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S1 Table. Selected mutations and sequences inserted in the dual reporter plasmid. Are indicated the inserted sequences corresponding to the indicated PTC.

Mutation		Inserted sequence	Mutation		Inserted sequence
c.178G>T	p.Glu60*	TGG GAT AGA **TAG** CTG GCT TCA	c.2537G>A	p.Trp846*$_{UAG}$	GTG ACT ACA **TAG** AAC ACA TAC
c.366T>A	p.Tyr122*	TCT ATC GCG **TAA** CTA GGC ATA	c.2538G>A	p.Trp846*$_{UGA}$	GTG ACT ACA **TGA** AAC ACA TAC
c.658C>T	p.Gln220*	GAG TTG TTA **TAG** GCG TCT GCC	c.2551C>T	p.Arg851*	ACA TAC CTT **TGA** TAT ATT ACT
c.825C>G	p.Tyr275*	GTT AAG GCA **TAG** TGC TGG GAA	c.3276C>A	p.Tyr1092*$_{UAA}$	TGG TTC TTG **TAA** CTG TCA ACA
c.868C>T	p.Gln290*	AAC TTA AGA **TAA** ACA GAA CTC	c.3310G>T	p.Glu1104*	ATG AGA ATA **TAA** ATG ATT TTT
c.1301C>G	p.Ser434*	AGT AAT TTC **TGA** CTT CTT GGT	c.3382A>T	p.Arg1128*	GGA GAA GGA **TGA** GTT GGT ATT
c.1397C>G	p.Ser466*$_{UGA}$	GGC AAG ACT **TGA** CTT CTA ATG	c.3472C>T	p.Arg1158*	AGC TTG ATG **TGA** TCT GTG AGC
c.1624G>T	p.Glu542*	TTG CAA CAG **TGA** AGG AAA GCC	c.3484C>T	p.Arg1162*	TCT GTG AGC **TGA** GTC TTT AAG
c.1657C>T	p.Arg553*	GGA GGT CAA **TGA** GCA AGA ATT	c.3587C>G	p.Ser1196*	ATT GAG AAT **TGA** CAC GTG AAG
c.1753G>T	p.Glu585*	ACA GAA AAA **TAA** ATA TTT GAA	c.3802C>T	p.Gln1268*	GGA GAA ATC **TAG** ATC GAT GGT
c.2125C>T	p.Arg709*	AAC TCT ATA **TGA** AAA TTT TCC	c.3846G>A	p.Trp1282*	ATA GTT CTT **TGA** GAA GGT GGA
c.2128A>T	p.Lys710*	TCT ATA CGA **TAA** AAA ACC ATT	c.3937C>T	p.Gln1313*	TGG AGT GAT **TAA** GAA ATA TGG
c.2299C>T	p.Gln767*	CGA AGG AGG **TAG** TCT GTC CTG	c.4168C>T	p.Gln1390*	ACT CTA AAA **TAA** GCA TTT GCT
c.2353C>T	p.Arg785*	AAC ATT CAC **TGA** AAG ACA ACA	c.4252G>T	p.Glu1418*	TTG GTC ATA **TAA** GAG AAC AAA
c.2491G>T	p.Glu831*	GAC TTA AAG **TAG** TGC TTT TTT			

S2 Table. Basal and drug induced readthrough levels. Values represent the median of n independent experiments. p-values are calculated using an unpaired Student t-test with α = 0.01.

Mutation	Basal (%)	*n*	Gentamicin (%)	*n*	*p Value*	Negamycin (%)	*n*	*P-value*
p.Glu60*	0.06 ± 0.02	*11*	0.47 ± 0.16	*5*	10^{-2}	0.13 ± 0.01	*5*	10^{-4}
p.Tyr122*	0.39 ± 0.19	*12*	1.85 ± 0.39	*8*	10^{-5}	0.32 ± 0.04	*5*	*ns*
p.Gln220*	0.04 ± 0.01	*12*	0.33 ± 0.11	*6*	10^{-3}	0.08 ± 0.01	*6*	10^{-7}
p.Tyr275*	0.03 ± 0.01	*12*	0.39 ± 0.15	*6*	10^{-2}	0.11 ± 0.05	*6*	10^{-2}
p.Gln290*	0.04 ± 0.01	*12*	0.08 ± 0.01	*6*	10^{-7}	0.03 ± 0.01	*6*	*ns*
p.Ser434*	0.34 ± 0.14	*12*	1.07 ± 0.19	*6*	10^{-4}	5.55 ± 1.35	*9*	10^{-5}
p.Ser466*	0.52 ± 0.08	*12*	2.47 ± 0.56	*5*	10^{-3}	1.72 ± 0.27	*6*	10^{-4}
p.Gly542*	0.08 ± 0.02	*9*	0.86 ± 0.63	*6*	10^{-2}	0.05 ± 0.03	*6*	*ns*
p.Arg553*	0.07 ± 0.02	*12*	0.51 ± 0.22	*6*	10^{-2}	0.12 ± 0.04	*6*	*ns*
p.Glu585*	0.04 ± 0.01	*9*	0.25 ± 0.04	*6*	10^{-4}	0.09 ± 0.09	*5*	*ns*
p.Arg709*	0.04 ± 0.01	*12*	0.20 ± 0.04	*6*	10^{-4}	0.34 ± 0.05	*6*	10^{-4}
p.Lys710*	0.03 ± 0.02	*12*	0.08 ± 0.06	*5*	*ns*	0.05 ± 0.02	*6*	*ns*
p.Gln767*	0.02 ± 0.01	*12*	0.12 ± 0.06	*6*	10^{-2}	0.03 ± 0.03	*6*	*ns*
p.Arg785*	0.06 ± 0.02	*12*	0.41 ± 0.35	*6*	10^{-4}	0.42 ± 0.12	*6*	10^{-3}
p.Glu831*	0.05 ± 0.02	*12*	0.21 ± 0.25	*6*	*ns*	0.02 ± 0.01	*6*	*ns*
p.Trp846*$_{UAG}$	0.03 ± 0.02	*12*	0.34 ± 0.10	*6*	10^{-3}	0.26 ± 0.04	*6*	10^{-4}
p.Trp846*$_{UGA}$	0.35 ± 0.19	*12*	2.70 ± 0.76	*5*	10^{-3}	1.54 ± 0.31	*6*	10^{-4}
p.Arg851*	0.05 ± 0.02	*12*	0.70 ± 0.17	*6*	10^{-3}	0.12 ± 0.09	*6*	10^{-3}
p.Tyr1092*	0.04 ± 0.02	*9*	0.14 ± 0.04	*6*	10^{-3}	0.06 ± 0.04	*5*	*ns*
p.Glu1104*	0.09 ± 0.02	*8*	0.16 ± 0.04	*6*	10^{-2}	0.35 ± 0.03	*6*	10^{-6}
p.Arg1128*	0.22 ± 0.02	*6*	1.02 ± 0.27	*6*	10^{-3}	0.52± 0.16	*6*	10^{-2}
p.Arg1158*	0.03± 0.01	*12*	0.05 ± 0.01	*6*	*ns*	0.17 ± 0.04	*6*	10^{-3}
p.Arg1162*	0.04 ± 0.01	*9*	0.39 ± 0.15	*6*	10^{-2}	0.07 ± 0.02	*9*	10^{-2}
p.Ser1196*	0.03 ± 0.01	*7*	2.53 ± 0.83	*6*	10^{-3}	0.19 ± 0.05	*9*	10^{-3}
p.Gln1268*	0.05 ± 0.02	*12*	0.46 ± 0.05	*9*	10^{-6}	0.67 ± 0.31	*6*	10^{-2}
p.Trp1282*	0.13 ± 0.02	*12*	0.74 ± 0.12	*6*	10^{-4}	0.40 ± 0.34	*6*	*ns*
p.Gln1313*	0.03 ± 0.03	*12*	0.41 ± 0.17	*6*	10^{-2}	0.06 ± 0.01	*6*	10^{-2}
p.Gln1390*	0.13 ± 0.02	*12*	0.15 ± 0.04	*6*	*ns*	0.15 ± 0.06	*6*	*ns*
p.Glu1418*	0.02 ± 0.01	*12*	0.48 ± 0.11	*6*	10^{-3}	0.02 ± 0.01	*6*	*ns*

