

Microbial Manipulation of Host Sexual Behavior

Overview: The transmission of sexually transmitted infections (STIs) depends on the sexual behavior of their hosts. Non-sexually transmissible microorganisms, including toxoplasma, rabies and many others have evolved the ability to alter host behavior in ways that facilitate transmission. While male mammals are generally expected to maximize opportunities for sexual activity because of their relatively low reproductive costs, females are expected to be selective in their choice of mates because of the high costs of pregnancy and lactation. An STI that decreased female sexual selectivity or otherwise increased female sexual proclivity would be expected to gain a substantive selective advantage over STIs without such traits. It is likely that STIs in nature have evolved these abilities. Discovering such microbes and pinpointing the mechanisms and nature of their action, represents an unexplored area of science.

Objectives: It is highly likely that STIs that alter female sexual behavior exist in the wider mammalian order. Whether or not such microbes currently infect humans remains unclear, so in addition to scanning human samples for novel STIs, we will look at rodents, a highly diverse group of mammals with an expected high diversity of underlying STIs. The program has three primary objectives: 1) obtain specimens from rodents and humans likely to be infected with STIs of interest; 2) identify known and unknown STIs in these human and rodent specimens; 3) use rodent lab models to examine the impact of identified STIs on host sexual behavior.

Technical approach: *The first step will be to procure STIs.* STI samples will be acquired from both existing collections* and targeted novel collections from highly promiscuous human populations and rodent species that exhibit appropriate promiscuity profiles. A combination of generic molecular approaches (e.g deep sequencing, viral microarrays) will be used to identify known and unknown STIs in human and rodent collections. *The second step will be to test known and unknown STIs for their impact on host sexual behavior.* STIs from humans and rodents will be cultured and adapted for use in rodent lab models. Adapted STIs will then be tested using controlled behavioral studies in established rodent lab models to determine the impact of STIs on host sexual behavior.

Budget & Timeline: The project includes a combination of internal studies and work conducted by subcontractors. Budget components include one field component (specimen acquisition) and three lab components (identification of STIs, adaptation of STIs to lab models, and testing of behavioral impact of STIs). The total requested budget for all components is US\$8.5m, with an expected timeline of 3 years.

Expected Outcomes: The project will assemble the largest collection of mammalian STIs ever obtained. It will identify novel STIs in rodent and human populations. And it will provide a test of the hypothesis that microbes manipulate host sexual behavior.

* Appropriate IRB revisions will be applied to existing collections.