

Does diversity increase within the amino acid sequences over time more within the rapid progressors compared to non-progressors?

Mia Huddleston and Avery Vernon-Moore

Two subjects from the nonprogressor and rapid progressor groups were chosen comparing each of their first and last visit clones.

Group	Subject	Number of Clones	Number of Mutations
Nonprogressors	Subject 13	10	5
Nonprogressors	Subject 12	12	11
Rapid Progressors	Subject 3	10	9
Rapid Progressors	Subject 10	17	24

Sequence alignment of rapid progressors shows large number of mutations from first to last

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S10V6-9 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRVFYATGEIIGDIRQA
S10V6-1 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRAFYATGEIIGDIRQA
S10V6-7 EVVIRSENFTDNAKTIIVHLNKAVEINCTRPNNNTRRSINMGPGRAFYATGDIIGDIRQA
S10V6-10 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRAFYATGEIIGDIRQA
S10V6-6 EVAIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRAFYATGDIIGDIRQA
S10V6-3 EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRALYTTGDIIGDIRQA
S10V6-2 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGDIIGDIRQA
S10V1-4 EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGEIIGDIRQA
S10V1-3 [2] EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGEITGDIRQA
S10V1-7 EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGEIIGDIRQA
S10V1-5 EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGEIIGDIRQA
S10V1-1 [2] EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGEIIGDIRQA
S10V1-6 EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRAFYTTGGIIGDIRQA
S10V1-2 [2] EVVIRSENFTDNAKTIIVQLNKSVEINCTRPNNNTRRSINMGPGRALYTTGEIIGDIRQA
S10V6-8 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNTRRSINMGPGRVFYTTGEIIGDIRQA
S10V6-5 EVVIRSENFTDNAKTIIVHLNKSVEINCTRPNNNKRKRITMGPGRALYTTGEIIGDIRQR
S10V6-4 EVVIRSENFTDNAKTIIVHLNESVEINCTRPNNNKRKRINMGPGRVLYTTGEIIGDIRQR
consensus EVVIRSENFTDNAKTIIVhLNksVEINCTRPNNNtRrsInMGPGRafYtTGeIiGDIRQA
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S10V6-9 HCNLSRTKWNDTLKQVVAKLREQFRNKTIIFTQSS
S10V6-1 HCNLSRTKWNDTLKQVVAKLREQFRNKTIIFTQSS
S10V6-7 HCNLSRTKWNDTLKQAVAKLREQFRNKTIIFTQSS
S10V6-10 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFTQSS
S10V6-6 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V6-3 HCNLSRTEWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V6-2 HCNLSRTEWNDTLKQAVDKLEQFRNKTIIFNQSS
S10V1-4 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-3 [2] HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-7 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-5 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-1 [2] HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-6 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V1-2 [2] HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V6-8 HCNLSRTKWNDTLKQVVDKLEQFRNKTIIFNQSS
S10V6-5 YCNLSRTKWNDTLKQGADKLEQFRNKTIIFNQSS
S10V6-4 YCNLSRTEWNDTLKQVVDKLEQFRNKTIIFNQSS
consensus hCNLSRTKWNDTLKQvvdKLrEQFRNKTIIFnQSS
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Sequence alignment of rapid progressors shows large number of mutations from first to last

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S3V6-6  DIVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V6-3  DIVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V6-1 [3] DIVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V6-5 [2] DIVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V6-4  DIVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V6-2 [2] DVVIRSANFTDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGRVYYTTGQIIIGDIRKA
S3V1-4  DVVIRSANFTNNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGKVYYTTGQIIIGDIRKA
S3V1-3  DVVIRSANFTNNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGKVYYTTGQIIIGDIRKA
S3V1-1 [7] DVVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGKVYYTTGQIIIGDIRKA
S3V1-2  DVVIRSANFSDNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGKVYYTTGQIIIGDIRKA
consensus DiVIRSANFsdNAKTILVQLNETVVMNCTRPGNNTRKRVTLGPGrVYYTTGQIIIGDIRKA

