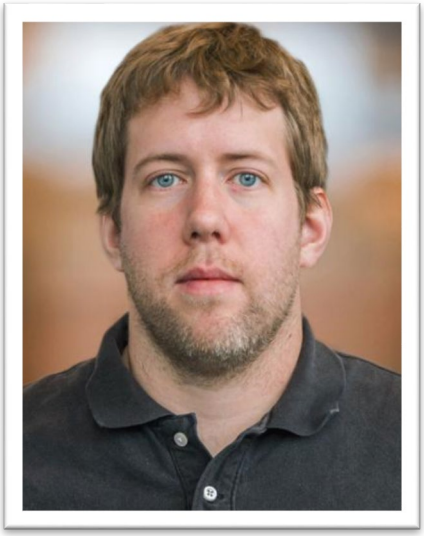
CENTER FOR RNA BIOMEDICINE



RNA Innovation Seminar

Monday, February 4, 2019 at 3:00pm
ABC Seminar rooms, Biomedical Research Science Building (BSRB), 109 Zina Pitcher

Andrew Robertson, PhD
Sherman Lab

"Towards the Treatment of HIV: Isolation and Structural Characterization of Natural Product Nef Inhibitors"

Abstract

HIV is an incurable, pandemic virus that has infected millions of people globally and continues to infect nearly 40,000 people each year in the United States. HIV establishes a latent infection in CD4+ T cells that is not affected by current antiretroviral treatments. Nef is an accessory protein encoded by Human Immunodeficiency Virus (HIV). One of the many functions of Nef is the down-modulation of Major Histocompatibility complex I (MHC-I), masking infection from the host immune system and allowing HIV infected cells to persist. In an ongoing collaborative effort, the laboratories of Dr. David Sherman and Dr. Kathleen Collins have been conducting work into the identification of lead-compound Nef-inhibitors from the Center for Chemical Genomics (CCG) natural product extract (NPE) library (University of Michigan, Life Sciences Institute). The Collins laboratory has developed a high throughput cell-based assay to test for inhibition of Nef dependent MHC-I down-modulation. Initial studies have determined that Nef inhibitors from these natural product extracts can reverse the effects of Nef, restoring cell surface levels of MHC-I, and potentially enabling detection and destruction of infected cells by the host immune system. A screen of 26,000 NPEs identified 11 samples possessing potent inhibition of Nef bioactivity. Purification and characterization of the pure active metabolites will be discussed.

Keywords: HIV, natural products, structural elucidation, bioprospecting