S3 Table. PTC associated exon skipping. Values represent the mean of n independent experiments. p-values are calculated using an unpaired Student t-test.

Exon	Name	Protein	Basal skipping (WT)	n=	Skipping (Mutation)	n=	*P*-value
3	c.178G>T	p.Glu60*	8 ± 3.2	7	32 ± 1.6	3	*< 0.001*
4	c.366T>A	p.Tyr122*	1 ± 0.5	6	2 ± 0.6	3	*ns*
10	c.1301C>G	p.Ser434*	2.5 ± 0.5	6	3.3 ± 0.3	6	*ns*
11	c.1397C>G	p.Ser466*$_{UGA}$	0	7	0	4	*ns*
12	c.1624G>T	p.Gly542*	0.3 ± 0.3	4	0.7± 0.1	4	*ns*
12	c.1657C>T	p.Arg553*	0.3 ± 0.3	4	6 ± 1.8	4	*< 0.001*
14	c.2353C>T	p.Arg785*	8 ± 2.0	8	44 ± 11.4	14	*< 10^{-6}*
15	c.2538G>A	p.Trp846*$_{UGA}$	3 ± 0.7	9	12 ± 2.6	5	*< 0.001*
20	c.3276C>A	p.Tyr1092*$_{UAA}$	3 ± 0.3	3	2 ± 1.3	3	*ns*
20	c.3310G>T	p.Glu1104*	3 ± 0.3	3	1 ± 2.0	3	*ns*
21	c.3382A>T	p.Arg1128*	0	4	0	4	*ns*
22	c.3484C>T	p.Arg1162*	0	8	0	4	*ns*
22	c.3587C>G	p.Ser1196*	0	8	0	5	*ns*
23	c.3846G>A	p.Trp1282*	0	4	0	3	*ns*
24	c.3937C>T	p.Gln1313*	0	6	0	4	*ns*

S4 Table. Major and minor amino acid identified by mass spectrometry in the absence and presence of paromomycin.

PTC	- paromomycin		+ paromomycin	
	Major	Minor	Major	Minor
UAA	Gln & Tyr	Lys	Gln & Tyr	Lys
UAG	Tyr	Lys & Gln	Tyr	Lys & Gln
UGA	Trp	Arg & Cys	Trp	Arg & Cys

S5 Table. Predicted Recoded CFTR channels. Are indicated the predicted recoded channels for the corresponding PTCs according to Blanchet et al (Gentamycin induced readthrough in the Yeast model). In bold are indicated the major recoded amino acids. ^{CF} indicates a known CF mutation, and ^{WT} indicates WT channels.

Mutation	PTC	Recoded Residue	*CFTR* variants	Tested *CFTR* variants
p.Glu60*	UAG	**p.Glu60Tyr,** -Gln, -Lys^{CF}	p.Glu60Lys	p.Glu60Tyr
p.Tyr122*	UAA	**p.Tyr122Gln -Tyr^{WT}, -**Lys	p.Tyr122His -Cys	p.Tyr122Gln -Lys
p.Ser434*	UGA	**p.Ser434Trp**, -Cys, -Arg	-	p.Ser434Trp
p.Ser466*	UGA	**p.Ser466Trp**, -Cys, -Arg	p.Ser466Leu	p.Ser466Trp
p.Gly542*	UGA	**p.Gly542Trp** -Cys, -Arg	p.Gly542Glu	p.Gly542Trp -Arg, -Cys
p.Arg553*	UGA	**p.Arg553Trp**, -Cys, -Arg^{WT}	p.Arg553Gly, -Gln	p.Arg553Trp
p.Arg785*	UGA	**p.Arg785Trp**, -Cys, -Arg^{WT}	-	p.Arg785Trp
p.Trp846*	UGA	**p.Trp846Trp**^{WT}, -Cys, -Arg	-	-
p.Tyr1092*	UAA	**p.Tyr1092Gln, -Tyr**^{WT}, -Lys	p.Tyr1092Cys, -His	p.Tyr1092Gln
p.Glu1104*	UAA	**p.Glu1104Gln, -Tyr** -Lys^{CF}	p.Glu1104Lys	p.Glu1104Gln -Tyr
p.Arg1128*	UGA	**p.Arg1128Trp**, -Cys, -Arg^{WT}	-	p.Arg1128Trp
p.Arg1162*	UGA	**p.Arg1162Trp,** -Cys, -Arg^{WT}	p.Arg1162Leu	p.Arg1162Trp
p.Ser1196*	UGA	**p.Ser1196Trp**, -Cys, -Arg	-	p.Ser1196Trp
p.Trp1282*	UGA	**p.Trp1282Trp**^{WT}, -Cys^{CF}, -Arg^{CF}	p.Trp1282Gly -Cys, -Arg,	-
p.Gln1313*	UAA	**p.Gln1313Gln**^{WT} **-Tyr**, -Lys	p.Gln1313Lys	p.Gln1313Tyr

