

Supplementary Material

Genetic Consequences of Antiviral Therapy on HIV-1

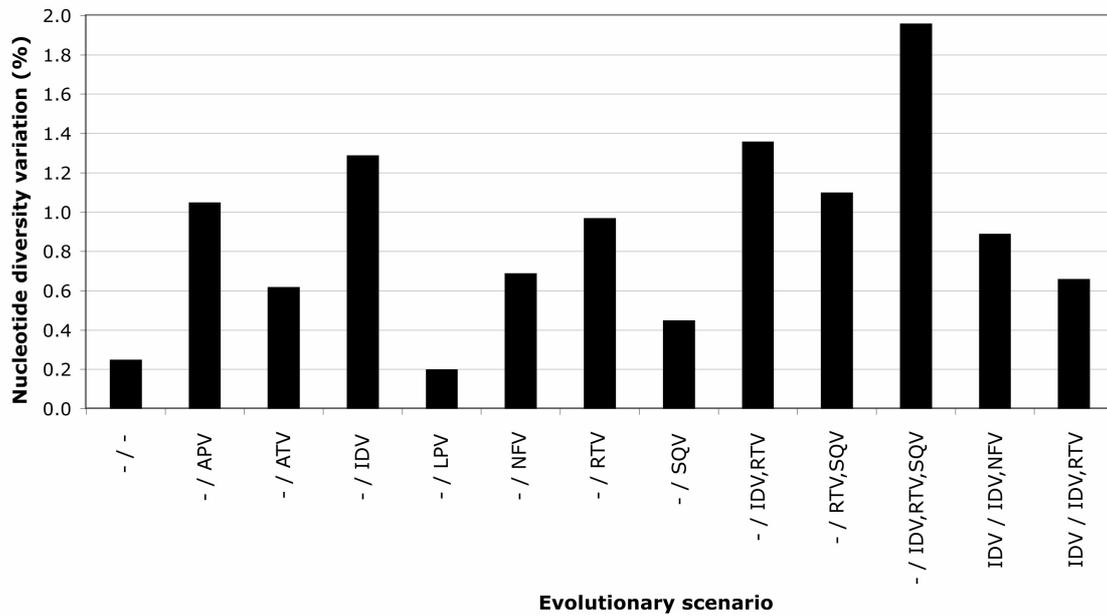


Figure S1. Nucleotide diversity variation. Variation of nucleotide diversity (pairwise nucleotide differences per site π) between the two datasets of each evolutionary scenario ($\pi_{\text{after treatment}} - \pi_{\text{before treatment}}$). “-” indicates naïve-treatment patients. Reference values are shown in Table S2.

