ABSTRACT Human immunodeficiency virus type-1 (HIV-1) is estimated to infect approximately 34 million people worldwide, including one million Americans. There is currently no vaccine, nor any effective microbicidal approach to prevent virus transmission. Our laboratory is working on two projects that are intended to address these gaps. First, we are using bacteriophage lambda as a scaffold to display the HIV-1 envelope glycoprotein in a dense, repetitive array that is expected to elicit more potent humoral immune responses against this key virus antigen. The fundamental concept is to try to develop a virus-like particle (VLP) vaccine that may share some of the strongly immunogenic properties of the recently developed vaccine for cervical cancer. Second, we are working towards the development of a novel microbicide capable of reducing the rate of sexual transmission of HIV-1 infection. This project is focused on cationic amyloid fibrils present in semen, termed the semen-derived enhancer of viral infection (SEVI). These fibrils bind HIV-1 virions and enhance viral infectivity by several orders of magnitude. We have identified small molecules which are capable of interfering with the ability of SEVI to enhance HIV-1 infection, with the long-term goal of using these materials (or derivatives of them) as part of an antiviral microbicide.