**Overall research plan:** My overall research goal is to investigate the evolutionary dynamics of HIV populations and to understand its implications for treatment design and search for cure. No cure is currently available for HIV infection and infected individuals depend on life-long treatment to avoid the progression of HIV-infection to AIDS. However, drug-resistance is easy to emerge due to the high mutation rate of the virus.

To understand how the virus is evolving, we infect the T-cells in-vitro with HIV and sequence the viral population after a few days to determine the rate of HIV evolution and the viral population structure. Doing this at several time points will document the evolutionary trajectory of the viral population. Tracking the genomic diversity in presence of drugs will shed light on the mechanisms by which drug-resistance mutations emerge and are maintained in an error-prone replication system.

The analysis of sequencing data from a single infection experiment revealed that several new mutations appeared within four days of infection, underlining the rapid rate of HIV evolution. We also reconstructed the genomic variants in the population spanning ~1k of the 10 kb viral genome using our novel computational method that can be applied to analyze sequencing data from any mixed population.

Additionally, we are investigating the effects of further increasing the mutation rate of the virus by using mutagenic drugs. Increasing the mutation rate beyond a limit causes the virus to lose the genetic information necessary to cause infection, a phenomenon called *lethal mutagenesis*. ~50% of Hepatitis C Virus (another rapidly mutating virus) infections are cured by this approach. Our initial results suggest that for HIV infections, the three-way interaction between the host, virus, and the drug is critical for lethal mutagenesis to provide a viable cure.

This highly interdisciplinary research is being carried out in my mentor Dr. Chris Adami’s (MMG, Physics) lab whose research focus is on study of evolution: evolutionary biology, evolution of intelligence and cognition, and so forth. Collaborators Dr. Yong-Hui Zheng (MMG) is an expert in HIV virology, and Dr. C. Titus Brown (MMG, Computer Science) is an expert in developing computational tools for analysis of sequencing data.

**Impact of participation on applicant's research and field:** This meeting will bring together highly respected HIV researchers from around the world, providing an excellent opportunity for interactions to receive feedback on my research and to form collaborations for my future research in interdisciplinary virology. The meeting’s sections on HIV diversity, host-virus interactions and co-evolution are of particular interest for my current and future research. My presentation will highlight the role of evolutionary dynamics of HIV populations in emergence of drug-resistance, and novel computational tools for analysis of population sequencing data will further the use of next-generation sequencing technologies in HIV research.

**Travel plan:** The funding is requested to attend two jointly held Keystone Symposia on “HIV Pathogenesis: Virus vs. Host”, and “HIV Vaccines: Adaptive Immunity and Beyond”, from March 9-14, 2014, at Banff, Alberta, Canada. The travel award will be used to pay towards lodging (conference discounted rate for the entire length of the meeting: USD 1076) and/or airfare.