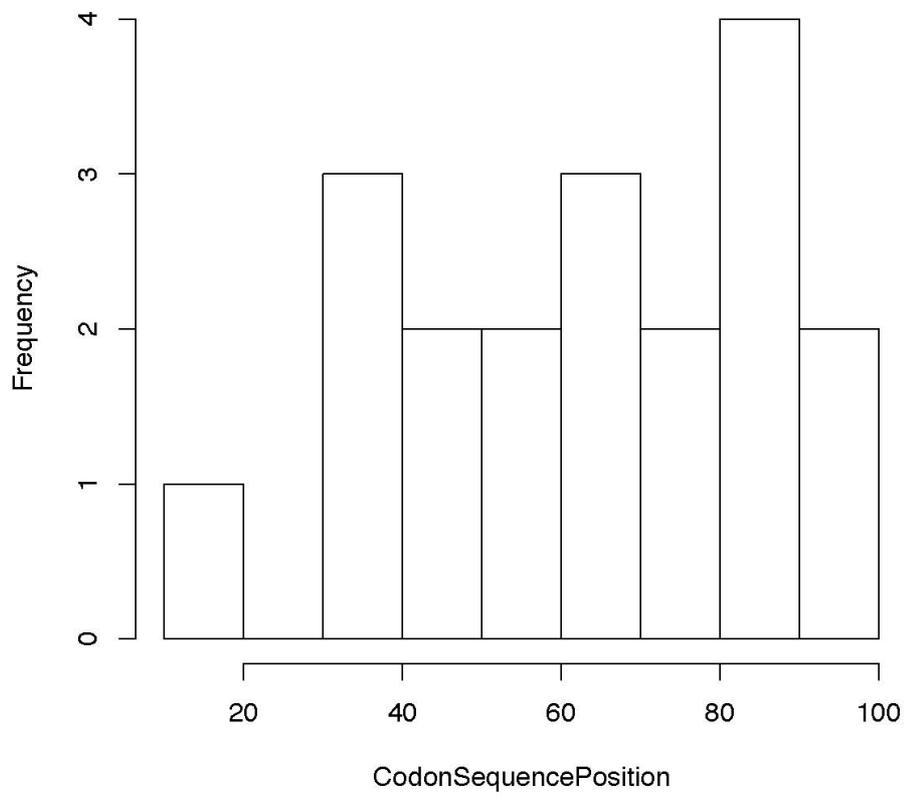


Figure S2. Histogram on the distribution of the significant nonsynonymous substitutions (95% CI), induced by the studied PIs, along the PR coding gene. Further details are included in Table S4.

Table S1. Estimates of overall mean distance with *MEGA*.

| Dataset | Overall mean distance | Standard error |
|------------------------------------|-----------------------|----------------|
| - / - (before treatment) | 0.001 | 0.000 |
| - / - (after treatment) | 0.002 | 0.001 |
| - / APV (before treatment) | 0.028 | 0.005 |
| - / APV (after treatment) | 0.050 | 0.006 |
| - / ATV (before treatment) | 0.034 | 0.005 |
| - / ATV (after treatment) | 0.045 | 0.007 |
| - / IDV (before treatment) | 0.029 | 0.005 |
| - / IDV (after treatment) | 0.050 | 0.006 |
| - / LPV (before treatment) | 0.052 | 0.007 |
| - / LPV (after treatment) | 0.051 | 0.008 |
| - / NFV (before treatment) | 0.003 | 0.001 |
| - / NFV (after treatment) | 0.003 | 0.001 |
| - / RTV (before treatment) | 0.038 | 0.006 |
| - / RTV (after treatment) | 0.051 | 0.007 |
| - / SQV (before treatment) | 0.047 | 0.007 |
| - / SQV (after treatment) | 0.052 | 0.006 |
| - / IDV,RTV (before treatment) | 0.059 | 0.010 |
| - / IDV,RTV (after treatment) | 0.072 | 0.009 |
| - / RTV,SQV (before treatment) | 0.055 | 0.010 |
| - / RTV,SQV (after treatment) | 0.074 | 0.010 |
| - / IDV,RTV,SQV (before treatment) | 0.050 | 0.007 |
| - / IDV,RTV,SQV (after treatment) | 0.072 | 0.008 |
| IDV / IDV,NFV (before treatment) | 0.057 | 0.008 |
| IDV / IDV,NFV (after treatment) | 0.069 | 0.010 |
| IDV / IDV,RTV (before treatment) | 0.073 | 0.008 |
| IDV / IDV,RTV (after treatment) | 0.083 | 0.010 |

Table S2. Estimates of nucleotide genetic diversity.

| Dataset | π |
|------------------------------------|--------|
| - / - (before treatment) | 0.0653 |
| - / - (after treatment) | 0.0678 |
| - / APV (before treatment) | 0.0376 |
| - / APV (after treatment) | 0.0481 |
| - / ATV (before treatment) | 0.0479 |
| - / ATV (after treatment) | 0.0541 |
| - / IDV (before treatment) | 0.0498 |
| - / IDV (after treatment) | 0.0627 |
| - / LPV (before treatment) | 0.0739 |
| - / LPV (after treatment) | 0.0759 |
| - / NFV (before treatment) | 0.0429 |
| - / NFV (after treatment) | 0.0498 |
| - / RTV (before treatment) | 0.0496 |
| - / RTV (after treatment) | 0.0593 |
| - / SQV (before treatment) | 0.0474 |
| - / SQV (after treatment) | 0.0519 |
| - / IDV,RTV (before treatment) | 0.0584 |
| - / IDV,RTV (after treatment) | 0.0720 |
| - / RTV,SQV (before treatment) | 0.0577 |
| - / RTV,SQV (after treatment) | 0.0687 |
| - / IDV,RTV,SQV (before treatment) | 0.0485 |
| - / IDV,RTV,SQV (after treatment) | 0.0681 |
| IDV / IDV,NFV (before treatment) | 0.0601 |
| IDV / IDV,NFV (after treatment) | 0.0690 |
| IDV / IDV,RTV (before treatment) | 0.0721 |
| IDV / IDV,RTV (after treatment) | 0.0787 |

