Structural Analysis of the Envelope GP120 V3 Loop for Some HIV-1 Variants Circulating in the Countries of Eastern Europe

A. M. Andrianov[1]

[1]*Institute of Bioorganic Chemistry, National Academy of Sciences of Belarus,*

Kuprevich Street, 5/2, 220141 Minsk, Republic of Belarus, andrianov@iboch.bas-net.by

YU.V. Kornoushenko[1]

[1]*Institute of Bioorganic Chemistry, National Academy of Sciences of Belarus,*

Kuprevich Street, 5/2, 220141 Minsk, Republic of Belarus, kornoushenko@iboch.bas-net.by

I.V. Anishchenko[2]

[2]*United Institute of Informatics Problems, National Academy of Sciences of Belarus,*

Surganov Street 6, 220012 Minsk, Republic of Belarus, anishchenko.ivan@gmail.com

V.F. Eremin[3]

[3]*The Republican Research and Practical Center for Epidemiology and Microbiology*

Filimonova street, 23 220114 Minsk, Republic of Belarus, veremin@mail.ru

A.V.Tuzikov[2]

[2]*United Institute of Informatics Problems, National Academy of Sciences of Belarus,*

Surganov Street 6, 220012 Minsk, Republic of Belarus, tuzikov@newman.bas-net.by

The V3 loop on gp120 from HIV-1 is a focus of many research groups involved in anti-AIDS drug development because this region of the protein is a principal target for neutralizing antibodies and a major determinant for cell tropism and syncytium formation. In this study, the nucleotide sequences of the *env* gene region coding the V3 loop were determined by DNA sequencing methods for four novel HIV-1 strains that circulate in the countries of Eastern Europe, such as Russia, Belarus, Ukraine, etc. Based on the empirical data, the 3D structures of the V3 loops associated with these viral modifications were generated by computer modeling and then compared to discover similarities in the spatial arrangement of this functionally important site of gp120.

The structural data on V3 obtained here validate the findings of our previous study [1] on the consensus sequences of the V3 loops from different viral subtypes as well as accord with

those of NMR spectroscopy, X-ray diffraction, and computer modeling. With this evidence, mutations in the region of the *env* gene coding V3 trigger off its substantial structural rearrangements. However, despite a wide range of the HIV-1 faces, this cryptic site of gp120 forms three conserved structural motifs, which relate to β-turns and contain residues critical for cell tropism. The data obtained also amplify the observations of a work [2], whereby the most variable sequence positions in the crown of the V3 loop cluster to a small zone on the surface of one face of the V3 hairpin conformation, specifically demonstrating a superiority of conserved 3D structure in this highly sequence-variable region.

Integration of the above information on the invariant motifs of the V3 loop with that on functioning of their individual amino acids makes it possible to believe that these sites of gp120 represent the HIV-1 Achilles' heel and may be used as the promising targets for the design of novel effective anti-HIV-1 drugs. Tools for computer-aided structural analysis, such as molecular docking, molecular dynamics, free energy simulations, QSAR modeling, etc., will likely be of great assistance in this effort.

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References

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