S6 Table. Maturation of recoded CFTR channels. CFTR maturation was assessed using the C/(B+C) ratio for each condition. Are indicated significant differences to WT maturation ratio under control conditions (ANOVA followed with Fisher test for p value calculation) and significant differences between untreated and treated with VX809 constructs (unpaired Student t-test).

	C/(B+C)	**n =**	*P*-value	**% to basal WT**	***VX809***	**n =**	*P*-value	**% to basal WT**
WT	91 ± 1.5	10		*100%*				
p.Phe508del	19 ± 1.4	9	$<10^{-4}$	*21%*	47 ± 2.8	7	$<10^{-4}$	*52%*
p.Glu60Tyr	19 ± 2.9	7	$<10^{-4}$	*21%*	73 ± 7.4	4	$<10^{-4}$	*80%*
p.Tyr122Lys	92 ± 2.3	4	*ns*	-				
p.Tyr122Gln	92 ± 2.5	4	*ns*	-				
p.Ser434Trp	88 ± 1.7	4	*ns*	-				
p.Ser466Trp	30 ± 3.4	6	$<10^{-4}$	*33%*	68 ± 3.5	4	$<10^{-4}$	*75%*
p.Gly542Trp	48 ± 3.7	7	$<10^{-4}$	*53%*	63 ± 4.3	5	*0.01*	*69%*
p.Gly542R	87 ± 3.7	6	*ns*	-				
p.Gly542C	88 ± 1.2	6	*ns*	-				
p.Arg553Trp	56 ± 4.0	6	10^{-3}	*61%*	74 ± 1.6	5	$<10^{-2}$	*81%*
p.Arg785Trp	92 ± 2.2	4	*ns*	-				
p.Glu1104Y	51 ± 6.7	6	$<10^{-4}$	*56%*	75 ± 3.7	4	*0.02*	*82%*
p.Glu1104Q	85 ± 2.7	4	*ns*	*93%*				
p.Tyr1092Q	94 ± 1.3	4	*ns*	-				
p.Arg1128Trp	90 ± 2.3	4	*ns*	-				
p.Arg1162Trp	90 ± 1.5	4	*ns*	-				
p.Ser1196Trp	93 ± 0.6	4	*ns*	-				
p.Gln1313Y	90 ± 1.9	4	*ns*	-				

S7 Table. Function of recoded CFTR channels. CFTR function was measured as the initial transport rate for each condition. Are indicated differences to WT transport rates under control conditions, (ANOVA followed with Fisher test for p value calculation). Differences between untreated constructs and constructs treated with VX770 or VX809/VX770 were evaluated using Student unpaired t-test.

Construct	Transport rate (mM/s) Basal	*n*	*WT* *P*-value	% to control WT	Transport rate (mM/s) VX770	*n*	*Effect of VX770* *P*-value	% to control WT	Transport rate (mM/s) VX809+VX770	*n*	*Effect of VX809+VX770* *P*-value	% to control WT
pTracer	0.04 ± 0.01	*20*		*15%*	0.05 ± 0.01	*10*	*ns*	*18%*	0.06 ± 0.01	*6*		*22%*
WT	0.27 ± 0.02	*14*	-	*100%*	0.52 ± 0.05	*10*	10^{-4}	*180%*				
p.Phe508del	0.04 ± 0.01	*10*	$<10^{-4}$	*15%*	0.06 ± 0.02	*5*	*ns*	*22%*	0.11 ± 0.02	*6*	10^{-4}	*41%*
p.Glu60Tyr	0.05 ± 0.02	*5*	$<10^{-4}$	*18%*	0.03 ± 0.01	*2*	*ns*	*11%*	0.18 ± 0.01	*4*	10^{-5}	*67%*
p.Tyr122Lys	0.14 ± 0.02	*6*	*0.002*	*52%*	0.37 ± 0.04	*5*	10^{-4}	*137%*				
p.Tyr122Gln	0.23 ± 0.02	*4*	*ns*	*85%*	0.51 ± 0.06	*3*	*0.02*	*190%*				
p.Ser434Trp	0.22 ± 0.02	*4*	*ns*	*82%*	0.45 ± 0.04	*3*	10^{-4}	*167%*				
p.Ser466Trp	0.04 ± 0.01	*5*	$<10^{-4}$	*15%*	0.04 ± 0.01	*2*	*ns*	*15%*	0.18 ± 0.01	*4*	10^{-6}	*67%*
p.Gly542Trp	0.09 ± 0.02	*6*	$<10^{-4}$	*33%*	0.19 ± 0.04	*3*	*0.03*	*70%*	0.26 ± 0.04	*3*	10^{-3}	*96%*
p.Gly542Cys	0.22 ± 0.02	*3*	*ns*	*81%*	0.43 ± 0.04	*3*	10^{-3}	*160%*				
p.Gly542Arg	0.26 ± 0.04	*4*	*ns*	*96%*	0.45 ± 0.03	*3*	10^{-3}	*167%*				
p.Arg553Trp	0.09 ± 0.01	*6*	10^{-4}	*33%*	0.17 ± 0.01	*3*	10^{-3}	*62%*	0.21 ± 0.01	*5*	10^{-4}	*78%*
p.Arg785Trp	0.34 ± 0.06	*6*	*ns*	*125%*	0.57 ± 0.08	*3*	*0.02*	*211%*				
p.Tyr1092Gln	0.15 ± 0.02	*6*	10^{-3}	*56%*	0.40 ± 0.06	*4*	*0.002*	*150%*				
p.Glu1104Gln	0.24 ± 0.04	*5*	*ns*	*89%*	0.37 ± 0.03	*3*	*0.03*	*140%*				
p.Glu1104Tyr	0.07 ± 0.05	*7*	$<10^{-4}$	*26%*	0.12 ± 0.02	*3*	*0.04*	*44%*	0.19 ± 0.01	*5*	10^{-4}	*70%*
p.Arg1128Trp	0.25 ± 0.05	*5*	*ns*	*92%*	0.44 ± 0.06	*3*	*0.02*	*160%*				
p.Arg1162Trp	0.29 ± 0.08	*3*	*ns*	*107%*	0.45 ± 0.13	*3*	*0.02*	*167%*				
p.Ser1196Trp	0.35 ± 0.03	*6*	*ns*	*130%*	0.66 ± 0.09	*5*	10^{-4}	*244%*				
p.Gln1313Tyr	0.31 ± 0.08	*5*	*ns*	*115%*	0.49 ± 0.14	*3*	*0.02*	*180%*				