S3V6-6  HCNLSRAGWNSTLERIAIKLREQFQNKTIAFNQSS
S3V6-3  HCNLSRAGWNNTLERIAIKLREQFQNKTIAFNQSS
S3V6-1 [3] HCNLSRAGWNNTLERIAIKLREQFQNKTIAFNQSS
S3V6-5 [2] HCNLSRADWNNTLERIAIKLREQFQNKTIAFNQSS
S3V6-4  HCNLSRADWNNTLERIAIKL-EEQFQNKTIGFNQSS
S3V6-2 [2] HCNLSRADWNNTLERIAIKLREQFQNKTIAFNQSS
S3V1-4  HCNLSRADWNNTLKRiAIKLREQFQNKTIVFNQSS
S3V1-3  HCNLSRADWNNTLKRiAIKLREQFQNKTIAFNQSS
S3V1-1 [7] HCNLSRADWNNTLKRiAIKLREQFQNKTIVFNQSS
S3V1-2  HCNLSRADWNNTLKRiAIKLREQFQNKTIAFNQSS
consensus HCNLSRADWNnTLerIAIKLrEQFQNKTIAFNQSS
```

Sequence alignment of non progressors shows less mutations per number of clones than rapid progressors from first to last visits.

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S12VB-1 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12V1-2 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12VB-8 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12V1-3 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12V1-1 [7] EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12VB-2 [2] EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12VB-3 [2] EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12VB-4 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12V1-4 EVVIRSVNFTDNART IIVQLNETSVE INCTRPNNMTRRSIP IGPGRIFYTTGEIIGDIRQA
S12VB-7 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYATGEIIGDIRQA
S12VB-6 EVVIRS RNFTDNARI IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYATGEIIGDIRQA
S12VB-5 EVVIRSVNFTDNART IIVQLNETVE INCTRPNNMTRRSIP IGPGRIFYATGEIIGDIRQA
consensus EVVIRSkNFtDNARi IIVQLNetVE INCTRPNNMTRRSIp IGPGRIFYtTGEIIGDIRQA

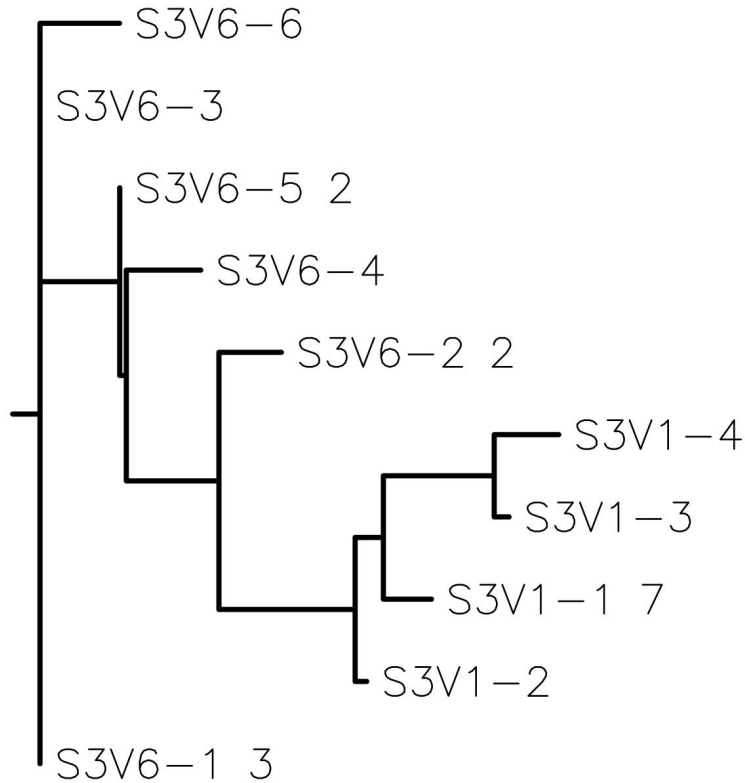
S12VB-1 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12V1-2 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-8 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12V1-3 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12V1-1 [7] BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-2 [2] BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-3 [2] BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-4 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12V1-4 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-7 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-6 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
S12VB-5 BCNLSRARWNETLKRQIVIKLREQFRNRTIVFSPSS
consensus BCNLSRARWnETLKRQIVIKLREQFRNRTIVFSPsS
```

