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***Short Communication***

# Comparison and Phylogenetic Analysis of HIV retroviral Gag Poly Protein Precursors

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## Abstract

*The human immunodeficiency virus type I (HIV-1) is a member of retrovirus family, initially synthesized as the central and core domain of the Gag polyprotein. These polyprotein precursors are produced from the unspliced genomic RNA on free ribosomes within the cytoplasm. The entire process of membrane binding, particle assembly and maturation may occur sometimes in the absence of certain viral envelope proteins. Gag molecules generally gather and capture the viral RNA. After this, it migrates towards the inner cell membrane and assemble into immature viral particles of the cell. They are mainly involved in assembly of virus like particles. Analysis of retroviruses including HIV, SIV and their precursors reveals new insights to study their proper functioning and mechanism of action. In this study, sequence alignments were performed to analyze the similarity and phylogenetic analysis helped to know the evolutionary relationships among these protein precursors. For, this various bioinformatics tools was used for analysis which will help to study their function and also the structural level predictions.*

**Keywords**: Gag, Capsid, Viral, Phylogenetic Analysis.

## Introduction

HIV-1 belongs to lentiviruses released by cell surface via budding and gathers at the plasma membrane. A host cell-derived lipid envelop enwraps the nascent viral capsid by protecting it from the external environment. Gag protein is the major protein encoded by all reteroviruses. It controls the gathering and assembling of HIV-1. Previous studies shown, virus-like particles are formed by gag protein in the absence of other viral proteins. Gag plays an important role to code for the precursor gag polyprotein which is processed by viral protease during maturation of matrix protein and capsid protein. Gag Protein belongs to family of reteroviruses. They play major role in assembly of virus like particles. Studies has proved gag as the main structural protein of retroviruses and HIV-1.

Gag has core ability to recognize specifically the genomic RNA, viral and host protein. These proteins plays many important functions and also contributes as a main traffic machinery to the cell membrane. Also, it plays an important role in correct assembly, budding and maturation of many new infectious particles. According to studies, the HIV-1 Gag proteins are involved in multiple complex mechanisms during the complete life cycle. Gag proteins are engaged in interactions with many other gag and viral proteins leading towards various diverse functions. Gag can often act as a precursor, because it can cleave by the viral protease (PR), which results in the virion internal structural proteins. Cleavage products released by gags like matrix, capsid and nucleocapsid are common to all retroviruses.

Simian immunodeficiency viruses (SIV) also belongs to family of lentiviruses that naturally infect different species[1,2]. Studies reported, transmission of SIVs from animals like chimpanzees and gorillas which leads towards emergence of human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2)[3-5]. According to some previous reports, high divergence was observed among these animals. Each primate species was found to be infected with one or sometimes more species-specific viruses. On the other hand, some cross-species transmission and recombination examples are also known[6-10].

All reported lentiviruses characterized have found to be rich with 18 cysteine residues which are conserved in external subunit of gp120. Scientist observed four cysteine pairs in SIV strains located in different putative domains of gp120[11]. These conserved motifs were also present in gag and other protein domains. Identification of HIV-1 disease and its primary source is of scientific and extreme importance. Hence, it is cleared that lentivirus is an immediate precursor of HIV-1 that infects chimpanzees of *Pan troglodytes* which belongs to a subspeciesin central part of west Africa[12,13]. It is also known about SIV strains which have been transmitted to humans resulting from various transmission events in the beginning of the twentieth century[14-16]. Also, a number of retroviral Gag proteins were found assembled with the membrane through some electrostatic interactions[17-21]. A variety of genes are found

to be involved in HIV which codes for several structural proteins present in all retroviruses. The studies shown, there are three major genes in HIV genome mainly, 5'gag-pol-env-3'. This gene encodes multiple structural proteins and essential enzymes. The *gag* gene is involved in maintaining the basic physical structure of the virus. Where as*pol* provides the basic mechanism by which retroviruses reproduce.

## Materials and Methods

Several computational tools were used for analysis of HIV, SIV and their protein precursor.

**Sequence Retrieval:** Sequences were retrieved from NCBI-Genbank data repository.

**Multiple Sequence Alignment:** Sequence alignment was performed by using T-Coffee computational tool.

**Phylogenetic Analysis:** Phylogenetic analysis was done using CLUSTALW software to study the evolutionary relationships among all these retrovirus protein precursors.

**Conserved domain Analysis:** The domain analysis showed various conserved regions. This was performed by using CDD analysis tool.

