

Combined treatment of bronchial epithelial Calu-3 cells with Peptide Nucleic Acids Targeting miR-145-5p and miR-101-3p: Synergistic Enhancement of the Expression of the Cystic Fibrosis Transmembrane Conductance Regulator (*CFTR*) Gene

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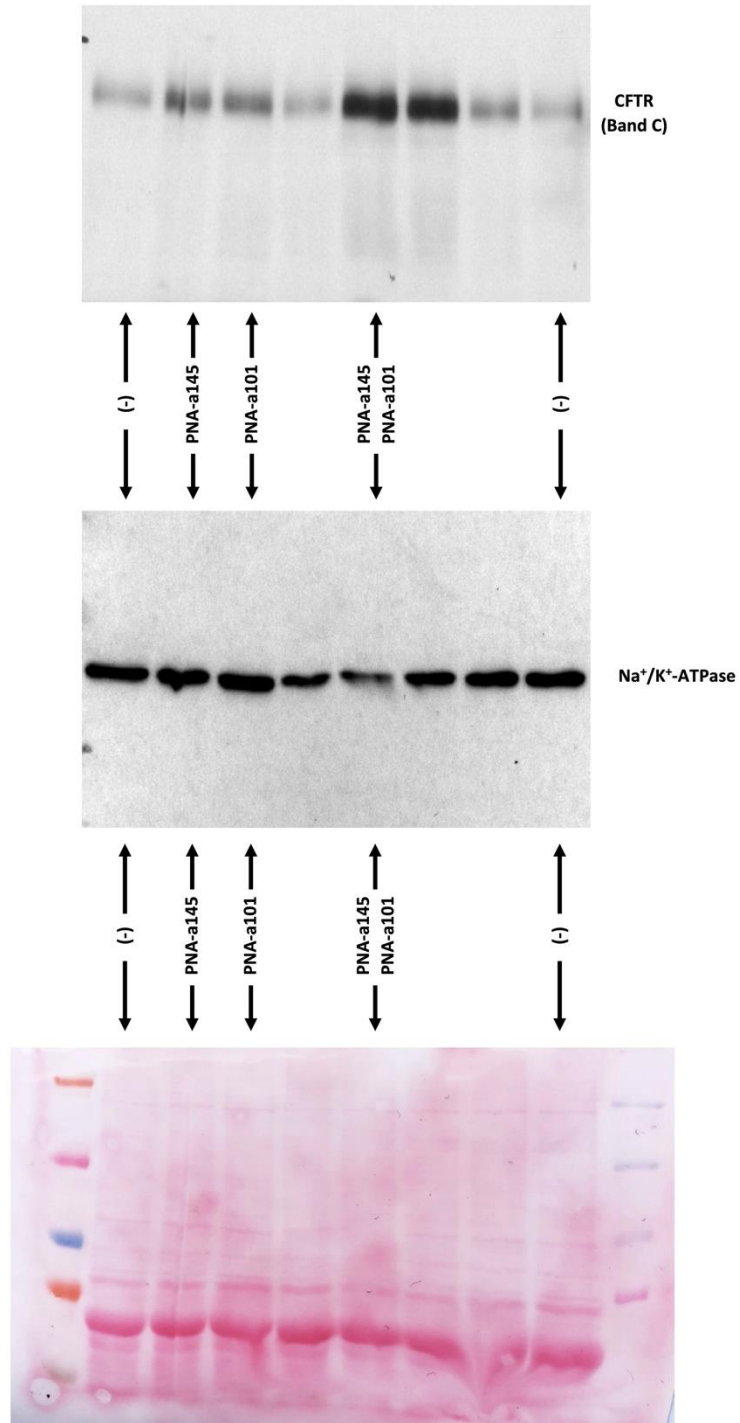
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SUPPLEMENTARY MATERIALS

FIGURE S1

Uncut version of the Western blotting data



These data have been used for Figure 3A, upper part of the panel (up) and Figure 3A, lower part of the panel (down).

