

# **Nonsynonymous Amino Acid Mutations in gp120 Binding Sites are Related to Progression of HIV-1**

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BIOL 368: Bioinformatics Laboratory  
Loyola Marymount University  
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# Outline

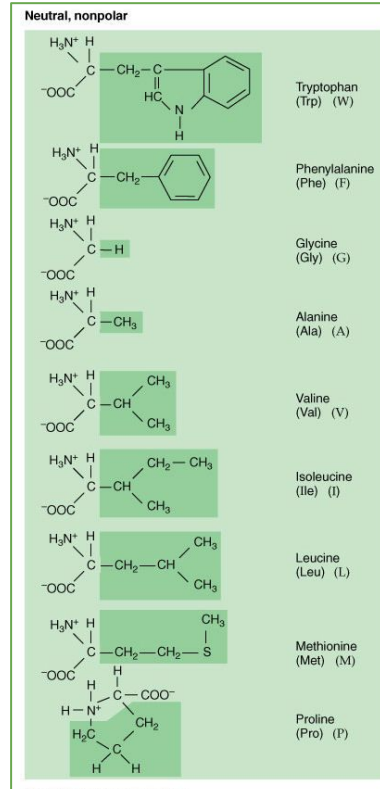
- 1. Nonsynonymous mutations in binding sites affects gp120 and CD4 binding.**
- 2. Variability of four subjects' clones were analyzed across two visits to determine structural and functional differences.**
- 3. Rapid progressors showed major mutations across all clones, but few highly variable amino acids appeared.**
- 4. Moderate progressors showed multiple major mutations at amino acids that interact with binding sites.**
- 5. Other studies identified position 317 in gp120 essential for antibody recognition.**

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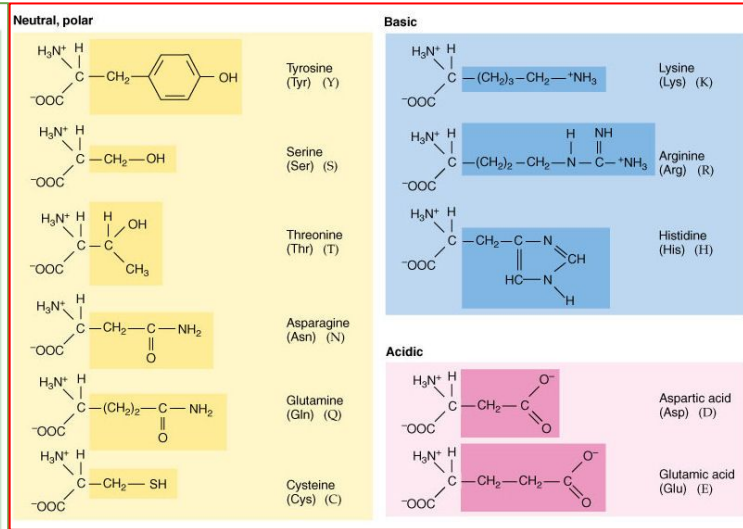
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# Amino Acids are Categorized According to R Groups

Hydrophobic



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Hydrophilic

Nonsynonymous amino acid mutations are mutations across these two groups.