S8 Table. Predicted readthrough response to negamycin. Skills were assigned for the level of readthrough, the occurrence of exon skipping and the function of the recoded channel to assess treatment response (Low, Moderate, or High). Additional CFTR directed co-therapies are indicated for the considered PTC.

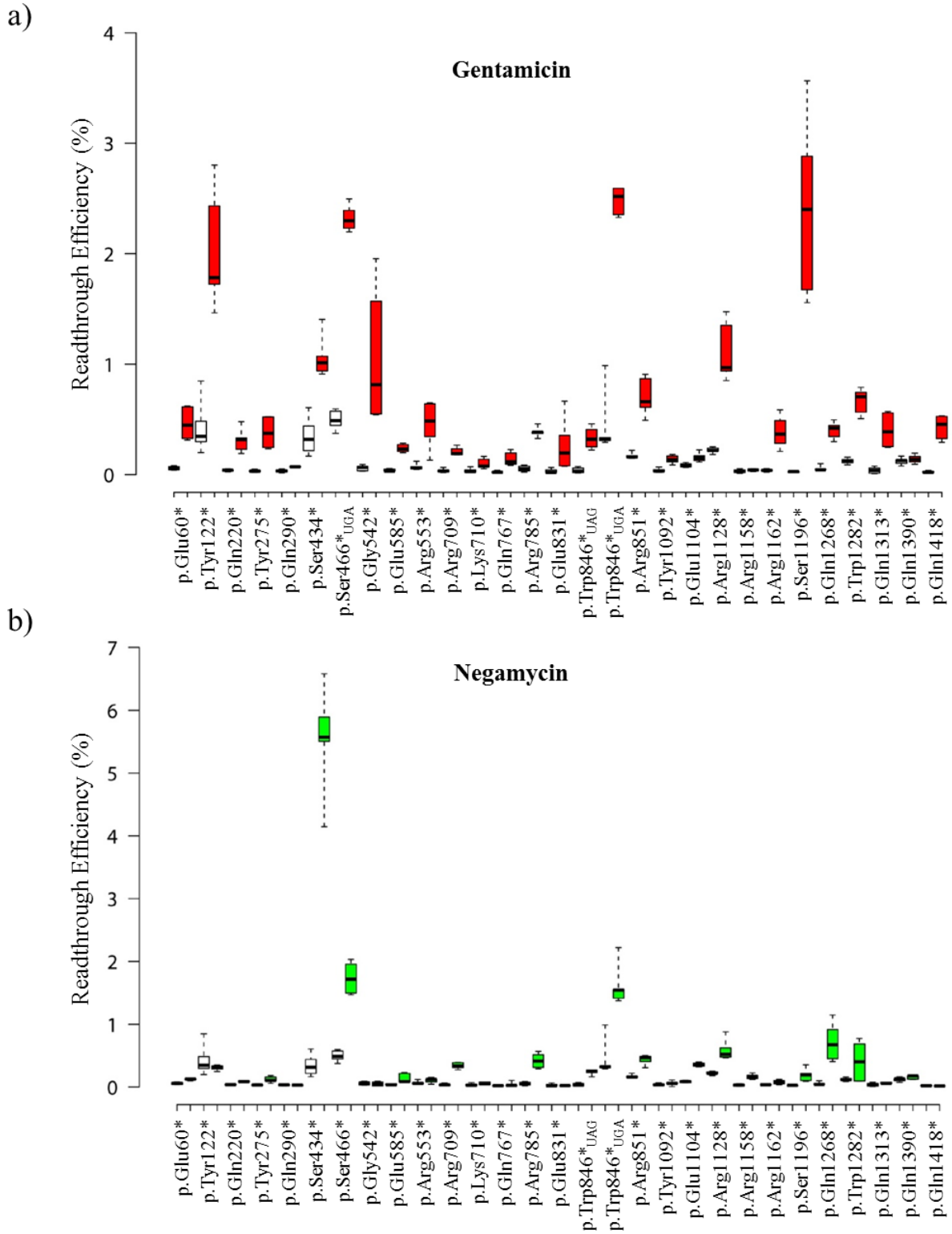
Mutation	Readthrough stimulation	Skipping	Function	Response	Additional treatment
p.Glu60*	Low	Low	Low	**Low**	Potentiator + Corrector
p.Tyr122*	Low	High	High	**Low**	Potentiator
p.Ser434*	High	High	High	**High**	Potentiator
p.Ser466*	High	High	Low	**Low**	Potentiator + Corrector
p.Gly542*	Low	High	Moderate	**Low**	Potentiator + Corrector
p.Arg553*	Low	Low	Moderate	**Low**	Potentiator + Corrector
p.Arg785*	Low	Low	High	**Low**	Potentiator
p.Trp846*$_{UGA}$	High	Low	High	**Low**	Potentiator
p.Tyr1092*	Low	High	Moderate	**Low**	Potentiator
p.Glu1104*	Low	High	Moderate	**Low**	Potentiator + Corrector
p.Arg1128*	Moderate	High	High	**Moderate**	Potentiator
p.Arg1162*	Low	High	High	**Low**	Potentiator
p.Ser1196*	Low	High	High	**Low**	Potentiator
p.Trp1282*	Low	High	High	**Low**	Potentiator
p.Gln1313*	Low	High	High	**Low**	Potentiator

S9 Table. Mismatches corresponding to amino acid incorporation. Major and minor amino acids identified by mass spectrometry are indicated in bold and in italic, respectively.