Table S3. Estimates of molecular adaptation with *Hyphy*.

| Dataset | <i>dN/dS</i> | 95%CI down | 95%CI up |
|------------------------------------|--------------|------------|----------|
| - / - (before treatment) | 0.456 | 0.456 | 0.457 |
| - / - (after treatment) | 0.445 | 0.445 | 0.445 |
| - / APV (before treatment) | 0.248 | 0.176 | 0.339 |
| - / APV (after treatment) | 0.315 | 0.236 | 0.410 |
| - / ATV (before treatment) | 0.222 | 0.172 | 0.281 |
| - / ATV (after treatment) | 0.254 | 0.201 | 0.315 |
| - / IDV (before treatment) | 0.301 | 0.263 | 0.342 |
| - / IDV (after treatment) | 0.379 | 0.340 | 0.422 |
| - / LPV (before treatment) | 0.264 | 0.222 | 0.312 |
| - / LPV (after treatment) | 0.269 | 0.227 | 0.315 |
| - / NFV (before treatment) | 0.235 | 0.217 | 0.253 |
| - / NFV (after treatment) | 0.268 | 0.250 | 0.286 |
| - / RTV (before treatment) | 0.242 | 0.190 | 0.303 |
| - / RTV (after treatment) | 0.302 | 0.246 | 0.367 |
| - / SQV (before treatment) | 0.250 | 0.201 | 0.306 |
| - / SQV (after treatment) | 0.268 | 0.220 | 0.322 |
| - / IDV,RTV (before treatment) | 0.233 | 0.163 | 0.322 |
| - / IDV,RTV (after treatment) | 0.244 | 0.178 | 0.325 |
| - / RTV,SQV (before treatment) | 0.206 | 0.147 | 0.279 |
| - / RTV,SQV (after treatment) | 0.271 | 0.204 | 0.351 |
| - / IDV,RTV,SQV (before treatment) | 0.264 | 0.184 | 0.363 |
| - / IDV,RTV,SQV (after treatment) | 0.529 | 0.412 | 0.666 |
| IDV / IDV,NFV (before treatment) | 0.402 | 0.310 | 0.510 |
| IDV / IDV,NFV (after treatment) | 0.495 | 0.395 | 0.611 |
| IDV / IDV,RTV (before treatment) | 0.329 | 0.261 | 0.409 |
| IDV / IDV,RTV (after treatment) | 0.442 | 0.360 | 0.536 |

Table S4. Number and position of positively selected sites and negatively selected sites. Only detected positively selected sites (PSSs) and negatively selected sites (NSSs) at 95% CI are shown. For each PSS the corresponding *p*-value is indicated after the parenthesis. “-” indicates naïve-treatment patients.

