

1 **Supplementary Table 1.** Primers used in the site-directed mutageneses

Mutation	Primer	Sequence (5'→3')
G16E	Forward	cttagttacagtaaaattagaggacagctgatagaagcc
	Reverse	ggcttctatcagctgtccctctaattttactgtaactaag
G17E	Forward	cttagttacagtaaaattaggggaacagctgatagaagcc
	Reverse	ggcttctatcagctgtccctctaattttactgtaactaag
I64M	Forward	gacaatatgatcagatacttatggaaatttgaggaaaaaggc
	Reverse	gcctttttccacaaattccataagtatctgatcatattgtc
K70R	Forward	cttatagaaatttgaggaaaaaggctataggtacagtgttagtagg
	Reverse	cctactaacactgtacctatagccctttttccacaaatttctataag
I72V	Forward	gaaatttgaggaaaaaggctgtaggtacagtgttagtagg
	Reverse	cctactaacactgtacctacagcctttttccacaaatttc

2 * Underlined bases correspond to the changes made to the original BD6-15 clone.

Supplementary Table 2. Primers used in the oligonucleotide ligation assays

Protease codon	Upstream primer	Target	Downstream primer
17	5'-GTTACAGTAAAATTAGGGGA <u>A</u> -3'	17E	5'-CAGCTGATAGAAGCCTTAT-3'
	5'-GTTACAGTAAAATTAGGGGG <u>G</u> -3'	17G	
64	5'-AATATGATCAGATACTTAT <u>G</u> -3'	64M	5'-GAAATTTGTGGAAAAAAGGC-3'
	5'-AATATGATCAGATACTTATA <u>A</u> -3'	64I	
72	5'-AATTTGTGGAAAAAAGGCT <u>G</u> -3'	72V	5'-TAGGTACAGTGTTAGTAGGA-3'
	5'-AATTTGTGGAAAAAAGGCT <u>A</u> -3'	72I	

* Underlined bases correspond to the discriminating nucleotide position between the two variants present in each head-to-head competition.