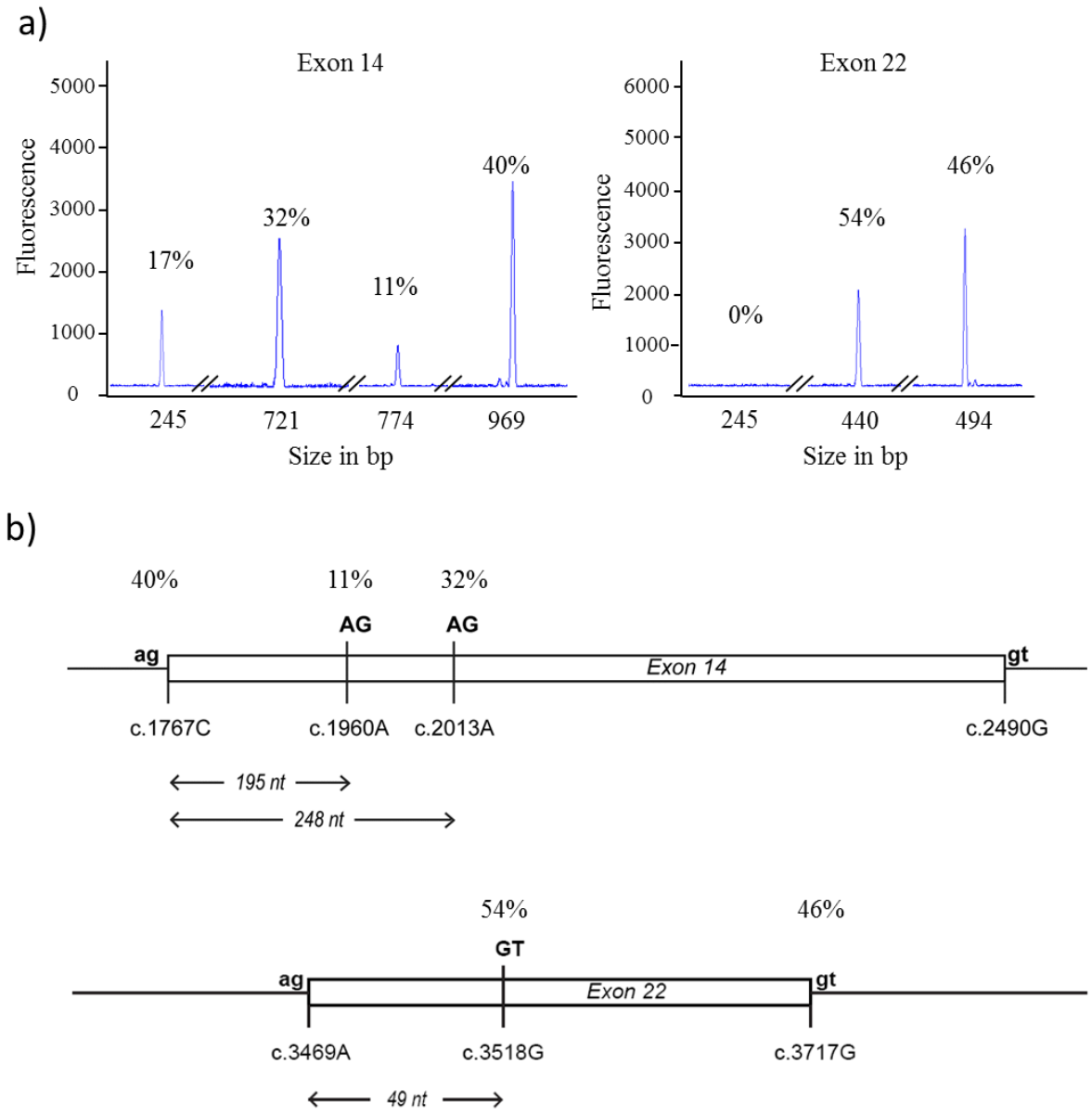
PTC	Mismatch position 1	Mismatch position 2	Mismatch position 3
UAA	**CAA (Gln)**	UUA (Leu)	**UAU (Tyr)**
	AAA (Lys)	UCA (Ser)	**UAC (Tyr)**
	GAA (Glu)	UGA (Stop)	UAG (Stop)
UAG	***CAG (Gln)***	UUG (Leu)	**UAU (Tyr)**
	AAG (Lys)	UCG (Ser)	**UAC (Tyr)**
	GAG (Glu)	UGG (Trp)	UAA (Stop)
UGA	***CGA (Arg)***	UUA (Leu)	***UGU (Cys)***
	AGA (Arg)	ACA (Thr)	***UGC (Cys)***
	GGA (Gly)	UAA (Stop)	**UGG (Trp)**

S10 Table. Primer sequences used to generate the corresponding minigene constructs. Are indicated both Forward (F) and Reverse primers (R) and the restriction enzyme used for cloning.