# Amino Acids in Binding Sites Must be Highly Specific for Proteins to Successfully Bind With Ligands

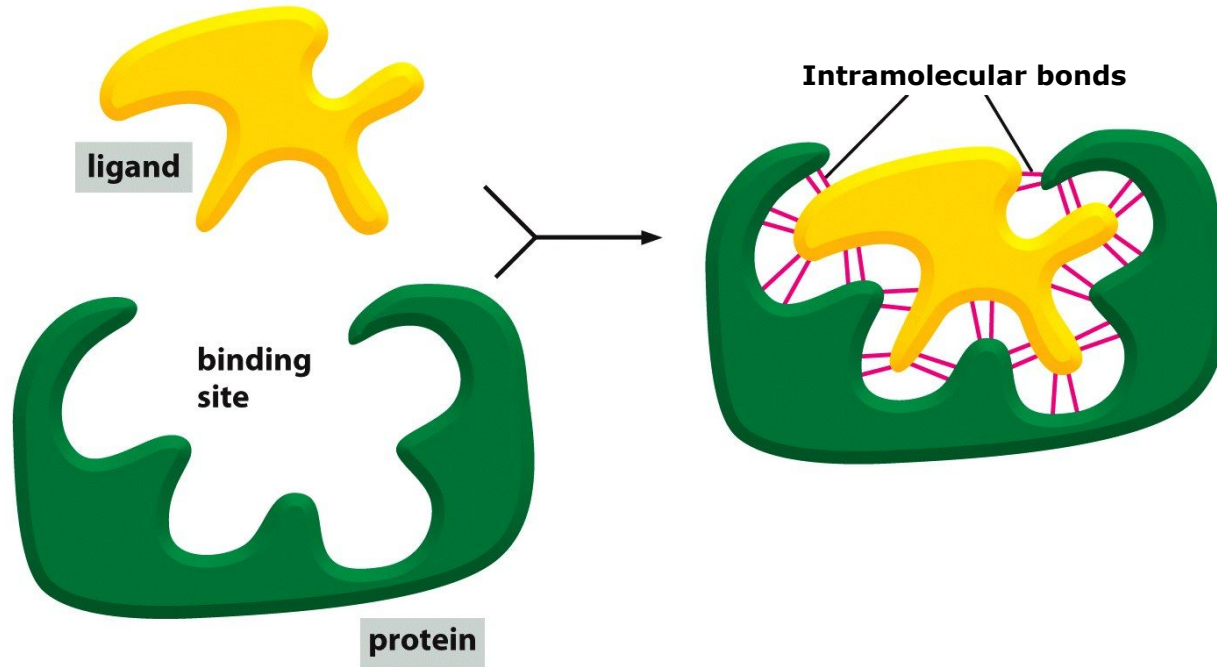
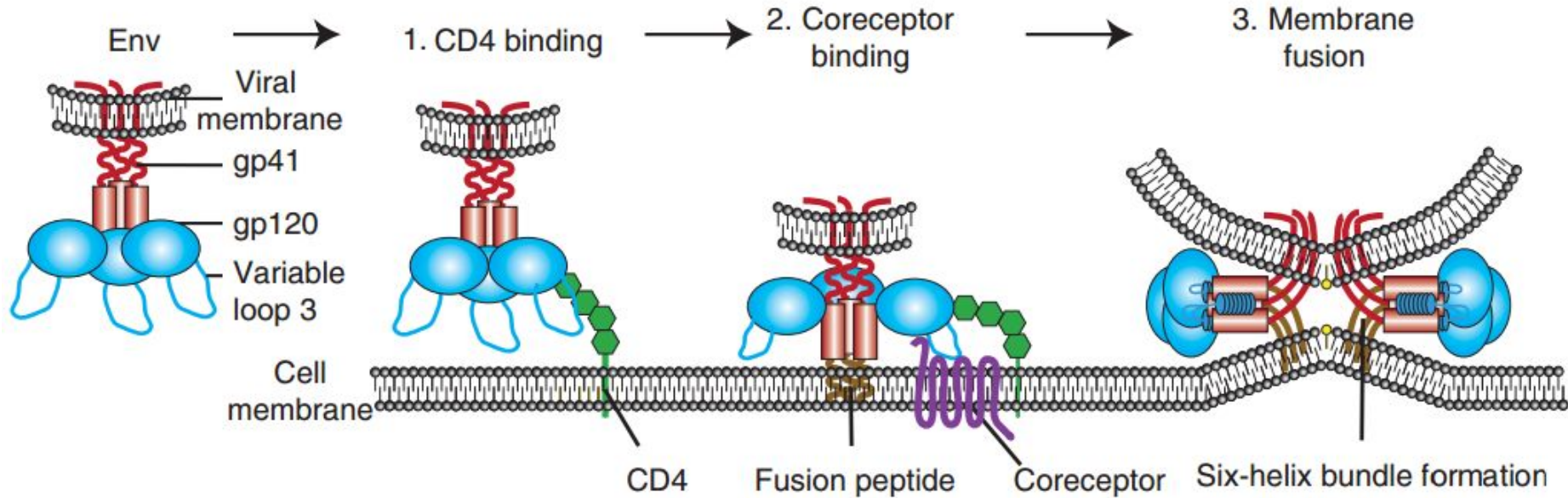


Figure 4-27 Essential Cell Biology 3/e (© Garland Science 2010)

# Interactions Between gp120 and CD4 cells Impact Progression of HIV-1



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# Mutations in Four Subjects' Protein Sequences Were Analyzed to Determine Functional Differences

**Question:** How do mutations in gp120 affect function of the protein?

**Hypothesis:** Nonsynonymous mutations in gp120 in key locations will most greatly affect protein function.

- Subjects 4(RP), 9(MP), 11(RP), and 14(MP)
  - Different progressor groups, but same dS/dN values
- Clones collected from Visit 1 and Visit 4
  - Compare extent of change in structure over time
- Amino acids 269 - 363 in gp120 analyzed



