

**Alexander M. Andrianov & Ivan V. Anishchenko  
(2009) Computational Model of the HIV-1 Subtype A  
V3 Loop: Study on the Conformational Mobility for  
Structure Based Anti-AIDS Drug Design, Journal of  
Biomolecular Structure and Dynamics, 27:2, 179-193,  
DOI: 10.1080/07391102.2009.10507308**

**Loyola Marymount University  
Department of Biology  
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**Zach, Matt, Mia, Will**

# Outline

- **The V3 loop and the molecular dynamic in regards to this study**
- **Three segments along the V3 region are compared showing similarities and conserved regions**
- **The most probable 3D structure of the V3 loop shows secondary structures in the immunogenic region and the N- and C- terminals**
- **cRMSD and aRMSD analyses show the immunogenic tip has more relativity and rigidity than the rest of the V3 loop**
- **The V3 loop was bound to CycA and FKBP to show the loop binds at more than one site.**
- **N- and C- terminals and immunogenic tip along the SA-V3 region of HIV-1 gene demonstrate promising sites for anti-AIDS drugs**
- **Future modeling on SB-V3 region using cRMSD and aRMSD to increase data sets would show consistency in results**

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# HIV Aspects

- **The virions enter the host cells through sequential interactions the CD4 cell surface receptors**
  - **After binding to the CD4 binding site, a 180 degree switch in the surface protein gp120 of the virus exposes the co-receptor binding site.**
  - **V3 loop of the glycoprotein gp120 is 35 residues long and highly variable plays a central role in the virus biology in human invasion and immune system interaction.**
- **The focus of this paper is to investigate the V3 loop, constructed by various adaptive and computational computer programs**

# HIV Aspects

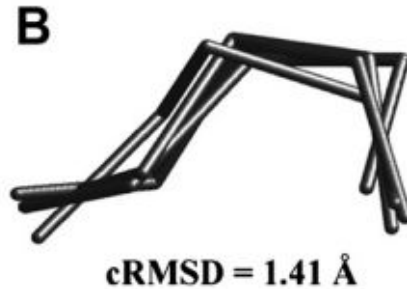
**This paper seeks to provide insight into the less-studied HIV 1 subtype A model**

- **Seeks to investigate this lack of knowledge through simulated computer media**
  - **Comparative modeling and simulated annealing**
  - **Collection of the low-energy structures to find a consensus amino acid sequence for the HIV-1 subtype A V3 loop.**
  - **Structural motifs in the HIV-1 V3 loops were located and analyzed**
  - **Examined the consistencies therein to identify characteristics of the V3 loop**

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# 3D structures of the individual segments 3-7, 15-19, and 28-32 of the HIV-1 subtype A V3 loop exhibit close structural similarity