Name	Primer sequence	Restriction enzyme used for cloning
Exon10_F	ccg**ctcgagt**gggtaattcagggttgctt	*XhoI*
Exon10_R	cgc**ggatcc**agcagctgggactacagcat	*BamHI*
Exon12_F	ccg**ctcgag**tttgtaaaatggacctatggatga	*XhoI*
Exon12_R	cgc**ggatcc**agtggcagggtctatgatgg	*BamHI*
Exon20_F	ccg**ctcgag**tgcttctggcttgagcctat	*XhoI*
Exon20_R	cgc**ggatcc**catttctcaacctggcgatt	*BamHI*
Exon22_F	ccg**ctcgag**ttgtgcagtgctgctcatag	*XhoI*
Exon22_R	cgc**ggatcc**tcacttgtttggcagaatgg	*BamHI*
Exon24_F	ccg**ctcgag**caaactaggaatttgttctaacagg	*XhoI*
Exon24_R	gcgc**tctaga**ccagtgaggagagaagtaggc	*XbaI*

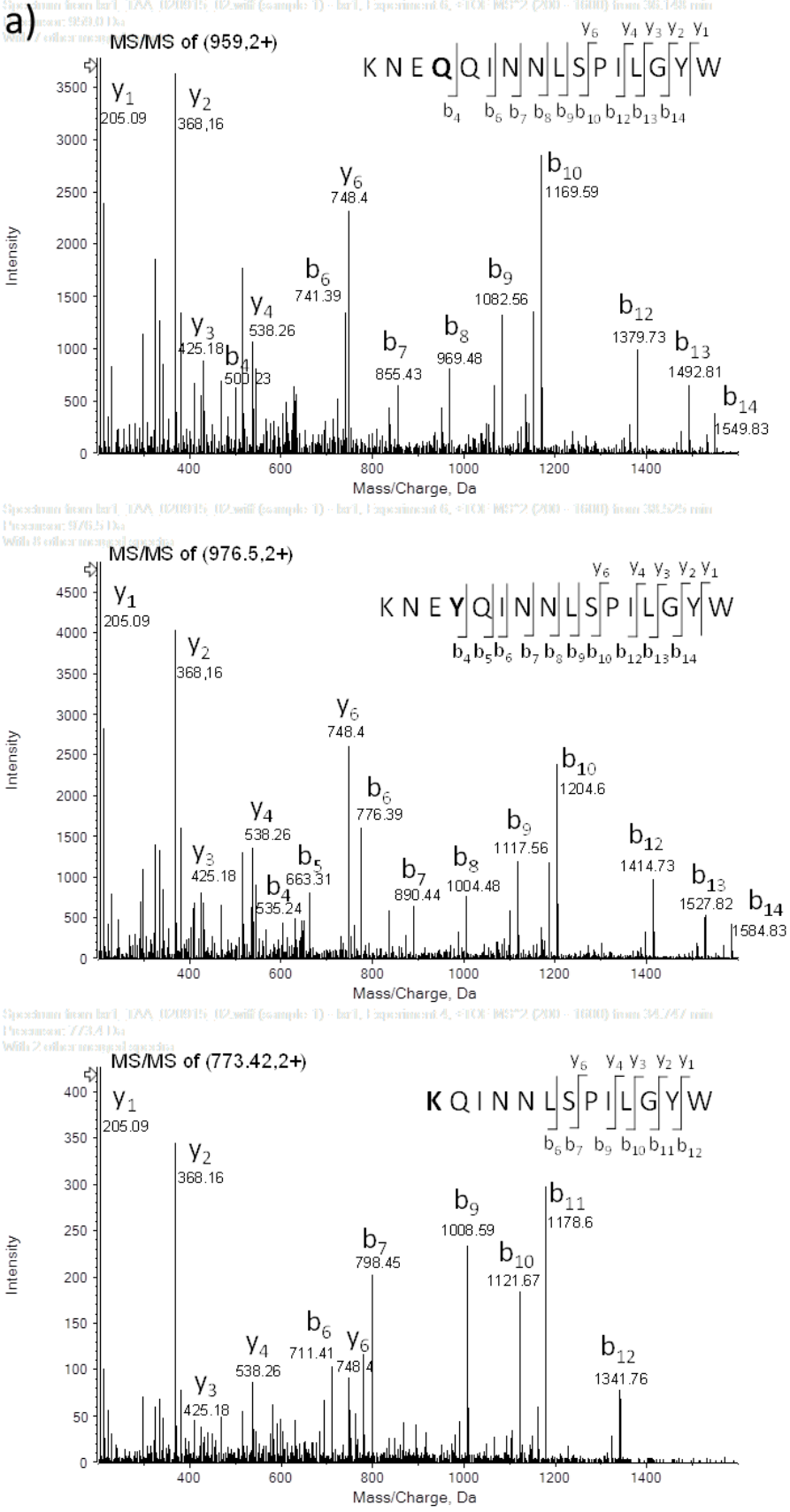


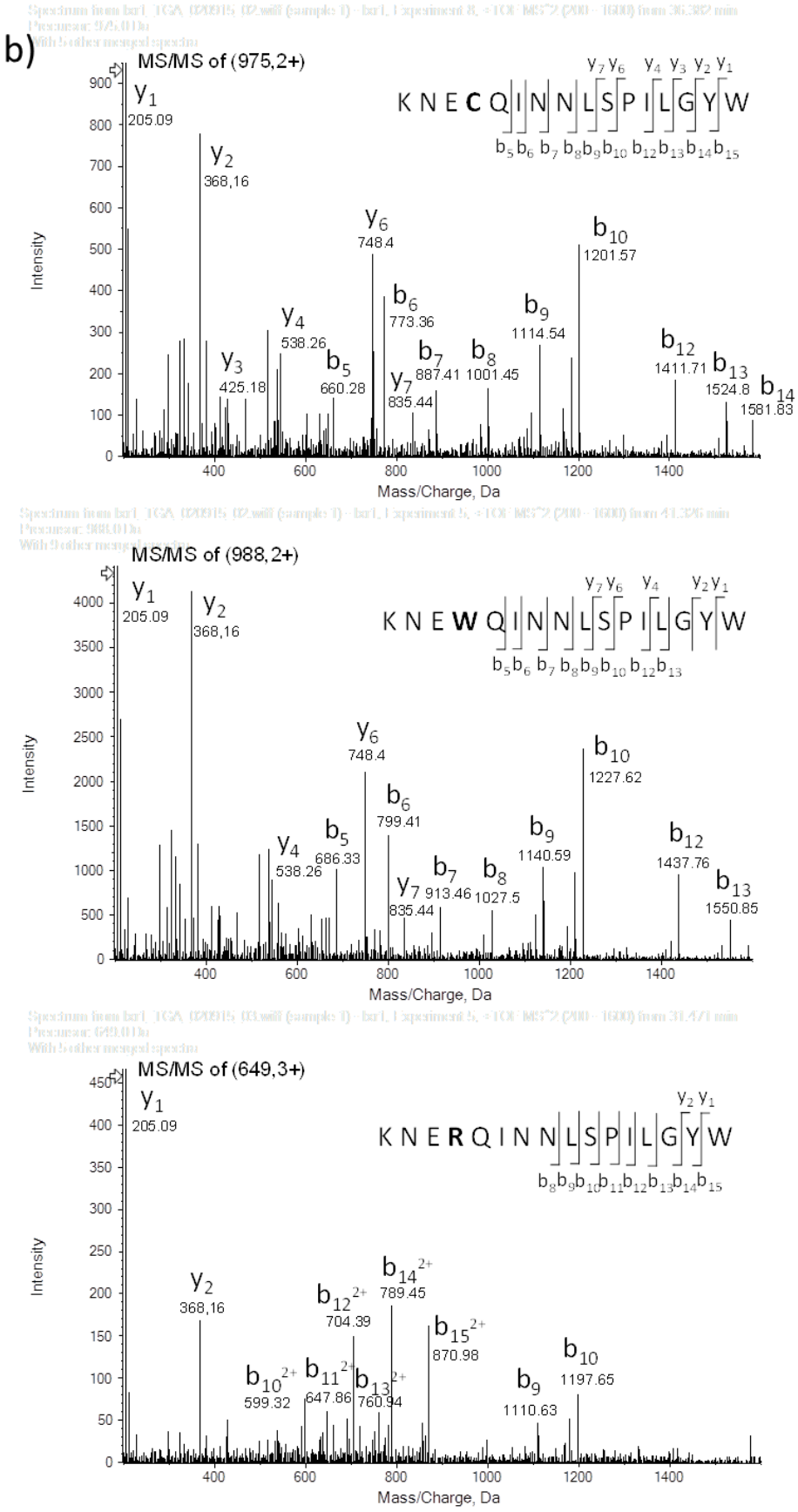
S1 Figure. Readthrough levels. Readthrough levels measured for the indicated CFTR PTC mutation, at basal state (empty boxes) and after incubation with gentamicin (a) (red boxes) or negamycin (b) (green boxes). Center lines show the medians; box limits indicate the 25th and 75th percentiles as determined by R software; whiskers extend 1.5 times the interquartile range from the 25th and 75th percentiles n>5 for all samples.



S2 Figure. Multiple transcripts produced with the constructs carrying CFTR exon 14 and exon 22. A. Examples of capillary electrophoresis analysis of RT-PCR products obtained from BEAS-2B cells transfected with indicated minigene. The corresponding size and relative amount for each peak is indicated. The peak at 245 bp corresponds to transcripts lacking the exon. B. Schematic representation of CFTR exons 14 and 22 indicating the position of the identified cryptic acceptor and donor sites. The amounts of corresponding transcripts are indicated in %.

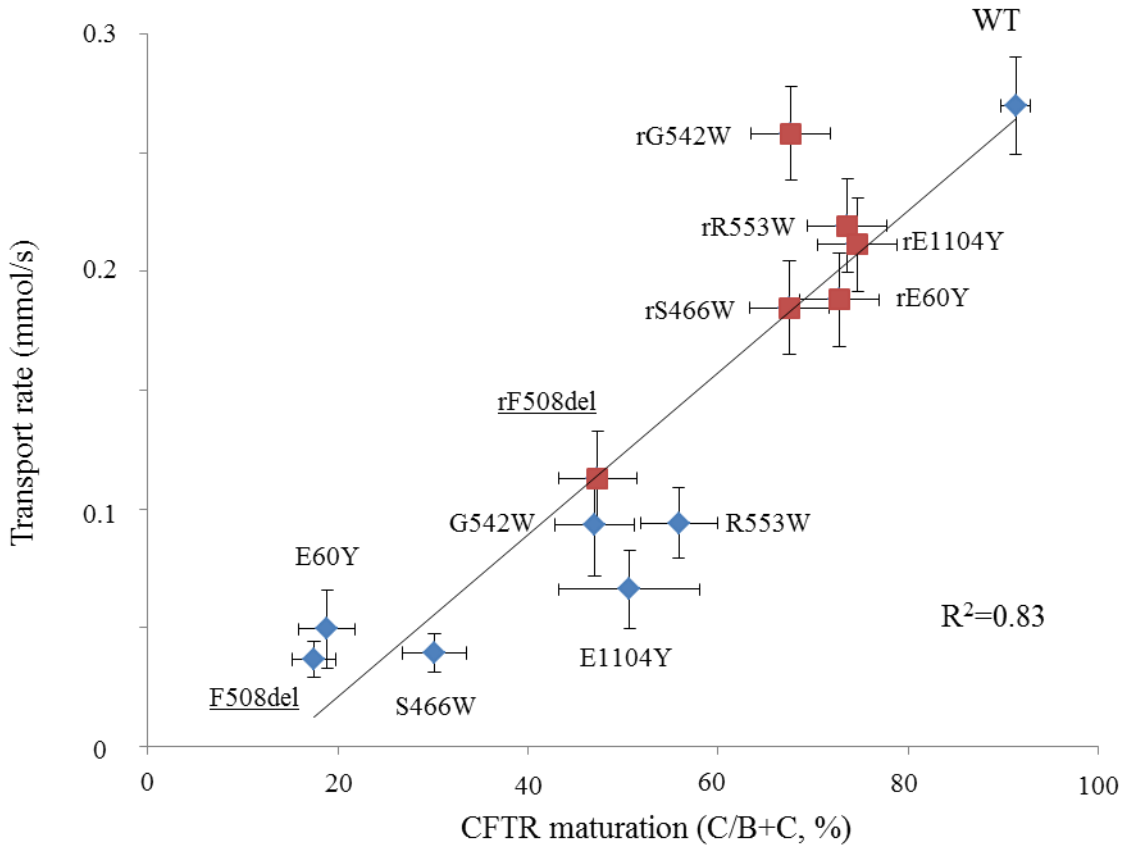
a)