# Subjects Have Identical dS/dN Values in Different Progressor Groups

Table 1. Summary data on 15 seroconverters

| Subject             | No. of observations | Baseline |                                                       |                                       | Annual rate of CD4 T cell decline | Slope of change in intravisit nucleotide differences per clone per year | Slope of divergence (% nucleotides mutated from baseline consensus sequence per year) | Median dS/dN |
|---------------------|---------------------|----------|-------------------------------------------------------|---------------------------------------|-----------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------|--------------|
|                     |                     | CD4      | Median intravisit nucleotide differences among clones | Virus copy number (×10 <sup>3</sup> ) |                                   |                                                                         |                                                                                       |              |
| Rapid Progressor    |                     |          |                                                       |                                       |                                   |                                                                         |                                                                                       |              |
| Subject 4           | 4                   | 1,028    | 0.90                                                  | 6.8                                   | −593                              | 4.64                                                                    | 2.09                                                                                  | 0.0          |
| Subject 10          | 5                   | 833      | 1.71                                                  | 99.3                                  | −363                              | 3.16                                                                    | 1.00                                                                                  | 0.2          |
| Subject 11          | 4                   | 753      | 2.27                                                  | 62.2                                  | −363                              | 1.11                                                                    | 0.32                                                                                  | 0.0          |
| Subject 15          | 4                   | 707      | 15.16                                                 | 171.0                                 | −362                              | −2.94                                                                   | 0.68                                                                                  | 0.7          |
| Subject 3           | 5                   | 819      | 1.82                                                  | 302.5                                 | −294                              | 0.53                                                                    | 0.74                                                                                  | 1.0          |
| Subject 1           | 3                   | 464      | 5.64                                                  | 307.6                                 | −117                              | 5.10                                                                    | 1.55                                                                                  | 0.3          |
| Moderate Progressor |                     |          |                                                       |                                       |                                   |                                                                         |                                                                                       |              |
| Subject 7           | 5                   | 1,072    | 2.27                                                  | 317.6                                 | −392                              | −0.79                                                                   | 1.35                                                                                  | 1.3          |
| Subject 8           | 7                   | 538      | 1.24                                                  | 209.0                                 | −92                               | 1.68                                                                    | 1.16                                                                                  | 0.5          |
| Subject 14          | 9                   | 523      | 1.00                                                  | 50.9                                  | −51                               | 1.69                                                                    | 0.60                                                                                  | 0.0          |
| Subject 5           | 5                   | 749      | 2.50                                                  | 260.6                                 | −41                               | 0.06                                                                    | 0.50                                                                                  | 1.4          |
| Subject 9           | 8                   | 489      | 9.49                                                  | 265.0                                 | −11                               | 1.58                                                                    | 1.21                                                                                  | 0.0          |
| Subject 6           | 7                   | 405      | 2.82                                                  | 321.4                                 | 52                                | 1.92                                                                    | 0.82                                                                                  | 0.4          |
| Nonprogressor       |                     |          |                                                       |                                       |                                   |                                                                         |                                                                                       |              |
| Subject 2           | 5                   | 715      | 1.64                                                  | 21.6                                  | 30                                | 1.32                                                                    | 0.49                                                                                  | 1.8          |
| Subject 12          | 6                   | 772      | 2.80                                                  | 5.1                                   | 44                                | 0.62                                                                    | 0.13                                                                                  | 0.9          |
| Subject 13          | 5                   | 671      | 0.87                                                  | 1.7                                   | 53                                | 0.53                                                                    | 0.28                                                                                  | 3.5          |

# Major Mutations in Protein Sequences were Measured According to the Number and Importance of Substitutions

- We measured the number of positions with:
  - Any amino acid substitutions
  - Major substitutions (hydrophobic to hydrophilic or vice versa)
  - Multiple major substitutions across clones