Sequence alignment of non progressors shows less mutations per number of clones than rapid progressors from first to last visits.

```
S13V1-1[5] EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V1-2[3] EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V1-3 EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V1-4 EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINMGPGRAPYASRGIIGDIRQA
S13V5-1[4] EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V5-2 EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V5-3 EIVIRFENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V5-4[2] EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V5-5 EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
S13V5-6 EIVIRSENFTNNARTI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA
consensus EIVIRSENFTNNARI IIVQLRESVEINCTRPGNNTRRSINIGPGRAPYASRGIIGDIRQA

S13V1-1[5] YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V1-2[3] YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V1-3 YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V1-4 YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V5-1[4] YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V5-2 YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V5-3 YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V5-4[2] YCNISRAKWDNTLRQVAARLREQFRNATIVFNQSS
S13V5-5 YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
S13V5-6 YCNISRAKWDNTLRQVAARLREQFRNATIVFNQSS
consensus YCNISRAKWDNTLGQVAARLREQFRNATIVFNQSS
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Rooted trees of each subject's first and last visits were unhelpful in identifying diversity changes over time.

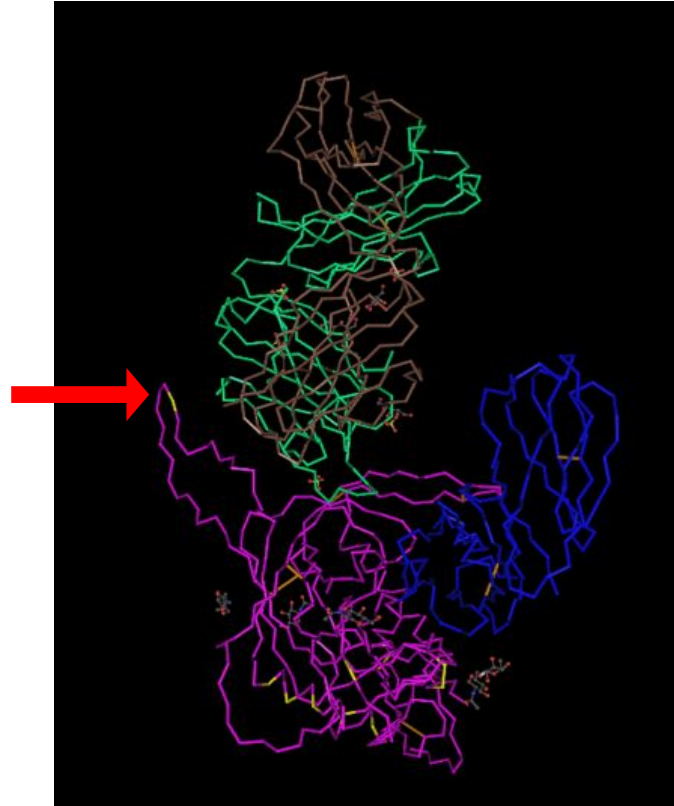


Clustldist shows higher rate of diversity among rapid progressors than non-progressors by comparing the distances of mutations from the first visit to the last per subject.

Progressor Type	Subject	Distance between first and last visit
Rapid	3	0.010
Rapid	10	0.137
Non	12	0.010
Non	13	0.021

Mutations are identified and located using structure of gp120 that Kwong et al. discovered.

- Subject 10's mutations can be visible in yellow
- One mutation can be seen in the V3 loop



The types of mutations may affect how the protein function would differ.

Subject	Number of major mutations	Number of minor mutations	Number of clones
3	4	5	10
10	14	10	17
12	7	4	12
13	3	2	10

Data suggests higher diversity among rapid progressor amino acid sequences than non-progressors, but a larger sample size is needed to confirm results

- Using more subjects would create a larger sample size
- More data points per subject could increase statistical evidence

Acknowledgements

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References

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