MS/MS of (959,2+)
K N E Q Q I N N L S P I L G Y W
y1 205.09
y2 368,16
y3 425.18
b4 500.23
y4 538.26
y6 748.4
b6 741.39
b7 855.43
b8 969.48
b9 1082.56
b10 1169.59
b12 1379.73
b13 1492.81
b14 1549.83
Intensity
Mass/Charge, Da
MS/MS of (976.5,2+)
K N E Y Q I N N L S P I L G Y W
y1 205.09
y2 368,16
y3 425.18
b4 535.24
b5 663.31
y4 538.26
y6 748.4
b6 776.39
b7 890.44
b8 1004.48
b9 1117.56
b10 1204.6
b12 1414.73
b13 1527.82
b14 1584.83
Intensity
Mass/Charge, Da
MS/MS of (773.42,2+)
K Q I N N L S P I L G Y W
y1 205.09
y2 368.16
y3 425.18
y4 538.26
b6 711.41
y6 748.4
b7 798.45
b9 1008.59
b10 1121.67
b11 1178.6
b12 1341.76
Intensity
Mass/Charge, Da

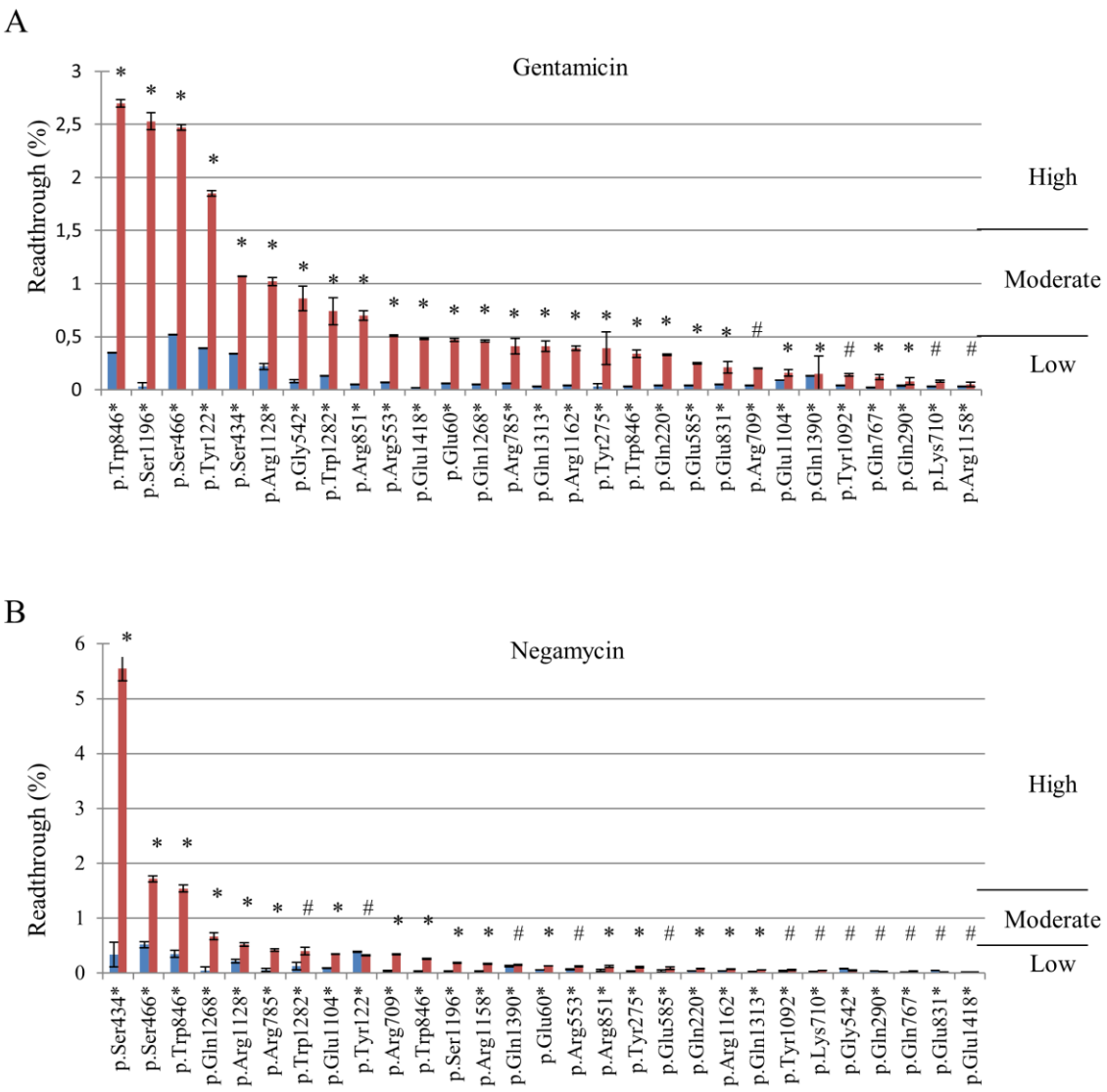


S3 Figure. **MS/MS spectra of the readthrough peptides in presence of paromomycin.** Panels show representative Triple-TOF MS/MS spectra for readthrough peptides, for the UAA/UAG (A) and UGA stop codons (B). No new amino acid is inserted in presence of

paromomycin (Q, Y, K for UAA/UAG and C, W, R for UGA). The identified fragments are annotated on the sequence and the Mascot ion scores (not shown) of readthrough peptides are significantly higher than the identity thresholds calculated at a FDR of 1%. One letter amino acid code was used for better visibility.



S4 Figure. Correlation between CFTR maturation and function. Plot of the maturation ratio vs channel function for the indicated mutation under basal conditions (bleu dots) and after VX809/VX770 treatment (red). Treated channels are indicated as rescued (r- before the name). One letter nomenclature was used for amino acids.



S5 Figure. **Classified readthrough response to gentamicin and negamycin.** Are indicated the levels of response considered as Low, Moderate and High.