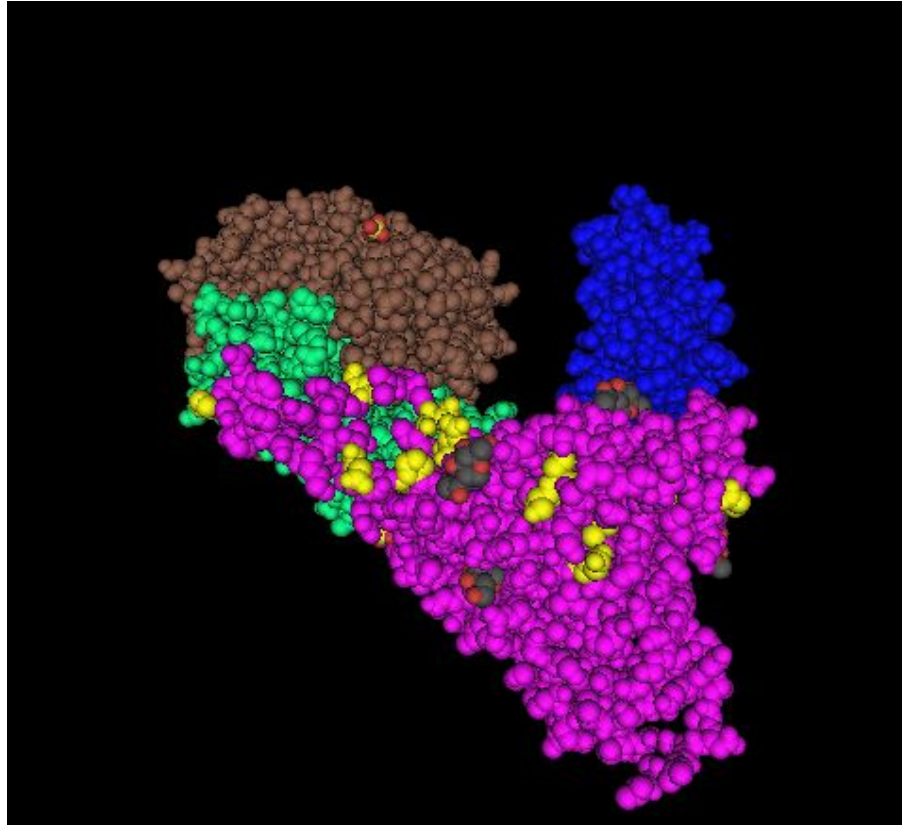
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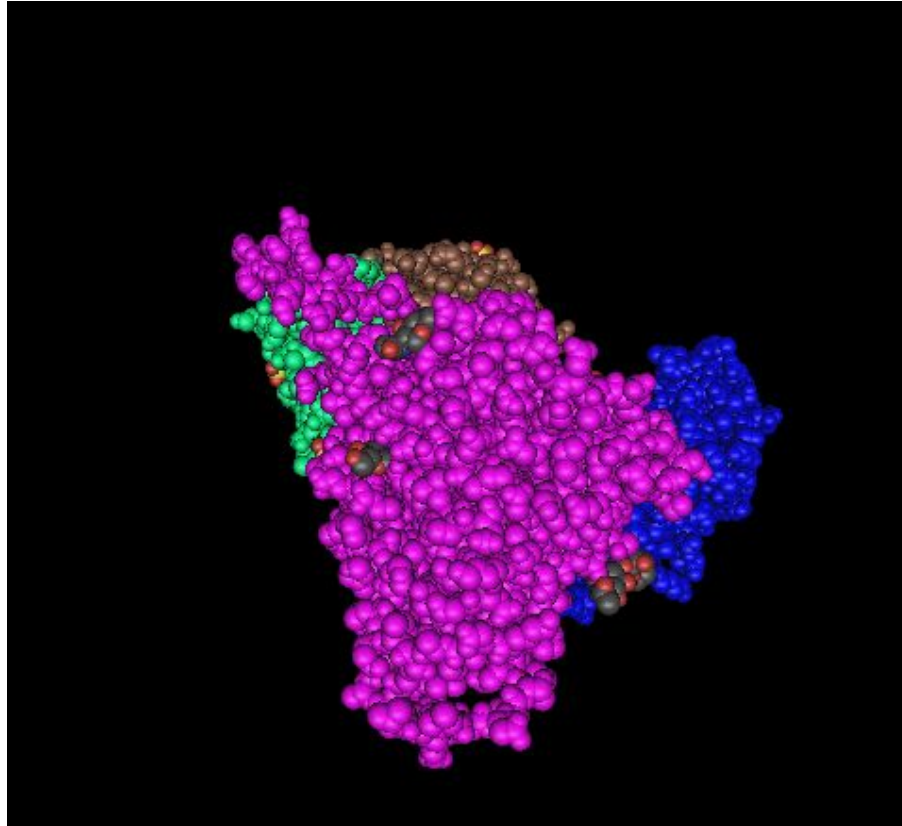
# Subject 4 (RP) Has Major Mutations at More Positions with Less Variability

|             |                                                                  |
|-------------|------------------------------------------------------------------|
| S4V4-11     | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RVGD IRQA  |
| S4V4-9      | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RVGD IRQA  |
| S4V4-12     | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RVGD IRQA  |
| S4V4-10     | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RVGD IRQA  |
| S4V4-3      | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RVGD IRQA  |
| S4V4-13     | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGLGSSSFYTTG-RIGD IRQA |
| S4V4-2      | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPGRSFYTTG-IVGD IRQA  |
| S4V4-8      | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-II GD IRQA |
| S4V4-5 [4]  | EVVIRSENFTHNARI IIVQLNESVEINCTRPDNNTVRRIP IGPSSSFYTTG-RIGD IRQA  |
| S4V4-1      | EVVIRSENFTHNARI IIVQLNRSVEINCTRPDNNTVRRIP IGPSSSFYTTG-RIGD IRQA  |
| S4V4-7      | EVVIRSENFTHNARI IIVQLNRSVEINCTRPNNNTIRRIP IGPGRAPYTTG-RIGN IRQA  |
| S4V4-4      | EVVIRSENFTHNARI IIVQLNRSVEINCTRPNNNTIRRIP IGPGRAPYTTG-RIGN IRQA  |
| S4V1-3 [3]  | EVVIRSENFTHNARI IIVQLNRSVEINCTRPNNNTIRRIP IGPGRAPYTTG-RIGD IRPA  |
| S4V1-1      | EVVIRSENFTHNARI IIVQLNRSVEINCTRPNNNTIRRIP IGPGRAPYTTG-RIGD IRPA  |
| S4V1-2 [11] | EVVIRSENFTHNARI IIVQLNRSVEINCTRPNNNTIRRIP IGPGRAPYTTG-RIGD IRQA  |
| Huang       | EVVIRSDNPTNNART IIVQLRESVEINCTRPQNTRKSI IGPGRAPYTTGE II GD IRQA  |
| consensus   | EVVIRSENFTHNARI IIVQLNESVEINCTRPdnnTVrkIP IGPg■FYTTG-riGdIRqA    |
|             |                                                                  |
| S4V4-11     | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-9      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-12     | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-10     | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-3      | HCNISRTK■NNTLRLLIANKLREQPGNRTIIFNQSS                             |
| S4V4-13     | HCNISRTK■NNTLRLLIANKLREQPGNRTIIFNQSS                             |
| S4V4-2      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-8      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-5 [4]  | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-1      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-7      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V4-4      | HCNILEAK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V1-3 [3]  | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V1-1      | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| S4V1-2 [11] | HCNISRTK■NNTLRLLIVNKLREQPGNRTIIFNQSS                             |
| Huang       | HCNISRTAK■NDTLRQIVIKLREQPGNRTIVFNRSS                             |
| consensus   | HCNI■rtK■NntLRLLIVnKLREQPgNRTIiFPqSS                             |

