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# A cell-free HTS assay to identify novel inhibitors of DC-SIGN/gp120 interaction to prevent early HIV-1 infection

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The current antiretroviral therapy (HAART) has several disadvantages including renal and hepatic toxicity as well as high cost. Measures are being undertaken for ARV therapy alternatives, particularly for the control of early HIV-1 infection. Dendritic cells (DCs) present in the mucosal tissue, together with $CD4^+$ T lymphocytes and macrophages, are among the first cells to encounter HIV-1. The dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin (DC-SIGN) molecule plays a crucial role in binding HIV-1 through the high affinity interaction with viral envelope glycoprotein gp120. DC-SIGN, a mannose-binding C-type lectin expressed on cells in the mucosal tissue of the rectum, uterus and cervix, facilitates early HIV-1 infection after sexual transmission. The study present herein reports a novel, specific and optimized high-throughput screening assay capable of quantifying the binding as well as the inhibition of DC-SIGN and gp120. First, the assay's linearity was established as it was miniaturized from a 96 to a 384 well format. Assay specificity was then determined through competitive inhibition while optimization occurred for DMSO tolerability (0.5%), Z' Factor (0.51), S/N (3.26) and CV% (5.1%). Previously recognized antagonists of DC-SIGN/gp120 binding were tested for assay validation to prove that it could detect inhibition. In conclusion, the assay was deemed ready for the high-throughput screening of potential agents that block the binding between these proteins so that they may be formulated into drugs that prevent early HIV-1 infection.