Pathology-2013

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference and Exhibition on
Pathology

August 05-07, 2013 Embassy Suites Las Vegas, USA

Development of aptamer-based HIV-1 entry inhibitor prophylactic drug

Grace London
CSIR Biosciences, South Africa

Abstract

AIDS remains a major public health problem globally, especially in Southern Africa where over 6.4 million people are infected by the most prevalent HIV-1 subtype C. To help stop the spread of HIV-1 subtype C, we isolated 2´-F-RNA aptamers against gp120, with a view of developing them as entry inhibitor drugs. In this study, we evaluated the neutralization activity of two aptamers (CSIR1.1 and UCLA1) against HIV-1 subtype C, their toxicity effects and mapped their epitopes on gp120. UCLA1 and CSIR1.1 were tested against a 32 Env pseudotyped panel from HIV-1 subtype C. In addition, UCLA1 was further tested against 10 clinical isolates in PBMC and MDM. We evaluated the cytotoxic effects of aptamers in target cells using ATP and PMTS proliferation assay and mapped their epitopes on gp120 by site directed mutagenesis. UCLA1 and CSIR1.1 neutralized infectivity of 79 % and 84 % pseudotyped viruses, respectively. UCLA1, further inhibited > 60 % of clinical isolates. We noted that, aptamers neutralized both R5 and X4 tropic viruses with mean IC_{50} value of 10 nM and did not affect cell viability after 72 hrs incubation with a concentration of 500 nM. The mapping studies revealed that CSIR1.1 and UCLA1 bind to conserved region of V1/V2 region and V3 loop on gp120. Our results showed that RNA aptamers prevent infection of HIV-1 subtype C by binding to conserved regions on gp120, without toxicity effects. This warrant further studies to develop RNA aptamer as prophylactic drugs to prevent infection of HIV-1 subtype C.

Biography

Grace, recently submitted her PhD for examination at University of Cape Town collaboration with CSIR (Council for scientific and industrial research). She completed part of her PhD at Scripps Research Institute after being awarded the Fogarty global scholarship and recently won a clinical excellence awards at the 6 th South African AIDS conference. Part of her PhD work was published as a conference proceeding in the Sep 2012 issue of the Retrovirology journal. She is the first author of a complete manuscript which will be submitted in a reputable journal.