## Subject 4 (RP) Had Major Mutations at 19 Positions



# Subject 4 (RP) Lacks Positions with Multiple Major Mutations



# Subject 11 (RP) Indicates Several Locations With Major Amino Acid Mutations

```

S11V4-7      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-4      -----EVIIRSENFsNNAKNIIVQLNESV
S11V1-2      -----EVIIRSENFsNNAKNIIVQLNESV
S11V1-3[4]   -----EVIIRSENFsNNAKNIIVQLNESV
S11V1-6      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-5      -----EVIIRSENFsNNAKNIIVQLNESV
S11V1-7      -----EVIIRSKNEfSNAKNIIVQLNESV
S11V1-1      -----EVIIRSKNEfSNAKNIIVQLNESV
S11V1-4      -----EVIIRSKNEfSNAKNIIVQLNESV
S11V1-5      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-3      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-1[2]   -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-8      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-2      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-9      -----EVIIRSENFsNNAKNIIVQLNESV
S11V4-6      -----EVIIRSENFsNNAKNIIVQLNESV
2B4C_G_Chain_G_ STVQCTHGIRPVVSTQLLLNGSLABEEVIRSDNEfTNAKTIIVQLKESV
consensus      -----EVIIRSENFsNNAKNIIVQLNESV

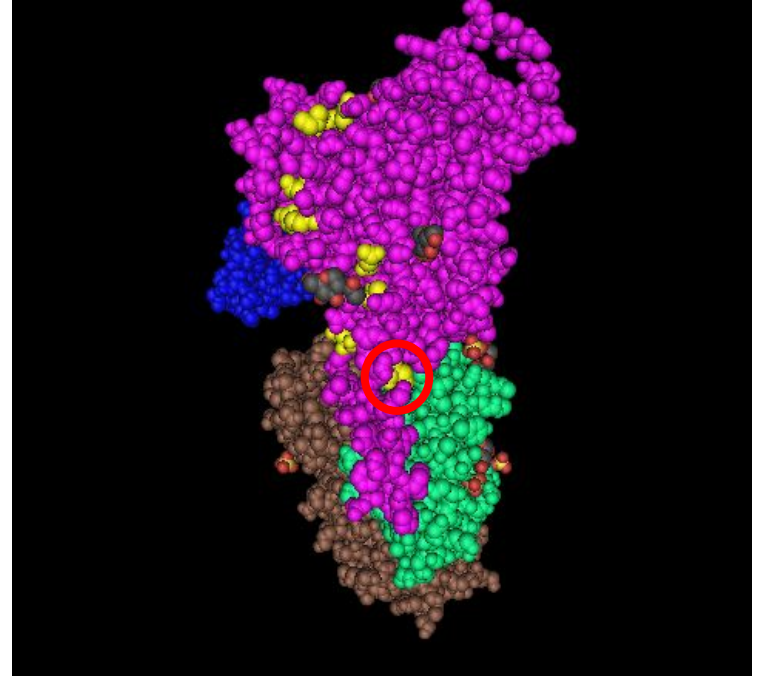
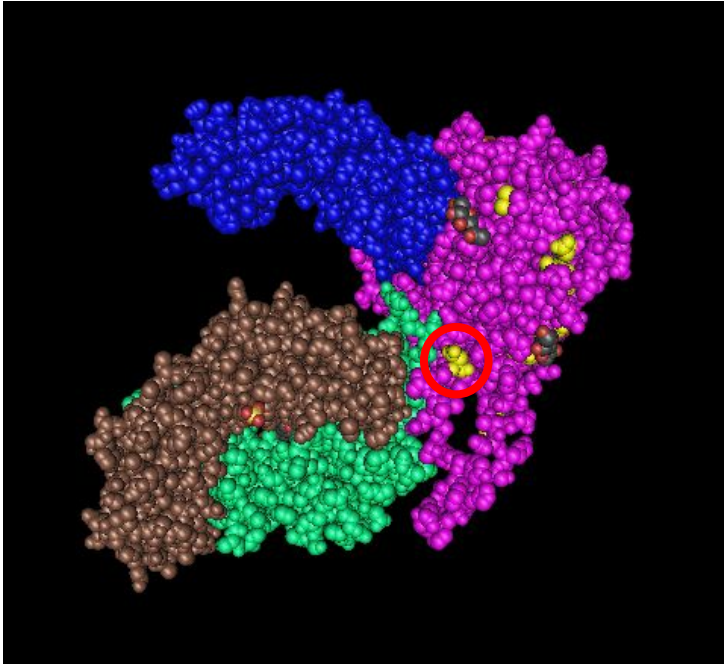
S11V4-7      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-4      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-2      VITCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-3[4]   VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-6      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-5      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-7      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-1      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-4      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V1-5      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-3      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-1[2]   VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-8      VINCTRPDNTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-2      VINCRPDYTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-9      VINCTRPDYTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
S11V4-6      VINCTRPDYTIKQRIIHIGPGRPFYTTG-IKGNIRQAHCNVsRGQWnKTL
2B4C_G_Chain_G_ EINCTRP-NQNTRKSIHIGPGRAFYTTGSIGDIRQAHCNIIRAKWnDTL
consensus      vInCtRPdntIkqriIHIGPGRpFYTTG-IkGnIRQAHCNVsrgqWnKTL

