Table S1:

Modulator	Type	Compound	Mechanism of action	Ref
Corrector	I	VX-809 (lumacaftor), VX-661 (tezacaftor)	Stabilization of MSD-NBD interface	[1]
	II	Corr4a	Stabilization of MSD2/NBD2	[1]
	III	VX-445 (elexacaftor)	Stabilization of NBD1	[2]
Potentiator	I	VX-770 (ivacaftor)	Phosphorylation-dependent, ATP-independent increase in P_O	[3]
	II	Apigenin	Co-potentiator, specific for NBD2 mutants, mechanism unknown	[3]
	III	VX-445 (elexacaftor)	Co-potentiator, mechanism unknown	[4]

Overview of the different CFTR modulator types with distinct mechanisms of action, used in this publication. CFTR modulators are grouped into different types based on distinct mechanisms of action and additive rescue effects when combined. In the current study, we conclude there are at least three different potentiator mechanisms, due to the clear additive effect of ivacaftor, elexacaftor and apigenin, in this manuscript studied on the class II/III/VI mutant N1303K [5, 6]. This is in line with the recent finding of the co-potentiator activity of elexacaftor on top of ivacaftor for F508del and other gating mutants [4], which we here extended to the triple potentiator combination for N1303K. Abbreviations: MSD: membrane spanning domain; NBD: nucleotide binding domain; P_O: open probability.

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