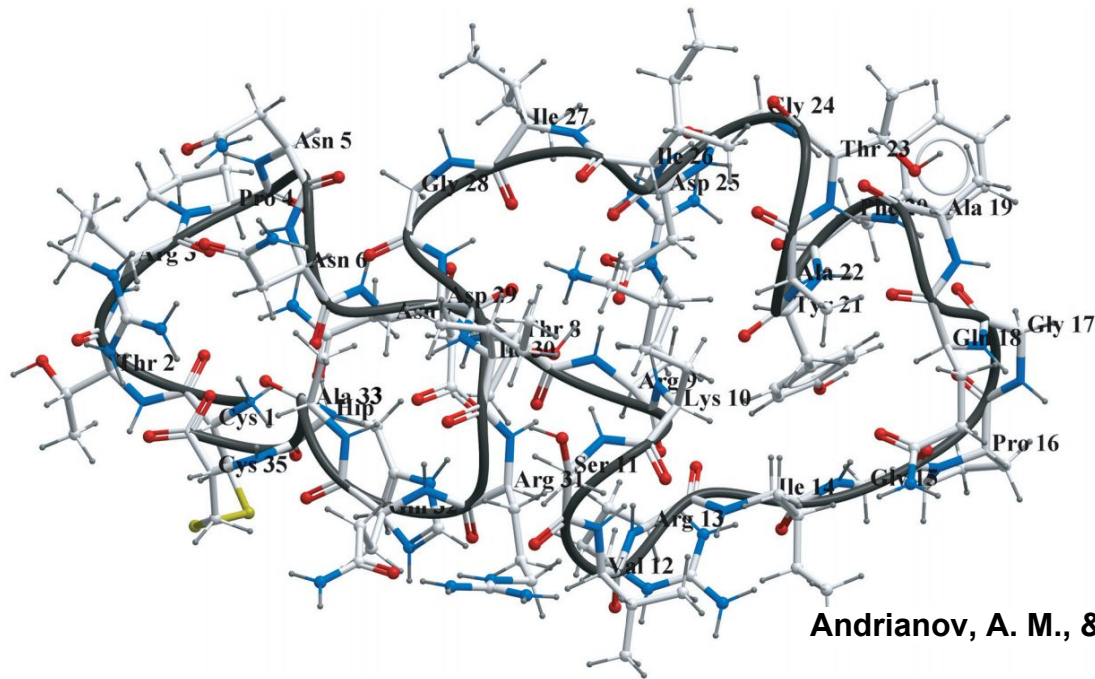


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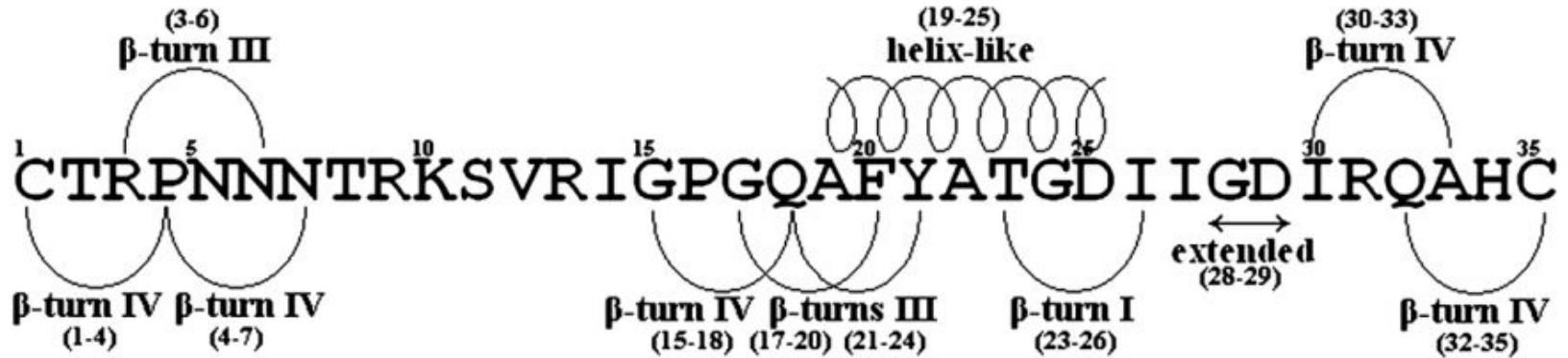


# The most probable 3D structure of the HIV-1 subtype A V3 loop shows beta turns and a small helical structure



Andrianov, A. M., & Anishchenko, I. V. (2009)

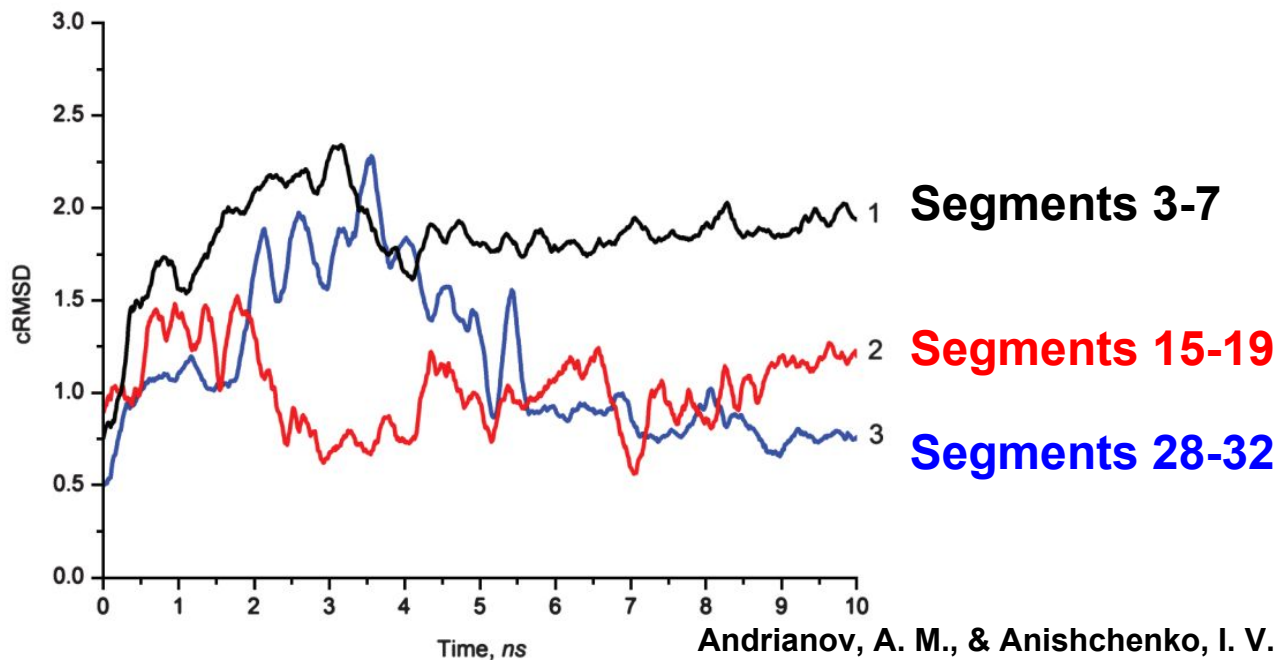
The immunogenic region and the N- and C-terminals are comprised mostly of beta turns and helical structures in the lowest-energy simulated conformation of the V3 loop