TABLE S1

List of miRNAs targeting CFTR and location of their binding sites within the CFTR 3'UTR sequence

miRNA	Binding sites	Reference
miR-505-3p	15 - 21	Viart et al., 2015
miR-943	56 - 62	Viart et al., 2015
miR-1827	97 - 104	Gilllen et al., 2011
miR-335-5p	170 - 183	Tavazoie et al., 2008
miR-377-3p	212 – 219 1549 - 1556	Viart et al., 2015
miR-145-5p	427 - 434	Gilllen et al., 2011 Oglesby et al., 2013 Viart et al., 2015 Fabbri et al., 2017 Lutful et al., 2017
miR-939-5p	477 - 483	Gilllen et al., 2011
miR-200b-3p	545 - 551	Bartoszewska et al., 2017
miR-143-5p	573 - 580	De Santi et al., 2018
miR-331-3p	740 – 746 1304 - 1310	Gilllen et al., 2011
miR-433-3p	1060 - 1067	Amato et al., 2013
miR-509-3p	1056 - 1063	Amato et al., 2013 Ramachandran et al., 2013
miR-384	1118 - 1125	Gilllen et al., 2011
miR-494-3p	1140 - 1147	Gilllen et al., 2011 Viart et al., 2015 Megiorni et al., 2011 Oglesby et al., 2013 Ramachandran et al., 2013

miR-607	1216 - 1223	Gilllen et al., 2011
miR-376b-3p	1250 - 1257	Gilllen et al., 2011
miR-223-3p	1475 - 1481	Oglesby et al., 2013
miR-101-3p	1508 - 1515	Megiorni et al., 2011 Hassan et al., 2012 Viart et al., 2015
miR-144-3p	1508 - 1514	Hassan et al., 2012
miR-600	1510 - 1517	Gilllen et al., 2011 Viart et al., 2015
miR-1290	1535 - 1542	Gilllen et al., 2011
miR-1246	1537 - 1544	Gilllen et al., 2011 Lukosevicius et al., 2022

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TABLE S2

List of the mRNAs targeted by miR-145-5p, miR-101-3p and miR-335-5p and list of the relative publications

miR-145-5p			
SOX9	Zhuang, et al. 2022	FLI1	Chen et al., 2021
YES1	Sun et al., 2022	NF- κ Bp65	Tu et al., 2021
Smad3	Ye at al., 2022 Shen et al., 2020	CDCA3	Gu et al., 2021 Chen et al., 2021
ABRACL	Fan et al., 2021	SOCS7	Zeng et al., 2021
TMOD3	Li et al., 2021	KLF4	Tuo et al., 2021
IGF1R	Capik et al., 2021	RBBP5	Xie et al., 2021
SERPINE1	Li et al., 2021	S1PR1	Gao et al. 2021
CDH22	Zeng et al., 2021	CD36	Yuan et al., 2021
MYO6	Yang et al., 2021	Smad2	Shen et al., 2020
WIP1	Sun et al., 2021	HDAC11	Wang et al., 2020
NRAS	Yu et al., 2021 Ding et al., 2020 Li et al., 2020	CPEB4	Liu et al., 2020
MEST	Yu et al., 2021	ABCC1	Zheng et al., 2020
MORC2	Su et al., 2021	BACH2	Liu et al., 2020 Li et al., 2020
BRD4	Wang et al, 2021	Smad4	Liu et al., 2020 Zhou et al., 2020
SPOP	Zhang et al., 2021	ANGPT2	Zhou et al., 2020
TGF- β 2	Qi et al., 2021	TNFAIP2	Li et al., 2020
PAK7	Chen et al., 2021	SPATS2	Dong et al., 2020
PXN	Lin et al, 2021	E2F3	Li et al., 2020
NOH-1	Tan et al., 2021	IGF1	Chen et al., 2020
AIFM1	Zhou et al., 2021	Notch1	Wei et al., 2020
NURR1	Jiang et al., 2021	ITGB8	Wei et al., 2020
CXCL1	Zhuang et al., 2021	CXCL3	Pei et al., 2020
ITGA2	Zhuang et al., 2021	CDK6	Shi et al., 2020 Shao et al., 2013
MUC1	Jara et al., 2021	SOX2	Tang et al., 2019
PLD5	Liu et al., 2021	FLT1	Lv et al., 2019 Dang et al., 2019
MAL2	He et al., 2021	KLF5	Zhou et al., 2019 Cao et al., 2020

