



Constructing a novel chimeric multiepitope vaccine against Simian immunodeficiency virus accessory proteins: Using hybrid deep learning algorithms and bioinformatics-driven tools

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ABSTRACT

Simian immunodeficiency virus (SIV), the evolutionary precursor of HIV, mirrors HIV in viral organization, transmission patterns, and disease progression in rhesus macaques. Because of these parallels, SIV serves as a practical model for exploring preventative strategies. This study aimed to examine SIV accessory proteins—Nef, Vif, Vpr, and Vpx—for their potential utility in vaccine construction using computational immunology and bioinformatics tools. Multiple epitope prediction platforms were employed to screen viral proteins and identify immunogenic regions meeting the criteria for antigenicity, lack of toxicity, and absence of allergenicity. Selected epitopes were assembled into a multiepitope construct using appropriate linkers and combined with the 50S ribosomal protein L7/L12 as an adjuvant. Structural modeling and refinement were followed by molecular docking against five Toll-like receptors (TLR2, TLR3, TLR4, TLR7, and TLR9). Stability and dynamic behavior were assessed using normal mode analysis and molecular dynamics simulations. An immune simulation model was applied to estimate the vaccine's immunological performance. Thirty candidate epitopes fulfilled all selection criteria and were incorporated into the final construct. The refined structure demonstrated favorable binding orientations with all examined TLRs. Computational stability analyses supported the structural integrity of the vaccine–receptor complexes. Immune simulations predicted strong antibody responses and activation of key cellular immune pathways. The findings suggest that the designed multiepitope construct has the potential to stimulate broad and durable immune responses against SIV. These results support further experimental evaluation and highlight the usefulness of *in silico* approaches in early vaccine design.

1. Introduction

Infectious diseases, particularly those with pandemic potential such as the ongoing HIV crisis, represent one of the most persistent and devastating challenges to global health. These diseases pose significant challenges to global health systems, disproportionately affecting public health resources, economies, and particularly vulnerable populations (Chahroudi et al., 2012).

Among various viruses, SIV is a retroviral member that originates from nonhuman primates (NHPs), specifically African apes and chimpanzees, and comprises multiple strains that induce chronic infections

across various NHP species. SIV exhibits high genetic homology with HIV, particularly with respect to structural, regulatory, and accessory genes, reflecting their common origin (Sharp and Hahn, 2010). Both viruses belong to the *Lentivirus* genus of the *Retroviridae* family and share critical features such as a long incubation period, persistent infection, and a sophisticated arsenal of immune-evasion mechanisms (Compton and Emerman, 2013). Although SIV and HIV are distinct primate lentiviruses, their related biology has made SIV an indispensable model for studying lentiviral pathogenesis, immune escape, and vaccine-induced protection in NHPs. SIV infection of macaques recapitulates the key features of human HIV-1 infection, including CD4 + T-cell depletion,

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.compbiolchem.2026.109316](https://doi.org/10.1016/j.compbiolchem.2026.109316).

Data availability

The original contributions presented in the study are included in the article/Supplementary material. Further inquiries can be directed to the corresponding authors.

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