| Scenario | DataSet | PSSs | NSSs |
|----------|---------|--|--|
| 1 | - | 0 | 93: 1,2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 36, 38, 39, 40, 41, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 |
| | - | 0 | 92: 1,2, 3, 4, 5, 6, 7, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 36, 38, 39, 40, 41, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99 |
| 2 | - | 1: 63 (0) | 26: 1, 3, 11, 17, 20, 22, 25, 27, 28, 31, 32, 34, 44, 47, 66, 67, 68, 70, 73, 74, 75, 79, 81, 83, 94, 98 |
| | APV | 2: 37 (0.00248), 63 (0.00002) | 34: 11, 12, 20, 21, 22, 25, 27, 28, 29, 32, 40, 44, 45, 46, 49, 54, 56, 66, 68, 79, 80, 81, 82, 83, 85, 86, 87, 88, 91, 94, 95, 96, 98, 99 |
| 3 | - | 1: 37 (0.01383) | 43: 7, 7, 9, 11, 16, 17, 20, 21, 22, 24, 25, 28, 30, 33, 34, 38, 39, 40, 43, 44, 46, 52, 58, 61, 65, 66, 68, 75, 76, 79, 80, 81, 83, 86, 87, 90, 91, 92, 94, 95, 96, 97, 99 |
| | ATV | 2: 63 (0.00404), 93 (0.03112) | 36: 7, 9, 11, 17, 20, 21, 22, 24, 25, 28, 34, 38, 39, 44, 46, 52, 58, 61, 65, 66, 68, 75, 76, 79, 80, 81, 83, 86, 87, 90, 91, 92, 94, 95, 96, 99 |
| 4 | - | 5: 10 (0.00008), 35 (0.01782), 37 (0.00002), 63 (0), 93 (0.03455) | 64: 1, 2, 3, 4, 5, 6, 7, 8, 9, 11, 16, 21, 22, 23, 24, 25, 26, 27, 29, 30, 32, 33, 38, 39, 40, 43, 45, 46, 48, 51, 52, 54, 58, 60, 61, 64, 65, 66, 67, 68, 73, 74, 75, 76, 78, 79, 80, 81, 82, 84, 85, 86, 87, 88, 90, 92, 94, 95, 96, 97, 98, 99 |
| | IDV | 7: 10 (0), 35 (0.01837), 37 (0.00024), 46 (0.04753), 63 (0.00198), 71 (0.04103), 93 (0.0121) | 58: 1, 2, 3, 4, 5, 7, 8, 9, 11, 16, 17, 21, 22, 23, 25, 26, 27, 30, 32, 34, 38, 39, 40, 43, 45, 47, 48, 51, 52, 53, 55, 58, 59, 60, 61, 65, 66, 67, 68, 70, 74, 75, 78, 79, 80, 81, 83, 85, 86, 87, 88, 92, 94, 95, 96, 97, 98, 99 |
| 5 | - | 3: | 54: |

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| | | 10 (0.01485), 37 (0.01689), 63 (0.00001) | 1, 2, 3, 4, 7, 9, 11, 14, 16, 17, 21, 22, 23, 24, 25, 27, 32, 38, 40, 43, 45, 48, 52, 54, 55, 56, 57, 58, 65, 66, 67, 68, 71, 72, 74, 75, 76, 78, 79, 80, 82, 83, 84, 86, 87, 88, 91, 92, 94, 95, 96, 97, 98, 99 |
| | LPV | 3: 10 (0.00749), 37 (0.02511), 63 (0.00017) | 54: 1, 2, 3, 7, 9, 11, 14, 16, 17, 21, 22, 23, 24, 25, 27, 32, 38, 40, 46, 48, 51, 52, 54, 55, 56, 57, 58, 65, 66, 67, 68, 69, 71, 72, 74, 75, 76, 78, 79, 80, 83, 86, 87, 88, 90, 91, 92, 94, 95, 96, 97, 98, 99 |
| 6 | - | 3: 19 (0.04020), 37 (0), 63 (0) | 86: 1,2, 3, 4, 5, 6, 7, 8, 9, 11, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 44, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 65, 66, 67, 68, 69, 70, 71, 73, 74, 75, 76, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 94, 95, 96, 97, 98, 99 |
| | NFV | 4: 10 (0.01775), 19 (0.00295), 37 (0), 63 (0) | 83: 1,2, 3, 4, 5, 6, 7, 8, 9, 11, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 36, 38, 39, 40, 42, 43, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 58, 59, 60, 61, 65, 66, 67, 68, 70, 71, 73, 74, 75, 76, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 94, 95, 96, 97, 98, 99 |
| 7 | - | 1: 63 (0.00020) | 39: 1, 2, 3, 6, 7, 11, 16, 17, 18, 22, 23, 27, 28, 33, 38, 40, 43, 45, 50, 52, 55, 56, 58, 61, 66, 68, 75, 78, 80, 81, 85, 87, 88, 91, 92, 94, 95, 96, 97 |
| | RTV | 1: 63 (0.00011) | 40: 1, 2, 3, 7, 11, 14, 16, 17, 18, 22, 23, 24, 27, 28, 38, 40, 46, 48, 50, 52, 55, 56, 58, 61, 66, 68, 75, 76, 78, 80, 81, 85, 87, 88, 92, 94, 95, 96, 97, 99 |
| 8 | - | 1: 63 (0) | 41: 2, 7, 9, 16, 17, 18, 20, 21, 23, 25, 27, 30, 33, 34, 40, 43, 44, 48, 52, 54, 55, 57, 58, 65, 66, 68, 70, 75, 76, 83, 86, 87, 88, 91, 92, 94, 95, 96, 97, 98, 99 |
| | SQV | 2: 35 (0.02464), 63 (0.00005) | 43: 1, 2, 7, 9, 16, 17, 18, 20, 21, 23, 24, 25, 27, 30, 31, 33, 34, 40, 43, 44, 51, 52, 54, 55, 66, 68, 70, 75, 76, 79, 82, 83, 86, 87, 88, 91, 92, 94, 95, 96, 97, 98, 99 |
| 9 | - | 1: 63 (0,00397) | 29: 4, 9, 14, 17, 21, 25, 29, 35, 37, 39, 40, 45, 48, 52, 54, 57, 66, 70, 72, 75, 80, 87, 88, 91, 94, 95, 96, 98, 99 |
| | IDV, RTV | 1: 63 (0,03740) | 29: 1, 7, 17, 18, 21, 25, 29, 39, 40, 45, 48, 52, 57, 61, 66, 70, 72, 75, 79, 80, 83, 87, 88, 91, 92, 94, 96, 98, 99 |