S11V4-7      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-4      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-2      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-3[4]   EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-6      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-5      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-7      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-1      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-4      EQVVRKLREqYGLNKTIvFKQPI-----
S11V1-5      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-3      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-1[2]   EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-8      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-2      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-9      EQVVRKLREqYGLNKTIvFKQPI-----
S11V4-6      EQVVRKLREqYGLNKTIvFKQPI-----
2B4C_G_Chain_G_ KQIVIKLREQYGDPNIVMHSFGGDPIVMHSFGGDFFYCNSAQLFN
consensus      eQvVrKLREqYgLNKTIvFkqpi-----

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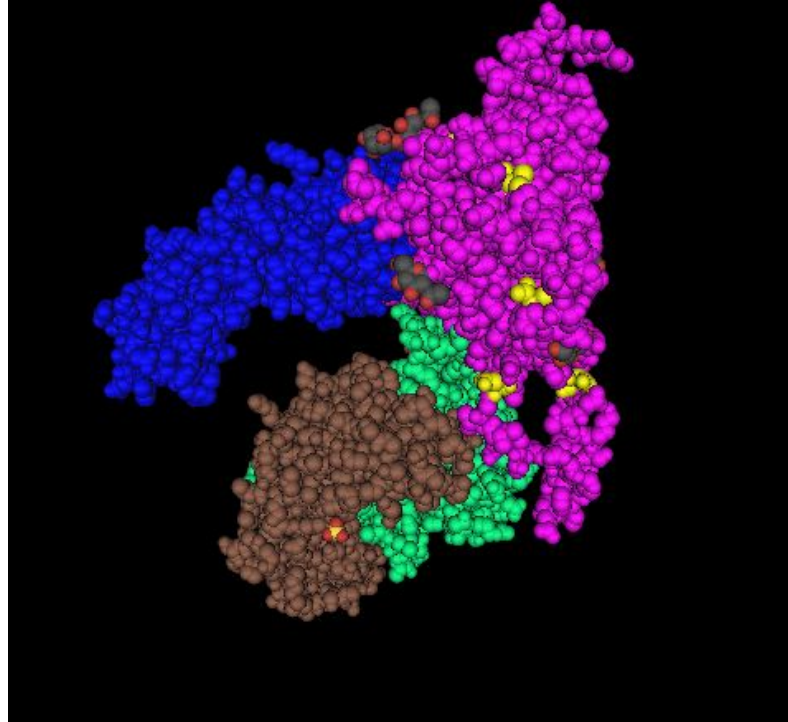


## Subject 11 (RP) Has Mutations on gp120 Near Antibody Interaction Sites





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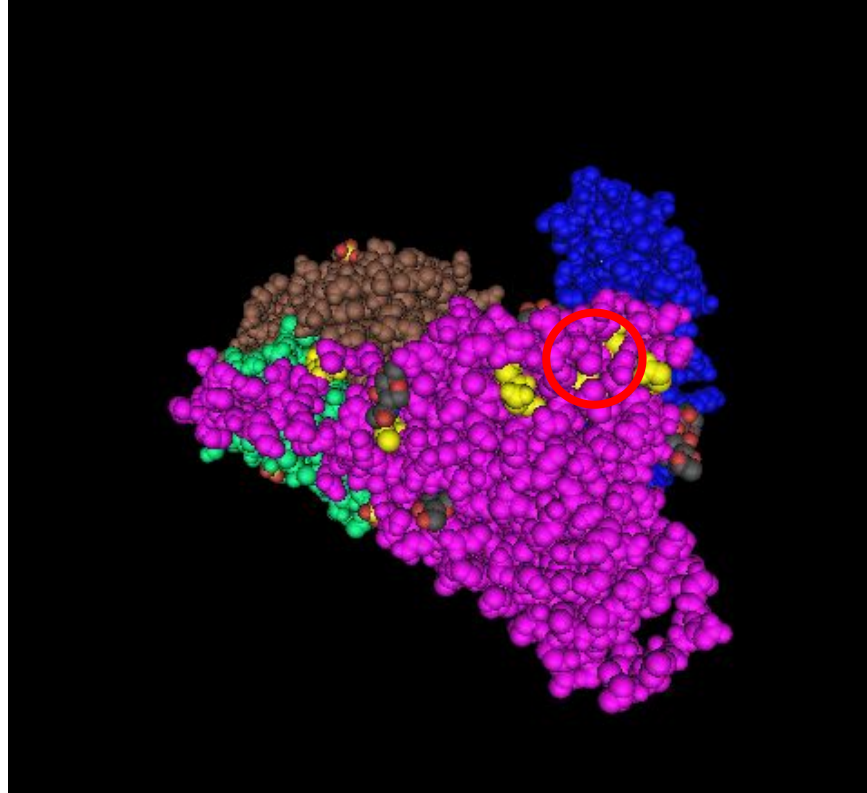
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# Subject 9 (MP) Indicates Several Positions with Major Mutations

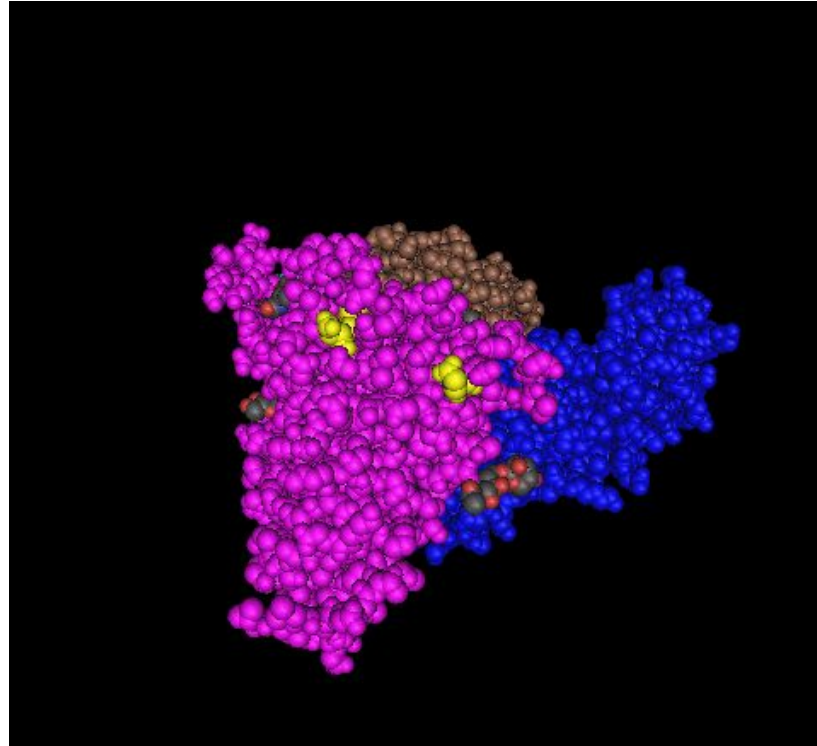
```
S9V1-4      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V1-1[2]   EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V1-2      EVVIRSANPTDNARTIIIVQLREHVEINCARPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-11     EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-2      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-10     EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-7      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-8      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-9      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-5      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-6      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-3      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-4      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V4-1      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V1-3      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
S9V1-5      EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA
Huang      EVVIRSDNPTDNARTIIIVQLRESVEINCTRPNNQNTKRSINIGPGRAPYATGTIIGDIRQA
consensus  EVVIRSANPTDNARTIIIVQLREHVEINCTRPNNNTRRSINIGPGRAPYATGTIIGDIRQA