## Results and Discussion

The human immunodeficiency virus type 1 gag protein shows expression is sufficient for efficient assembly of virus-like particles in mammalian cells. The sequence alignments and phylogenetic analysis shows the evolutionary relationships.

**HIV 1 Sequence Retrieval:** >gil9626453:450-1739 Human T-lymphotropic virus 1, complete genome.

**SIV Sequence Retrieval:** >gil9627204:897-5314 Simian immunodeficiency virus, complete genome

ATGGGCCAAATCTTTTCCCGTAGCGCTAGCCCTATTCCGCGGCCGCCCCGGGGGCTGGCCGCTCATCACT
GGCTTAACTTCCTCCAGGCGGCATATCGCCTAGAACCCGGTCCCTCCAGTTACGATTTCCACCAGTTAAA
AAAATTTCTTAAAATAGCTTTAGAAACACCGGTCTGGATCTGCCCCATTAACTACTCCCTCCTAGCCAGC
CTACTCCCAAAAGGATACCCCGGCCGGGTGAATGAAATTTTACACATACTCATCCAAACCCAAGCCCAGA
TCCCGTCCCGCCCCGCGCCGCCGCCGCCGTCATCCTCCACCCACGACCCCCCGGATTCTGACCCACAAAT
CCCCCCTCCCTATGTTGAGCCTACAGCCCCCCAAGTCCTTCCAGTCATGCACCCACATGGTGCCCCTCCC
AACCACCGCCCATGGCAAATGAAAGACCTACAGGCCATTAAGCAAGAAGTCTCCCAAGCGGCCCCTGGAA
GCCCCCAGTTTATGCAGACCATCCGGCTTGCGGTGCAGCAGTTTGACCCCACTGCCAAAGACCTCCAAGA
CCTCCTGCAGTACCTTTGCTCCTCCCTCGTGGCTTCCCTCCATCACCAGCAGCTAGATAGCCTTATATCA
GAGGCCGAAACTCGAGGTATTACAGGTTATAACCCCTTAGCCGGTCCCCTCCGTGTCCAAGCCAACAATC
CACAACAACAAGGATTAAGGCGAGAATACCAGCAACTCTGGCTCGCCGCCTTCGCCGCCCTGCCAGGGAG
TGCCAAAGACCCTTCCTGGGCCTCTATCCTCCAAGGCCTGGAGGAGCCTTACCACGCCTTCGTAGAACGC
CTCAACATAGCTCTTGACAATGGGCTGCCAGAAGGCACGCCCAAAGACCCCATTTTACGTTCCTTAGCCT
ACTCTAATGCAAACAAAGAATGCCAAAAATTACTACAGGCCCGAGGGCACACTAATAGCCCTCTAGGAGA
TATGTTGCGGGCTTGTCAGGCCTGGACCCCCAAAGACAAAACCAAAGTGTTAGTTGTCCAGCCTAAAAAA
CCCCCCCCAAATCAGCCGTGCTTCCGGTGCGGGAAAGCAGGCCACTGGAGTCGGGACTGCACTCAGCCTC
GTCCTCCCCCTGGGCCATGCCCCCTATGTCAAGATCCAACTCACTGGAAGCGAGACTGCCCCCGCCTAAA
GCCCACTATCCCAGAACCAGAGCCAGAGGAGGATGCCCTCCTATTAGATCTCCCCGCCGACATCCCACAC
CCAAAAAACTCCATAGGGGGGGAGGTTTAA