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| 10 | - | 1: 37 (0.00600) | 28: 1, 3, 9, 14, 16, 17, 20, 27, 40, 47, 54, 56, 66, 67, 70, 74, 75, 76, 79, 82, 85, 86, 87, 88, 94, 95, 96, 98, 99 |
| | RTV, SQV | 2: 35 (0.04481), 37 (0.03160) | 32: 1, 2, 3, 9, 14, 15, 16, 17, 18, 20, 27, 40, 56, 57, 61, 65, 66, 67, 68, 75, 79, 81, 83, 85, 87, 88, 91, 92, 94, 95, 96, 98, 99 |
| 11 | - | 1: 77 (0.01112) | 12: 15, 22, 29, 40, 51, 60, 72, 74, 83, 84, 91, 94, |
| | IDV, RTV, SQV | 6: 54 (0.01354), 63 (0.02167), 77 (0.00462), 82 (0.03294), 90 (0.03597), 93 (0.00623) | 13: 15, 16, 17, 20, 22, 27, 45, 52, 67, 68, 83, 94, 99 |
| 12 | IDV | 3: 10 (0.00240), 63 (0.00946), 82 (0.04698) | 20: 14, 17, 22, 25, 40, 45, 52, 66, 68, 75, 79, 80, 86, 87, 91, 94, 95, 96, 98, 99 |
| | IDV, NFV | 5: 10 (0.00068), 46 (0.00118), 62 (0.02108), 63 (0.00088), 90 (0.02295) | 28: 1, 3, 4, 9, 14, 16, 17, 18, 22, 25, 28, 40, 45, 52, 55, 56, 58, 61, 68, 75, 79, 83, 86, 87, 94, 95, 96, 99 |
| 13 | IDV | 1: 10 (0.00026) | 36: 1, 3, 4, 5, 6, 7, 8, 9, 11, 14, 17,, 21, 23, 25, 30, 32, 34, 40, 43, 48, 52, 68, 70, 73, 75, 78, 79, 80, 85, 86, 87, 92, 94, 95, 96, 99 |
| | IDV, RTV | 4: 10 (0.00026), 57 (0.04403), 72 (0.01765), 82 (0.03577) | 30: 1, 2, 3, 4, 5, 6, 7, 9, 11, 17, 21, 23, 25, 26, 27, 30, 40, 43, 48, 52, 68, 70, 75, 80, 87, 92, 94, 95, 96, 99 |