S9V1-4      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V1-1[2]   HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V1-2      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-11     HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-2      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-10     HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-7      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-8      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-9      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-5      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-6      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-3      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-4      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V4-1      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V1-3      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
S9V1-5      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
Huang      HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
consensus  HCNISGARWMDTLRQIVERLREQFENRTIVFNHSS
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## Subject 9 (MP) Has Non-Surface Mutations



# Subject 9 (MP) Has Multiple Major Mutations on Its Surface



# Subject 14 (MP) Indicates Multiple Major Mutations Between Clones at an Interaction Site

```

S14V1-4      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMTGPGRAPYATGDII
S14V1-3      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V1-6      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V1-5      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V1-1[?]   -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V1-2      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V4-7[2]   -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V4-8      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII
S14V4-9[2]   -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGAI
S14V4-1      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGAI
S14V4-6      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGNII
S14V4-4      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGNII
S14V4-3      -----EVVIRSENFPTNNAKIIVQPNESVEINCTRPNNNTRRSIMIGPGRAPYATGRI
S14V4-2      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGRI
S14V4-1D     -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGRI
S14V4-5      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGAI
2B4C_G_Chain_G_ GSIABEEVVIRSDNFTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGEII
consensus      -----EVVIRSENFPTNNAKIIVQLNESVEINCTRPNNNTRRSIMIGPGRAPYATGDII