**Figure-1**
**Shows sequence retrieval of Human T-lymphotropic virus 1 from Genbank-NCBI**

ATGGGCGGGGGTCACTCAGCACTGTCAGGGAGAAGCCTCGACACGTTCGAGAAGATTAGGCTACGTCCGA
ACGGGAAAAAGAAGTACCAAATTAAACATTTAATATGGGCAGGAAAAGAAATGGAACGATTTGGGTTACA
TGAGAAACTTTTAGAAACAAAAGAAGGCTGTCAAAAAATCATAGAAGTTTTAACCCCGTTGGAACCGACA
GGCTCCGAGGGGCTAAAAGCTCTGTTTAATTTGTGCTGCGTCATTTGGTGCATTCACGCAGAACAGAAAG
TGAAAGACACAGAGGAAGCTGTAGTAACAGTTAAGCAACACTACCATCTAGTGGACAAAAATGAGAAAGC
AGCTAAAAAGAAAAATGAGACAACAGCGCCACCTGGTGGCGAATCAAGAAATTACCCAGTAGTAAATCAG
AATAATGCCTGGGTACACCAGCCTTTGTCTCCGCGCACGTTAAATGCGTGGGTCAAATGCGTGGAGGAAA
AAAGGTGGGGAGCAGAAGTAGTCCCCATGTTCCAAGCACTCTCAGAGGGATGTCTCTCCTATGATGTAAA
TCAGATGCTCAATGTAATAGGAGACCATCAGGGGGCATTACAAATTCTTAAGGAAGTCATTAATGAAGAA
GCAGCAGAGTGGGACAGGACACACAGACCACCAGCTGGCCCGTTACCAGCAGGGCAGCTAAGAGACCCGA
CAGGGTCAGATATAGCAGGAACTACCAGCTCAATTCAGGAACAAATAGAGTGGACCTTCAATGCCAATCC
AAGAATAGACGTAGGGGCACAATACAGAAAATGGGTTATTTTGGGCTTACAAAAGGTAGTGCAGATGTAC
AATCCCCAAAAGGTCCTAGACATTCGACAGGGACCTAAAGAACCCTTCCAGGACTATGTAGACAGATTCT
ATAAAGCCCTGAGAGCAGAACAAGCACCACAGGATGTTAAAAATTGGATGACACAAACTTTGCTTATCCA
GAATGCCAATCCGGATTGTAAATTGATTCTGAAAGGATTGGGAATGAATCCAACCTTGGAGGAAATGCTA
ATAGCTTGCCAGGGAGTAGGAGGGCCACAACATAAGGCTAAGCTAATGGTAGAAATGATGAGTAATGGAC
AGAATATGGTCCAAGTGGGACCTCAGAAAAAGGGCCCCCGAGGGCCGCTAAAATGCTTTAATTGTGGCAA
ATTTGGACATATGCAAAGGGAATGCAAGGCACCAAGACAGATCAAATGCTTTAAGTGCGGCAAAATTGGC
CATATGGCAAAAGACTGCAAGAATGGACAGGCAAATTTTTTAGGGTATGGCCATTGGGGAGGAGCGAAAC
CAAGAAATTTTGTGCAATACAGAGGAGACACAGTTGGTCTGGAACCAACAGCCCCCCCAATGGAAACAGC
TTACGATCCAGCAAAGAAGCTCCTCCAGCAGTATGCAGAGAAGGGACAGCGCCTGAGAGAGGAGAGAGAA
CAGACAAGGAAACAGAAGGAGAAAGAAGTGGAGGATGTTTCCTTGAGCTCCCTCTTTGGAGGAGACCAAT
GAAACGAGTCATCATAGAAGGAACGCCAGTGCAAGCCTTGTTAGATACAGGAGCAGATGACACTATAATT

