

An Analysis of Enzyme Kinetics Data for Mitochondrial DNA Strand Termination by Nucleoside Reverse Transcriptase Inhibitors

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Supplemental Information: Model parameter values.

TABLE S1. Kinetic parameters k_{cat} (1/s) for base pairings when previously inserted nucleotide is correct (a Watson-Crick pair).

Base pairings	T	G	C	A
T	25	0.08	0.1	0.0036
G	0.012	37	0.003	0.1
C	0.16	0.066	43	0.042
A	0.013	1.16	0.038	45

Values were taken from Lee and Johnson (45) in which the previous base pair is A:T

TABLE S2. Kinetic parameters K_m (μ M) for base pairings when previously inserted nucleotide is correct.

Base pairings	T	G	C	A
T	0.6	800	540	25
G	180	0.8	140	160
C	200	150	0.9	250
A	57	70	360	0.8

Values were taken from Lee and Johnson (45) in which the previous base pair is A:T

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TABLE S3. Estimated k_{cat} (1/s) kinetic parameters for base pairings when previously inserted nucleotide is a point mutation (a non-Watson-Crick pair).

Base pairings	T	G	C	A
A	0.52	0.00052	0.00052	0.00052
C	0.00052	0.52	0.00052	0.00052
G	0.00052	0.00052	0.52	0.00052
T	0.00052	0.00052	0.00052	0.52

The k_{cat} values for insertion of C onto G measured by Johnson and Johnson (40-41) where the previous base pairing is a non-Watson-Crick base pairing of T:T as opposed to A:T. This value was assumed an approximation of those for other Watson-Crick pairings based on similarities of k_{cat} values in Table A1 for Watson-Crick base pairings (A:T, C:G). Values for non-Watson-Crick base pairing were made based on the observation from TABLE S1 that k_{cat} values are approximately 1000 times less for non-Watson-Crick base pairing than for Watson-Crick base pairing.

TABLE S4. Estimated K_m (μ M) kinetic parameters for base pairings when previously inserted nucleotide is a point mutation.

Base pairings	T	G	C	A
A	404	40400	40400	40400
C	40400	404	40400	40400
G	40400	40400	404	40400
T	40400	40400	40400	404

The K_m values for insertion of C onto G measured by Johnson and Johnson (40-41) where the previous base pairing is a non-Watson-Crick base pairing of T:T as opposed to A:T. This value was assumed an approximation of those for other Watson-Crick pairings based on similarities of K_m values in Table S2 for Watson-Crick base pairings (A:T, C:G). Values for non-Watson-Crick base pairing were made based on the observation from TABLE S2 that K_m values are approximately 100 times greater for non-Watson-Crick base pairing than for Watson-Crick pairing.

TABLE S5. Exonuclease and Disassociation by polymerase-gamma reaction rates when previous base pair is a Watson-Crick pairing vs. non Watson-Crick.

Previous base pairs	Exonuclease rate (1/s)	Disassociation rate (1/s)
Watson-Crick pair	0.05	0.02
Non-Watson-Crick pair	0.4	0.2

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Supplemental Information: Other results

TABLE S6. IC₅₀ values (μM) for the strand termination on the mtDNA heavy strand. NA – not applicable, meaning that the probability of strand termination never exceeded 50%.

Analog	IC ₅₀ values (μM)		
	High dNTP levels	Medium dNTP levels	Low dNTP levels
d4T-TP	6.75×10 ⁻⁴	3.60×10 ⁻⁴	7.50×10 ⁻⁵
ddA-TP	5.20×10 ⁻⁴	4.00×10 ⁻⁴	9.80×10 ⁻⁵
ddC-TP	8.90×10 ⁻⁴	5.80×10 ⁻⁴	1.30×10 ⁻⁴
FIAU-TP	1.44×10 ⁻³	8.30×10 ⁻⁴	1.60×10 ⁻⁴
FTC(+)-TP	1.40×10 ⁻²	1.00×10 ⁻²	2.20×10 ⁻³
acyclovir-TP	2.85×10 ⁻²	1.14×10 ⁻²	1.79×10 ⁻³
3TC(+)-TP	8.8×10 ⁻²	5.60×10 ⁻²	1.36×10 ⁻²
ddI-TP	0.33	0.23	5.75×10 ⁻²
3TC(-)-TP	1.50	1.00	0.19
TDF-TP	1.45	1.06	0.26
AZT₂₀₀₁-TP	3.00	1.94	0.37
AZT₂₀₀₇-TP	NA	NA	143
CBV-TP	NA	NA	2.22
FTC(-)-TP	NA	NA	30.9