```

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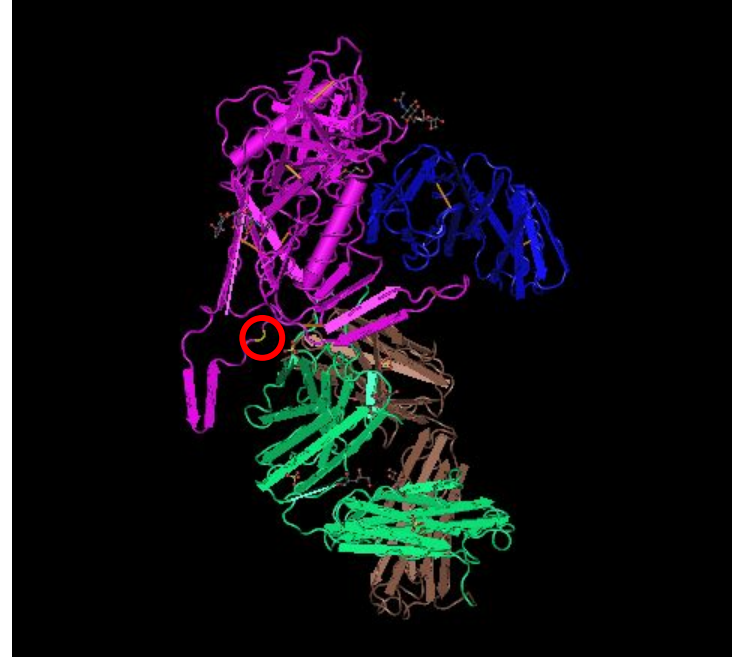
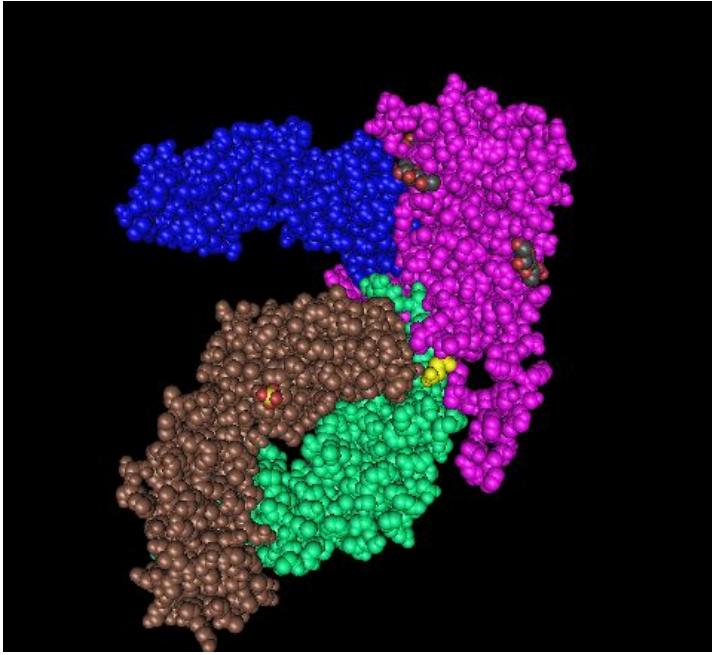
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S14V1-4      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V1-3      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V1-6      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V1-5      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V1-1[?]   GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V1-2      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-7[2]   GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-8      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-9[2]   GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-1      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-6      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-4      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-3      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-2      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-1D     GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
S14V4-5      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----
2B4C_G_Chain_G_ GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSSGGDPEIVMHSFNCGEFF
consensus      GDIRQABCNLSRAKWNNTLRQIVYKLRQFGNNKTIIFNQSS-----

```



# Subject 14 (MP) Indicates Multiple Major Mutations Between Clones at an Interaction Site



# Outline

1. Nonsynonymous mutations in binding sites affects gp120 and CD4 binding.
2. Variability of four subjects' clones were analyzed across two visits to determine structural and functional differences.
3. Rapid progressors showed major mutations across all clones, but few highly variable amino acids appeared.
4. Moderate progressors showed multiple major mutations at amino acids that interact with binding sites.
5. **Other studies identified position 317 in gp120 essential for antibody recognition.**



## Subject 9 and 14 Carry Mutations at an Antibody Recognition Site

- “HIV-1 Env-gp120 include sites in the antibody binding regions at the crowns of the V2 (Sites 169, 181) and V3 (Site 317) variable loops”
  - Edlefsen et al. (2015)
- Both are moderate progressors with identical mutations at this position
- Mutations at this site may increase ability of antibodies to neutralize virus

## Future Work

- See if mutations at site 317 persist in other subjects in each progressor group
- Human serum could be used to test neutralization susceptibility of each subject to antibody responses similar to Kirchherr et al. (2011)

## Summary

- 1. Nonsynonymous mutations in binding sites affects gp120 and CD4 binding.**
- 2. Variability of four subjects' clones were analyzed across two visits to determine structural and functional differences.**
- 3. Rapid progressors showed major mutations across all clones, but few highly variable amino acids appeared.**
- 4. Moderate progressors showed multiple major mutations at amino acids that interact with binding sites.**
- 5. Other studies identified position 317 in gp120 essential for antibody recognition.**

# Acknowledgements



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