

The Medicinal Chemistry Seminar Series presents:

## **Dr. Nichole Klatt**

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"Novel mechanisms underlying microbiome-mediated influence on human health"

## 1544 North University Building 11:00am Thursday, September 7th, 2023

## Abstract:

Antiretrovirals (ARVs) have transformed HIV into a manageable disease, and are highly effective in preventing progression to AIDS in people living with HIV. However, continued low levels of viral persistence and inflammation are commonly found in ARV-suppressed individuals that lead to increased comorbidities, and have been associated with dysbiosis of the bacteria in the gastrointestinal (GI) tract. These dysbiotic bacteria may perpetuate HIV persistence by driving persistent inflammation. Further, we have recently shown that dysbiotic vaginal bacteria can metabolize ARVs used for HIV prevention, which results in reduced drug bioavailability and efficacy of HIV prevention. Recent studies have also demonstrated that GI bacteria can robustly metabolize several drug classes, and we have demonstrated this can affect ARV drug levels in vitro. However, it is unclear whether GI bacteria may alter ARV levels and HIV persistence in HIV-infected individuals. Furthermore, dysbiotic bacteria drive persistent inflammatory responses that further HIV persistence. We utilized retrospective and prospective samples from HIV-infected and uninfected individuals, as well as novel mechanistic culture assays, in order to assess the contribution of the microbiome to HIV and Covid disease either by drug metabolism, persistent inflammation, or combination thereof. inhibition while minimizing undesired clinical side effects when administering these compounds to fighting bacterial infections.