Xenophagy in HIV infection: actual knowledge and future therapies

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Background
HIV (human immunodeficiency virus) is able to escape from the immune response and antiretroviral drugs. Despite this, HIV depends on its ability to avoid intrinsic cellular defenses. The presence of virulence factors against autophagy proves the essential role of xenophagy in HIV infection. Xenophagy response is also implicated in antigen presentation extending its function to adaptive immunity.

Objectives and methods
The objective of the study is to define the xenophagy response during HIV infection and propose a therapy strategy or investigation line. To achieve this, I have focused on recent publications and literature about the subject and bioinformatics analysis tools. Protein structure analysis and homology searches were performed with pBLAST, FATCAT and T-Coffee servers. Template construction was achieved with SwissModel software. Docking studies have been carried out with AutoDock4.0, ClusPro, SwarmDock, ZDOCK and RosettaDock softwares. The modeling of the best clusters obtained from docking studies was performed with ROSET server. The images were generated with UCSF Chimera software and Photoshop CS6.

HIV disturbs autophagy

Proteins involved in autophagy disruption

Proposed therapy

To counteract nef could be the best way to fight against HIV infection. The use of beclin-1 mimetic peptide would retain nef and block its mediated effects. The peptide will be based on the 267-299 region of beclin-1 previously described by Shoji-Kawata, S. et al. (Nature 2013) and will cover from 55 to 121 nef residues, this represents over 30% of total viral protein.

This peptide, combined with common ART (antiretroviral) cocktails would be able to stop HIV progression. Other autophagic enhancers could be added, but there is not enough description to ensure their efficacy.

Expected results

Diffusion plan

In order to spread this theory and its arguments the best way would be the publication in an high impact journal of this area. Also to contact researchers to collaborate with them in further investigation. This work will be presented to Universitat Autònoma de Barcelona and will remain at their DOD (digital documents deposit).

Conclusions

Beclin-1 mimetic peptide is a great candidate to target nef

Bibliography
Killian, M. S. Dual role of autophagy in HIV-1 replication and pathogenesis. AIDS Research and Therapy 9, 16 (2012).

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