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Poster presentation

P12-16. Biochemical and immunological characterization of the plant-derived candidate HIV-1 mucosal vaccine CTB-MPR

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Background

One of the targets of a future multi-component vaccine against HIV-1 should be one of the virus' chief mucosal penetration processes, namely epithelial transcytosis. We further reported that fusion proteins based on the membrane proximal region (MPR) of gp41, playing a key role in the transcytotic process, and the mucosal targeting subunit B of cholera toxin (CTB) are successful immunogens eliciting such transcytosis blocking immune responses and that such proteins can be produced in plants

Methods

Here, we report on the molecular characterization of CTB-MPR expressed in bacteria and transgenic plants and its immunological properties.

Results

We show that bacterially and plant-produced CTB-MPR can be purified to homogeneity. The MPR domain could specifically and reversibly self-associate. The affinities of the mAbs 4E10 and 2F5 to CTB-MPR from either source were equivalent to their affinities toward an MPR peptide. The fusion protein's affinity to GM1-ganglioside was comparable to that of native CTB. Mice and rabbits immunized with CTB-MPR shwoed modest anti-MPR antibody response, but a prime-boost immunization with CTB-MPR and a second MPR-based immunogen elicited a stronger response. These Abs strongly blocked the epithelial transcytosis of primary clade B and D isolates in a human tight epithelial model. The Abs recognized epitopes at the N-terminal portion of the MPR peptide, away from the neutralizing epitopes and were not effective in neutralizing infection of CD4+ cells. These results indicate distinct vulnerabilities of two separate interactions of HIV-1 with human cells – Abs against the C-terminal portion of the MPR can neutralize CD4+-dependent infection, while Abs targeting the MPR's N-terminal portion can effectively block GalCer-dependent transcytosis

Conclusion

We conclude that Abs induced by MPR-based immunogens may provide broad protective value independent of infection neutralization and that plant-based expression can be a viable alternative for the production of subunit HIV-1 vaccine candidates.