

Figure S1. Molecular modeling of APE1 protein variants. The wild-type APE1 amino acid sequence was obtained (NCBI accession# AF488551) and changed as per the mutations examined here (Q51H, I64V, P112L, D148E, R237C, G241R, P311S, and A317V). The PDB structure of wild-type APE1 was PDB ID# 1DE8, and the variant models were generated using SWISS-MODEL PDB2PQR (http://pdb2pqr.sourceforge.net/). The modeling was analyzed in UCSF Chimera software by overlaying the wild-type amino acids (white backbone, red amino acid) with the variant residue (grey backbone, blue amino acid) to compare alterations in protein integrity.

Figure S2



Figure S2. AP-DNA binding of wild-type and R237C APE1 proteins. (A) Wildtype or R237C variant protein (0.1 to 30 ng, as designated) were incubated with ³²Plabeled 18F NMR DNA (100 fmol), and the binding reactions were resolved on a nondenaturing polyacrylamide gel as described in Materials and Methods. Standard phosphorimager analysis was employed to visualize unbound substrate (DNA) and the APE1-substrate complex (C), with a representative gel image shown. NE = no enzyme. **(B)** Plot of the three independent data points for each protein at the indicated protein concentration. The line of best fit is shown. Table S1. Variant primer set for the indicated amino acid change and each oligonucleotide nameand sequence.The mutated codon is underlined.

Change	Oligonucleo	tide name and sequence (5'-3'):
Q51H	Q51H-For:	GAC CCC CCA GAT <u>CAC</u> AAA ACC TCA CCC AG
	Q51H-Rev:	CTG GGT GAG GTT TTG TGA TCT GGG GGG TC
164V	l64V-For:	AAC CTG CCA CAC TCA AG <u>G TC</u> T GCT CTT GGA ATG TG
	I64V-Rev:	CAC ATT CCA AGA GCA GAC CTT GAG TGT GGC AGG TT
P112L	P112L-For:	TGA ACT TCA GGA GCT G <u>CT T</u> GG ACT CTC TCA TCA AT
	P112L-Rev:	ATT GAT GAG AGA GTC CAA GCA GCT CCT GAA GTT CA
D148E	D148E-F0f:	CTTACG GCA TAG GC <u>G AG</u> G AGG AGC ATG ATC AGG
	DI40E-Rev.	CET GAT CAT GET CET CET CGE CTA TGE CGT AAG
R237C	R237C-For	
112070	R237C-Rev	CCG AAG CCT TGG CAC TCT TGT GGC GTG
G241R	G241R-For:	GAG CGC CAA GGC TTC AGG GAA TTA CTG CAG G
	G241R-Rev:	CCT GCA GTA ATT CCC TGA AGC CTT GGC GCT C
P311S	P311S-For:	TCG GCA GTG ATC ACT GT <u>T CT</u> A TCA CCC TAT ACC TA
	P311S-Rev:	TAG GTA TAG GGT GAT AGA ACA GTG ATC ACT GCC GA
A317V	A317V-For:	ATC ACC CTA TAC CTA <u>GTA</u> CTG TGA GGA TCC GGC
	A317V-Rev:	GCC GGA TCC TCA CAG TAC TAG GTA TAG GGT GAT

Table S2. Amplification primers used in *APE1* **exonic sequencing.** The underlined portion is the region complementary to the APE1 genomic sequence. The remaining portion of the oligonucleotide is the binding site for M13 forward and reverse primers used in direct sequencing of the PCR product.

Exon	Oligonucleotide sequence (5'-3')
Exon 1&2	Fex1_2: GTTTTCCCAGTCACGAC <u>GAGGCTAAGCGTCTCCGTCAC</u> Rex1_2: AGGAAACAGCTATGACCAT <u>CTGCGACTTCTTCACAAACC</u>
Exon 3	Fex3: GTTTTCCCAGTCACGAC <u>GGTTTGTGAAGAAGTCGCAG</u> Rex3: AGGAAACAGCTATGACCA <u>TCCTGAAGGCTAAACGGAGAA</u>
Exon 4	Fex4: GTTTTCCCAGTCACGAC <u>GAATATTGTGCTGCTTGACTC</u> Rex4: AGGAAACAGCTATGACCAT <u>GGGAAAGCAATCAAGAGGTG</u>
Exon 5	Fex5: GTTTTCCCAGTCACGAC <u>TTGCTAATTCTCTATCTCTG</u> Rex5: AGGAAACAGCTATGACCAT <u>GAGTGTTTAAAGAAGGAATGG</u>