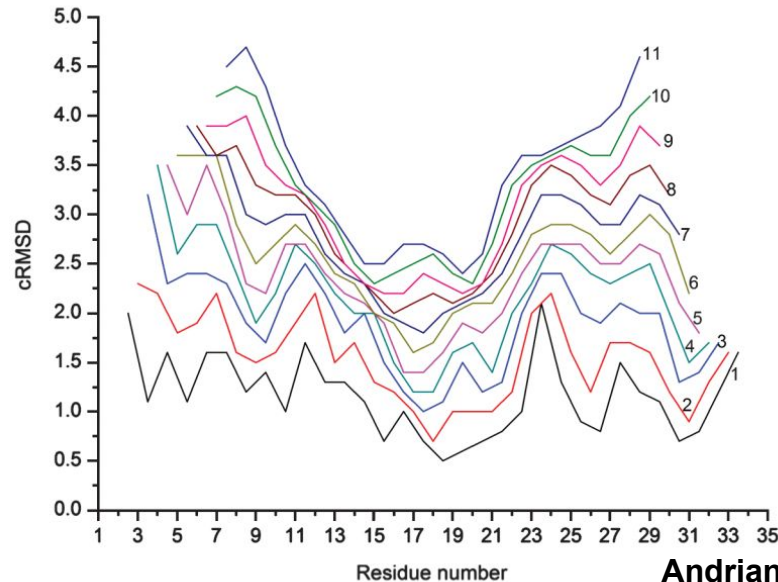
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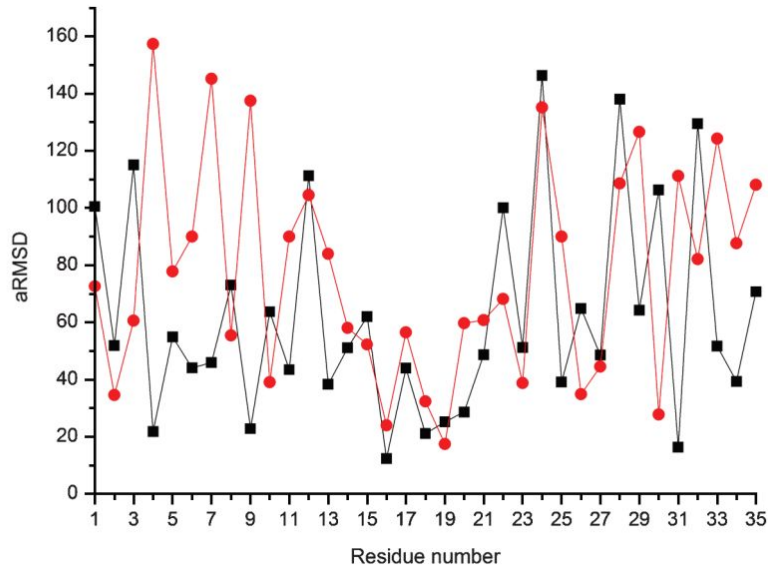
**Graphic 1 shows the least conserved structure, while Graphic 2 shows the most conserved structure based on cRMSD analysis**



