inflammatory pathways such as PPARγ.



What is to be gained from undergraduate research. There are many skills gained during my research experience that will certainly aid me in the future. The experience at the lab taught me how to think in order to generate new ideas and effectively solve problems.

A photo of myself. Working at NIMML has been the most rewarding and important experience in my undergraduate studies. It has been the bridge between my academics and the real world. I have been taught many new laboratory techniques but more importantly I learned to think creatively and apply my knowledge into designing a solution for a problem and then executing it.

Nutritional Immunology and Molecular Medicine Laboratory Group Picture