**Figure-2**

**Sequence retrieval of Simian immunodeficiency virus from Genbank-NCBI**

>gi|568815592:c31357212-31353868 Homo sapiens chromosome 6, GRCh38.p2 Primary Assembly
AGTTCTAAAGTCCCCACGCACCCACCCGGACTCAGAGTCTCCTCAGACGCCGAGATGCTGGTCATGGCGC
CCCGAACCGTCCTCCTGCTGCTCTCGGCGGCCCTGGCCCTGACCGAGACCTGGGCCGGTGAGTGCGGGTC
GGGAGGGAAATGGCCTCTGCCGGGAGGAGCGAGGGGACCGCAGGCGGGGGCGCAGGACCTGAGGAGCCGC
GCCGGGAGGAGGGTCGGGCGGGTCTCAGCCCCTCCTCACCCCCAGGCTCCCACTCCATGAGGTATTTCTA
CACCTCCGTGTCCCGGCCCGGCCGCGGGGAGCCCCGCTTCATCTCAGTGGGCTACGTGGACGACACCCAG
TTCGTGAGGTTCGACAGCGACGCCGCGAGTCCGAGAGAGGAGCCGCGGGCGCCGTGGATAGAGCAGGAGG
GGCCGGAGTATTGGGACCGGAACACACAGATCTACAAGGCCCAGGCACAGACTGACCGAGAGAGCCTGCG
GAACCTGCGCGGCTACTACAACCAGAGCGAGGCCGGTGAGTGACCCCGGCCCGGGGCGCAGGTCACGACT
CCCCATCCCCCACGTACGGCCCGGGTCGCCCCGAGTCTCCGGGTCCGAGATCCGCCTCCCTGAGGCCGCG
GGACCCGCCCAGACCCTCGACCGGCGAGAGCCCCAGGCGCGTTTACCCGGTTTCATTTTCAGTTGAGGCC
AAAATCCCCGCGGGTTGGTCGGGGCGGGGCGGGGCTCGGGGGACTGGGCTGACCGCGGGGCCGGGGCCAG
GGTCTCACACCCTCCAGAGCATGTACGGCTGCGACGTGGGGCCGGACGGGCGCCTCCTCCGCGGGCATGA
CCAGTACGCCTACGACGGCAAGGATTACATCGCCCTGAACGAGGACCTGCGCTCCTGGACCGCCGCGGAC
ACGGCGGCTCAGATCACCCAGCGCAAGTGGGAGGCGGCCCGTGAGGCGGAGCAGCGGAGAGCCTACCTGG
AGGGCGAGTGCGTGGAGTGGCTCCGCAGATACCTGGAGAACGGGAAGGACAAGCTGGAGCGCGCTGGTAC
CAGGGGCAGTGGGGAGCCTTCCCCATCTCCTATAGGTCGCCGGGGATGGCCTCCCACGAGAAGAGGAGGA
AAATGGGATCAGCGCTAGAATGTCGCCCTCCGTTGAATGGAGAATGGCATGAGTTTTCCTGAGTTTCCTC
TGAGGGCCCCCTCTTCTCTCTAGACAATTAAGGAATGACGTCTCTGAGGAAATGGAGGGGAAGACAGTCC
CTAGAATACTGATCAGGGGTCCCCTTTGACCCCTGCAGCAGCCTTGGGAACCGTGACTTTTCCTCTCAGG
CCTTGTTCTCTGCCTCACACTCAGTGTGTTTGGGGCTCTGATTCCAGCACTTCTGAGTCACTTTACCTCC
ACTCAGATCAGGAGCAGAAGTCCCTGTTCCCCGCTCAGAGACTCGAACTTTCCAATGAATAGGAGATTAT
CCCAGGTGCCTGCGTCCAGGCTGGTGTCTGGGTTCTGTGCCCCTTCCCCACCCCAGGTGTCCTGTCCATT
CTCAGGCTGGTCACATGGGTGGTCCTAGGGTGTCCCATGAAAGATGCAAAGCGCCTGAATTTTCTGACTC
TTCCCATCAGACCCCCCAAAGACACACGTGACCCACCACCCCATCTCTGACCATGAGGCCACCCTGAGGT
GCTGGGCCCTGGGTTTCTACCCTGCGGAGATCACACTGACCTGGCAGCGGGATGGCGAGGACCAAACTCA
GGACACTGAGCTTGTGGAGACCAGACCAGCAGGAGATAGAACCTTCCAGAAGTGGGCAGCTGTGGTGGTG
CCTTCTGGAGAAGAGCAGAGATACACATGCCATGTACAGCATGAGGGGCTGCCGAAGCCCCTCACCCTGA
GATGGGGTAAGGAGGGGGATGAGGGGTCATATCTCTTCTCAGGGAAAGCAGGAGCCCTTCAGCAGGGTCA
GGGCCCCTCATCTTCCCCTCCTTTCCCAGAGCCGTCTTCCCAGTCCACCGTCCCCATCGTGGGCATTGTT
GCTGGCCTGGCTGTCCTAGCAGTTGTGGTCATCGGAGCTGTGGTCGCTGCTGTGATGTGTAGGAGGAAGA
GTTCAGGTAGGGAAGGGGTGAGGGGTGGGGTCTGGGTTTTCTTGTCCCACTGGGGGTTTCAAGCCCCAGG

**Figure-3**

**Sequence retrieval of homosapiens chromosome 6 from Genbank-NCBI**

**Sequence Alignment**: Sequence alignments results are shown in Figure-4. The comparison showed the highly conserved regions, regions with less similarity and regions with poor alignment having gaps. The sequences were analyzed by using T-Coffee and CLUSTALW multiple sequence alignment tool. By analyzing these genes, it will be easy to study related evolutionary pathways among them.

**Phylogenetic Tree:** Analysis results shows the Neighbour-joining tree without distance corrections. The tree shows evolutionary emergence of these genes from ancestors. Each gene was assigned a particular identification ID by T-Coffee. These were assigned distances according to their evolutionary distances. The results are shown in Figure-5.

