Retrovirology

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Oral presentation

Microbicide development: multiple targets, multiple mechanisms

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Heterosexual transmission is the leading mode of HIV-1 infection worldwide, with women particularly vulnerable to HIV-1 infection as they often cannot control sexual encounters or insist on condom use. In the absence of an effective vaccine there is an urgent need to develop alternative prevention strategies. The immediate events between exposure to infectious virus and the establishment of infection are still poorly understood. Defining the mechanisms of HIV-1 transmission, the target cells involved and how the virus attaches to and fuses with these cells is revealing new ways to block the sexual spread of the virus. Initial efforts to develop vaginal microbicides focused on killing the virus through membrane disruption using surfactants, and blocking viral entry using polyanionic compounds that interact with the positively charged areas of the viral envelope proteins, many of which are currently in phase II/III trials. However recent advances in HIV pathogenesis and therapeutics are now bringing a wide range of new products into the development pipeline that specifically target different stages in the viral life cycle. This talk will present rigorous pre-clinical evaluation of candidate microbicides prior to selection for clinical trials, providing considerable savings in costs and time, given the expense and length of formal efficacy trials. Selection criteria include: high activity against cell free and cell associated virus in mucosal explant models; low irritation potential based on a range of preclinical irritation assays; high in vitro activity in the presence of semen; and effectiveness in animal models using challenge virus that is relevant to sexual HIV transmission. This presentation discussed how our increasing knowledge of the ways in which HIV-1 is transmitted has sharpened the development of new, more sophisticated intervention strategies based on the application of vaginal or rectal microbicides.