Novel Approaches to HIV Prevention

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There is no effective vaccine to protect against HIV infection today, and none will be available for the foreseeable future. The lack of an effective HIV vaccine is in part due to the structural properties of the viral envelope glycoprotein, which possesses highly variable amino-acid sequences along with extensive glycosylation that shield the virus from many anti-envelope antibodies. As an alternative strategy, our group is pursuing the use of antibodies as agents for passive administration to prevent HIV infection. We have engineered a number of bi-specific monoclonal antibodies that have remarkable potency and breadth against the virus in vitro. We have in hand a number of constructs with 100% breadth against a large panel of HIV strains with potency in the nM range. Several of these constructs are now being advanced as candidates for clinical development. In addition, our group has pursued a slow-release formulation of an integrase inhibitor (cabotegravir, formerly known as GSK744LA) against HIV. The pharmacokinetic profile of this drug in humans suggests that it could be administered as an injectable once every 2-3 months. In protection experiments against repeated low-dose virus challenges in monkeys, this drug has shown 100% protection. We firmly believe that long-acting cabotegravir is a promising agent for HIV prevention in high-risk populations. We are finishing a Phase-2 study at this time, and multiple Phase-3 efficacy studies are anticipated in high-risk African women as well as in male homosexual populations in the coming year.