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Three-dimensional modeling of DCIR and identification of new drugs blocking HIV-1 attachment and propagation

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Introduction

The HIV-1 pandemic continues to expand while no effective vaccine is yet available. Finding new therapeutic targets and drugs is therefore crucial. We have previously shown that the dendritic cell immunoreceptor (DCIR), a C-type lectin receptor expressed in dendritic cells (DCs), acts as an attachment factor for HIV-1 to DCs and contributes to HIV-1 transmission to CD4+ T lymphocytes (CD4TL). Directly involved in HIV-1 infection, DCIR is expressed in apoptotic or infected CD4TL and promotes trans-infection to bystander cells. The aim of the present study is to characterize the extracellular domain of DCIR and to test chemical inhibitors of HIV-1 attachment thereto.

Results

We present the first three-dimensional model of DCIR structure. Based on this structure, several inhibitors were selected to target viral interaction with the carbohydrate recognition domain and the EPS motif. Preliminary screening using Raji-CD4-DCIR cells identified two inhibitors that decreased HIV-1 attachment and propagation. These inhibitors did not affect the proliferation of peripheral blood mononuclear cells.

Conclusions

The results of this study thus suggest structures for novel molecules capable of blocking HIV-1 transmission by DCs and CD4TL.

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