Overall objectives

1) identify and obtain specimens from sexually transmitted infections (STIs) expected to alter host sexual behavior
2) determine which of the procured STIs have the potential to increase female sexual drive
3) capture intellectual property around such STIs and compounds derived directly or indirectly from them
4) sell to or collaborate with a pharmaceutical or biotech concern capable of mass commercialization of resulting methods, intellectual property, and/or compounds.

Case for support:

1) Business: a female 'viagra' will have substantial quality of life impact on consumers and create huge financial value to the companies that develop and market it
2) Science: the finding that microbes alter host sexual behavior would add an important new twist to the basic science of the evolution of parasite manipulation of host behavior

Rationale: the transmission of sexually transmitted infections (STIs) depends on the sexual behavior of their hosts. Other non-sexually transmissible microorganisms, including toxoplasma, rabies and a range of 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 capacities. It is likely that STIs in nature have evolved these abilities. Discovering such microbes and interrogating the mechanisms and nature of their action, represent unexplored areas of science. The expectation of their existence provides a justifiable path to the identification of agents and/or compounds that have the potential to boost the sexual drive of females.

Risk and limitations: the study is inherently risky. While it is highly likely that STIs that alter female sexual behavior exist in the wider mammalian order, whether or not they current infect humans remains unclear. Challenges exist in successfully culturing newly identified STIs and adapting microbes to standardized lab models for testing. Finally, any new STIs will be relatively easy to test for efficacy in animals but costly and otherwise challenging to test in humans, and it is possible that success in animal models will not translate into human efficacy. Risks can be mitigated by simultaneously conducting animal and human studies, increasing the probability of identifying at least a single mammalian agent that modifies female sexual behavior. Risks can also be mitigated by the consideration of exits at early milestones. For example, after identifying a particular microorganism that alters female sexual behavior in an animal model. Human testing and drug development,

in this scenario, can be passed to an acquiring entity or development partner, such as one of the many large biotech of pharmaceutical company that desire to increase their pipelines.

Technical approach: The most rapid route toward success will likely include simultaneous studies in humans and animal populations. A human STI altering human sexual behavior would be the most obvious and direct hit, yet ironically it will be difficult to identify such affects since studies in humans would need to be indirect (eg inaccurate questionnaire approaches rather than experimental infection studies) and because some human agents might be difficult to adapt to an experimental lab animal system. Of the animal models, rodents appear to make the most sense. They exist in tremendous diversity in nature, which means that their underlying STI diversity will also be large. Sampling and laboratory studies of rodents are widely accepted, with limited ethical and regulatory concerns, and rodent models are considered reasonable models for human physiology. We also know enough about rodent populations in nature that we can use ecological approaches to target those species most likely to have substantial biological conflict between female host behavior and STI transmission. For example, lek-forming species where small numbers of males get most copulations are not ideal – similarly monogamous species are not ideal. Given the diversity of rodents, many tens of species will have an appropriate promiscuity profile for the search.

Research elements

1) Procure known STIs
    a. Human: obtain previously cultured collections of known human STIs
    b. Rodent: obtain previously cultured collections of known rodent STIS
2) Procure unknown STIs
    a. Human: subject existing vaginal lavage and semen specimens to deep sequencing in an attempt to identify unknown human STIs
    b. Rodent: obtain specimens from wild rodent species within targeted promiscuity profile and subject them to deep sequencing in an attempt to identify unknown rodent STIs
3) Determine impact of agents on behavior
    a. Culture candidate STIs obtain from studies above
    b. Study candidate STIs using controlled behavioral studies with laboratory rodent populations to determine impact of sexually transmitted agents on rodent sexual behavior
4) Determine mechanism of action for STIs that influence sexual behavior