INTRODUCTION
HIV-1 infection and its concomitant disease - Aids, remain major public health problems in southern Africa. While current antiretroviral drugs have prolonged the quality of life for many HIV-positive individuals, they do not eliminate the virus [2, 3]. This is compounded by the rapid emergence of drug resistant HIV-1 strains. For these reasons, a search for novel antiretroviral agents with modalities different from those currently in use remains a high priority. As a novel strategy to combat the HIV/AIDS epidemic, we have recently discovered and described small nucleic acid ligands called aptamers with antiviral activity [1, 4]. These aptamers prevent HIV-1 infection by binding to gp120, which is the viral surface envelope glycoprotein necessary for the earliest stage of infection called entry. In this study we used in silico molecular modelling coupled with biochemical experiments to delineate the interaction of one of the aptamers called B40 with gp120, with a view of using the information to develop the aptamer as a novel HIV-1 entry inhibitor drug.

RESULTS AND DISCUSSION
B40 aptamer interfaces with gp120 binding to host cell natural receptors. Using real-time surface plasmon resonance technology (BIAcore®), we showed that the B40 aptamer interfered with interaction of gp120 with CCR5 and soluble human CD4 receptors (Figure 1). C4D and CCR5 are physiological receptors expressed on target host cells that are exploited by the virus for entry and infection.

The 840-gp120 interface is stabilised by a network of hydrogen bonds. The 10 gp120 amino acids that h-bond to the B40 aptamer are shown in Table 1. As a result, the B40-gp120 interface is primarily stabilised by a hydrogen bonding network between charged amino acids of gp120 and the oxygen atoms in the backbone of the B40 aptamer.

Point mutations of core residues on gp120 disrupt binding of B40 aptamer. Mutating a series of amino acid residues, one at a time, on the predicted gp120 interface, disrupt binding of the B40 aptamer as measured by the BIAcore® (Figure 2). The B40 aptamer binds to core conserved residues on gp120 (Table 1). This data suggests that the aptamer binds to functional core conserved residues on gp120 that the virus cannot afford to mutate without losing fitness and selective advantage.

The B40-gp120 interface is stabilised by a network of hydrogen bonds. The 10 gp120 amino acids that h-bond to the B40 aptamer are shown in Table 1. As a result, the B40-gp120 interface is primarily stabilised by a hydrogen bonding network between charged amino acids of gp120 and the oxygen atoms in the backbone of the B40 aptamer.

SUMMARY AND CONCLUSION
• The B40 aptamer that potently and broadly prevents HIV-1 infection binds to core conserved residues on gp120.
• The aptamer binds to functional core conserved residues on gp120 that the virus cannot afford to mutate without losing fitness and selective advantage.
• The aptamer prevents HIV-1 infection by direct steric hindrance and also by causing distant non-productive conformational changes in gp120 that affect virion-receptor interactions.

Molecular interaction of gp120 and B40 aptamer: A potential new HIV-1 entry inhibitor drug

CSIR scientists are developing small, artificially-engineered molecules called aptamers as potential new HIV-1 entry inhibitor drugs.

REFERENCES