**Gag Protein Conserved domains:** Domains are functional and conserved region of protein. The gag protein was analysed to find the conserved domains by using domain analysis software like CDD and pfam.The gag protein belongs to superfamily p19. The reults shows its covered area starts from 149 and ends at 325 position (Figure-6).


**Figure-4**
**Shows T-Coffee Multiple Sequence Alignment (MSA)**

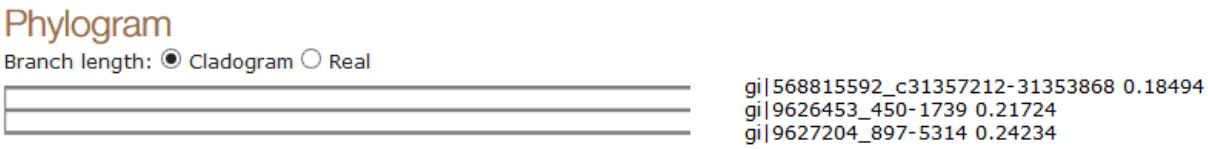


**Figure-5**
**Shows the obtained Phylogenetic tree from CLUSTALW**

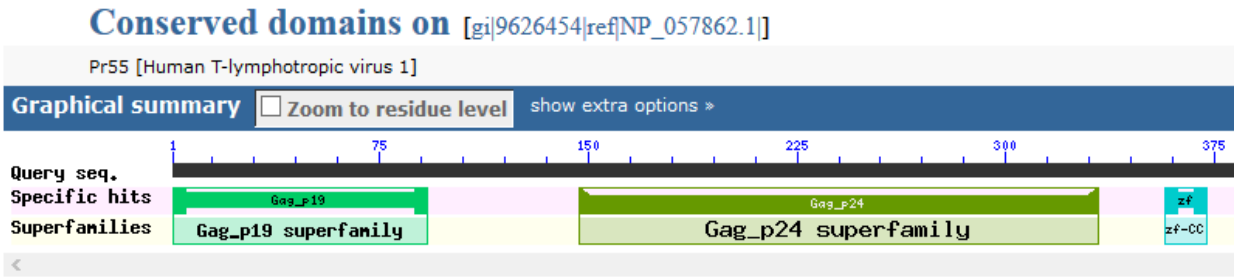


**Figure-6**
**Shows the conserved domains of Gag polyprotein precursor**

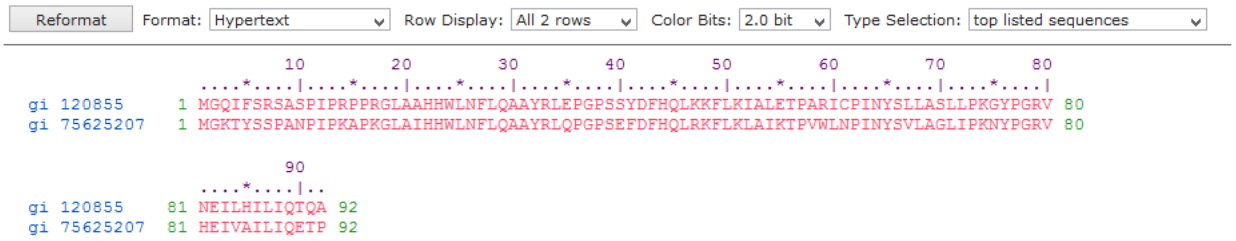


**Figure-7**
**Shows the conserved regions of Gag protein from pfam database**

**Discussion:** The human immunodeficiency virus protein is found to be synthesized as the core domain of the Gag polyprotein. Gag polyprotein is considered as a 231-amino-acid protein. Studies shown various molecular mechanisms involved in the assembly of the virus particle from the Gag protein but still some are not well understood. Assembly of human immunodeficiency virus (HIV) particles takes place at outer surface of infected cells mainly plasma membrane. The major structural proteins of HIV originate as Pr55GaF and as a Gag polyprotein precursor. For efficient assembly of virus like particles in mammalian cells the expression of human immunodeficiency virus type 1 (HIV-1) Gag polyprotein is found variable. But in some cases, it is sufficient. These particles found with diameter of 100–150 nm and are roughly spherical containing several thousand Gag molecules.

## Conclusion

Analysis of these proteins predicted many conserved regions within the domains. The Phylogenetic analysis shown the evolutionary relationships and also the ratio of similarity among different genes encoding proteins in all retroviruses. Therefore, it is easier to study the structural proteins and to analyze the conserved domains of these proteins which are mainly responsible for causing HIV disease.

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