Retrovirology

Poster presentation

P17-02. PolyCTLDesigner: the software for constructing highly efficient polyepitope immunogens. Application to HIV-1

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Background

Design of the artificial polyepitope immunogens capable of eliciting high levels of the CD8+ CTL responses to the most of contained epitopes is a promising approach in creation of an efficient vaccine against HIV-1. When designing such immunogens, it is necessary to provide their processing to liberate the epitopes and present them to the immune system. We have demonstrated that DNA vaccine construct encoding poly-CTL-epitope immunogen which contains N-terminal ubiquitin and residues ensuring the proteasome processing of polyepitope construct and transport liberated determinants through the endoplasmic reticulum where they bind to MHC class I molecules is most optimal for stimulating the maximal CD8+ CTL responses. These results inspired us to create PolyCTLDesigner software, intended for designing optimal polyepitope antigens.

Methods

The PolyCTLDesigner program utilizes the models of Toes et al. (2001) to predict the proteasomal/immunoproteasomal processing, the models of Peters et al. (2003) to predict the interactions between peptides and TAPs, and is integrated with the TEpredict program which was developed earlier http://tepredict.sourceforge.net.

Results

PolyCTLDesigner allows the user to select the minimal set of epitopes with the known (or predicted) specificity towards various allelic variants of MHC class I molecules covering the overall selected repertoire with a specified redundancy. This program makes it possible to select the flanking sequences for optimizing the binding of selected peptides with TAP and joins the obtained peptide fragments into a polyepitope construct to provide the liberation of potential epitopes by proteasomal and/or immunoproteasomal processing. More detailed information about PolyCTLDesigner is available at http://tepredict.sourceforge.net/PolyCTLDesigner.html.

Conclusion

The developed software realizes the rational approach to designing highly immunogenic poly-CTL-epitope vaccine constructs and can be used for designing new candidate polyepitope HIV-1 vaccines capable of eliciting high levels of the T-cell-mediated immune responses to the most selected epitopes.