Research

Bats as reservoirs for emerging zoonotic disease

Bats are the purported reservoir hosts for several of the world's most virulent emerging human diseases, including Hendra and Nipah henipaviruses, Ebola and Marburg filoviruses, and SARS and MERS coronaviruses. Bats appear to host these viruses without experiencing extensive morbidity or mortality, leading researchers to ask whether bats might be uniquely adapted for their roles as pathogen hosts. I bridge field ecology, cellular immunology, and quantitative epidemiology to investigate both **within-host** and **population** level questions related to this research theme. The fitting of dynamic models to time series data represents an underlying theme in my work, though I derive my data from a variety of laboratory and field sources–with a particular focus on viral infections in Madagascar fruit bats.

Within-host: What is the pathology of viral infections in bat hosts?

Recent work has demonstrated that some species of Old World Fruit Bat constitutively express the cytokine, Interferon-alpha, meaning that they have perpetually-primed antiviral immune systems (Zhou et al. 2016). This unique immunity likely plays a role in bats' capacities to resist or tolerate viral infections that cause extreme virulence in other mammalian hosts. As a graduate student, I studied the dynamics of bat viruses *in vitro*, modeling the spread of infection across a monolayer of bat cells under differing assumptions of the innate antiviral immune status. As a Miller Fellow, I am exploring the evolutionary underpinnings and consequences of generalist anti-viral immune systems, using both theoretical and empirical laboratory methods.

Population-level: What are the dynamics underpinning the persistence of bat viruses in a population?

Classic epidemiological modeling explores the dynamics of perfectly immunizing childhood infections, under which hosts are typically born susceptible (S), become infectious (I) as juveniles, then recover (R) via immune responses retained for life. In the simplest example, infections are maintained in a population by constant re-supply of susceptible births. Many bat species reproduce in annual or biannual birth pulses, meaning that susceptible re-supply is restricted within a year. Such a system suggests that bat viruses may be governed by more nuanced dynamics than standard SIR–be they longer infectious periods, latent periods for persistent infections, or periodic waning immunity. To elucidate these dynamics, I fit candidate mechanistic models to age-structured prevalence and seroprevalence data, which I collect from the field in collaboration with Christian Ranaivoson of the Institut Pasteur de Madagascar. As part of an NIH-funded research initiative, we are longitidunally sampling Malagasy fruit bat populations to construct the time series needed to parse our hypotheses.

Bridging from host to population: What underpins seasonality in bat viral dynamics?

In many instances, zoonotic emergence of bat viruses into human and other animal hosts shows a marked seasonality, which appears to be mediated by the annual reproductive calendar of the bat host in question (Plowright et al. 2015, Schmidt et al. 2017). Bridging across scales from within-host viral control to population-level and even cross-species transmission, we are tracking immune parameters in conjunction with infection status as part of our longitudinal surveillance project in Madagascar. The importance of seasonal forcings has long mediated inference into infection dynamics in other disease systems (i.e. Ferrari et al. 2008, Grenfell et al. 2002). However, we are often unable to identify the true driver of seasonal transmission–be it seasonal variation in between-host contact patterns, within-host immune profiles, or both. In the case of bat viral dynamics, where hypotheses of both classic susceptible pulsing and within-host viral latency are under consideration, it becomes ever more important to understand the true driver of this seasonality.