# Pinching of lines in residues 11-17 and 21-25 represent rigidity on either side of the immunogenic tip



# Graphical representation of the aRMSD analysis of phi and psi bonds shows the immunogenic tip as the valley between residues 11 and 21

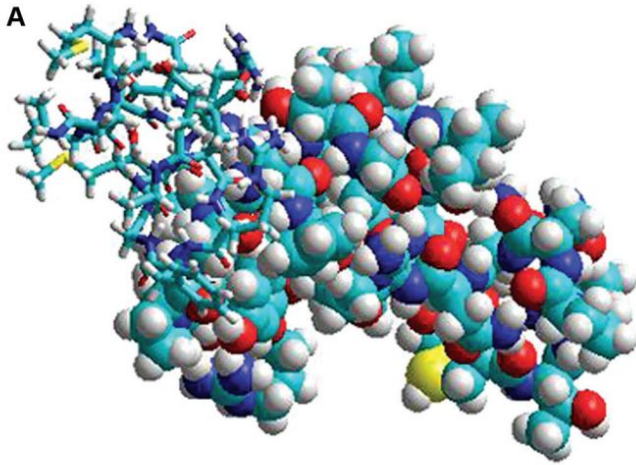


- Red = psi bonds
- Black = phi bonds

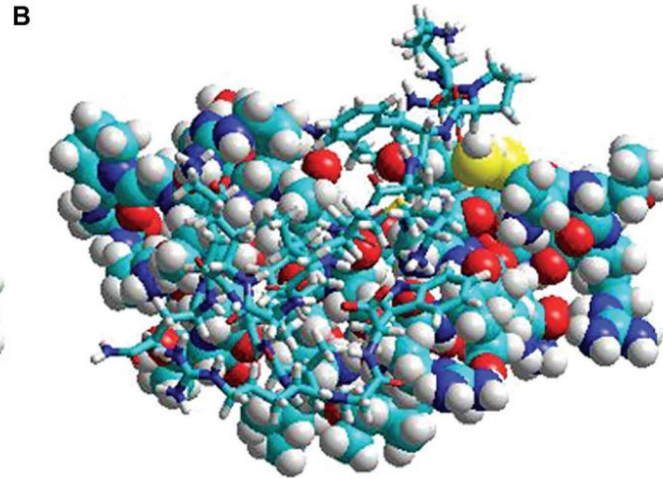
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# Binding sites of peptides can occur at more than one site along the V3 Loop



**CycA**



**FKBP**



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# **N- and C- terminals and Immunogenic tip of the SA-V3 loop may be promising targets for anti-AIDS drug development**

- **Information can be used to target cells and induce neutralizing antibody response**
- **Inflexible regions of SA-V3 regions act as HIV-1 “achilles heel”**
- **These findings can improve immunogenicity of AIDS drugs**
- **Provides a potential strategy for treating HIV and preventing AIDS progression by identifying a potential weakness within the virus**

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# **3D models of SB-V3 regions must be created to verify conserved segments of the SA-V3 region and study the V3 loop under varying conditions**

- **Models should be created and interpreted using the SB-V3 region to increase available data**
- **General consistency of the rigid segments proving to be promising for anti-AIDS medication will confirm analysis**
- **cRMSD and aRMSD calculations should be performed to compare SB to SA and determine consistency of rigid segments in the V3 region**
- **Different forms of the loop should be studied under varying conditions, subsequent data can be used in the synthesis of potential vaccines**

# Summary

- **Various programs and virtual constructions of V3 loop and thorough analysis of the generated models**
- **Three segments along the V3 region are compared showing similarities and conserved regions**
- **The most probable 3D structure of the V3 loop shows secondary structures in the immunogenic region and the N- and C- terminals**
- **N- and C- terminals and immunogenic tip along the SA-V3 region of HIV-1 gene demonstrate promising sites for anti-AIDS drugs**
- **Future work in 3D modeling and analysis of HIV-1 subtype B would show consistency in results for rigid segments along the gene**

# Acknowledgments

**Department of Biology  
Loyola Marymount University**

**Dr. Kam Dahlquist**



## References

- **Andrianov, A. M., & Anishchenko, I. V. (2009). Computational model of the HIV-1 subtype A V3 loop: Study on the conformational mobility for structure-based anti-AIDS drug design. Journal of Biomolecular Structure and Dynamics, 27(2), 179-193. DOI: 10.1080/07391102.2009.10507308**