ARF6	Zhong et al., 2021 Wang et al., 2021 Hsu et al., 2020	Sema3A	Liu et al., 2019
TOP2A	Du et al., 2021	TPT1	Jian et al., 2019 Du et al., 2019
Arhgap24	Zhang et al., 2021	RAB18	Wang et al., 2019
Srgap1	Zhang et al., 2021	RHBDD1	Niu et al., 2019
ROCK1	Cheng et al., 2021 Zhuang et al., 2021	FSCN1	Gao et al., 2019
SF-1	Liang et al., 2021	TGFbetaR2	García-García et al., 2019 Dong et al., 2021
FGF5	Zhu et al., 2021 Zhang et al., 2019	DUSP6	Wu et al., 2019 Gu et al., 2019
SOX4	Zhu et al., 2021	CDK6	Sun et al., 2019
TRPC6	Whang et al., 2021	MYD88	Sun et al., 2019
HMGA2	Tan et al., 2021	CTGF	Hang et al., 2019
TLR4	Jiang et al., 2021 Jin et al., 2019 Jara et al., 2021	PCBP2	Wang et al., 2019
PAFAH1B2	Xu et al., 2021	AKT3	Feng et al., 2019
VRK2	Mu et al., 2021	NEDD9	Yu et al., 2019
TRIM2	Xu et al., 2021	MTDH	Wang et al., 2015
TBX15	Zheng et al., 2021	SOX11	Chang et al., 2017
ATF3	Pan et al., 2021	ADAM17	Yang et al., 2014
EGFR	Cho et al., 2011	CFTR	Fabbri et al., 2017
ABRACL	Fan et al., 2021	JAM-A	Yang et al., 2020
CD40	Yuan et al., 2017	HBXIP	Jiang et al., 2019
BNIP3	Du et al., 2017	WNT2B	Li et al., 2019
UHRF1	Matsushita et al., 2016	AMAD19	Wang et al., 2019
FOXO1	Hao et al., 2018	REV3L	Chen et al., 2019
CCND2	Jin et al., 2020	EPHA4	Cai et al., 2019
TP53	Sheykhhasan et al., 2021	PAI-1	Liu et al., 2020
NUAK1	Xiong et al., 2018	TAGLN2	Zhang et al., 2018
STAT1	Gregersen et al., 2010	MRP1	Zhan et al., 2016
ADD3	Ye et al., 2017	PAK1	Kou et al., 2014
PDE8A	Booiman et al., 2014	ABCG2	Shi et al., 2014
DNMT3A	Li et al., 2020	TWIST	Shi et al., 2014
VEGFA	Zou et al., 2012	TNFRSF11B	Wang et al., 2017
HDAC2	Noh et al., 2013	LMNB2	Su et al., 2020

SP1	Zhu et al., 2014	p70S6K1	Xu et al., 2012
FKBP3	Zhu et al., 2017	OTC4	Hu et al., 2012
ERBB2	Sheykhhasan et al., 2021	HMGB3	Xie et al., 2020
PDGFRB	Xu et al., 2017	LRP5	Cai et al., 2020
MAPK1	Yang et al., 2018	LASP1	Wang et al., 2016
CBFB	Fukuda et al., 2015 Ostenfeld et al., 2010	SLC7A1	Wang et al., 2018
PPP3CA	Ostenfeld et al., 2010	C-MYC	Shao et al., 2013
CLINT1	Ostenfeld et al., 2010	SWAP70	Chiyomaru et al., 2011
IRS1	Guo et al., 2012	ESR1	Hu et al., 2018
NUDT1	Cho et al., 2011		

miR-335-5p

ARGLU1	Zhao et al., 2022	TPX2	Gu et al., 2020
TTK	Suyal et al., 2022	SNIP1	Xie et al., 2019
HBP1	Lu et al., 2021	IGF1R	Qi et al., 2019
MAPK10	Gao et al., 2021	LDHB	Zhang et al., 2019
SLC2A4	Li et al., 2021	ROCK1	Du et al., 2019
Oct4	Ji et al., 2021	OTC4	Yang et al., 2019
OCT4A	Taheri Bajgan et al., 2021	RB1	Shi et al., 2012
COL11A1	Kang et al., 2021	ZEB2	Sun et al., 2014
CCNB2	Wang et al., 2020	SOX17	Yang et al., 2014
ADCY3	Zou et al., 2020	RASA1	Wang et al., 2010
JNK3	Wang et al., 2020	BCL2L2	Liu et al., 2018
ROCK1	Li et al., 2020 She et al., 2020	ICAM1	Luo et al., 2018
SIX2	Jia et al., 2020	PYGO2	Qian et al., 2021
CUL4B	Yu et al., 2020	ZEB1	Zhang et al., 2018
NUCB2	Huo et al., 2020	CFTR	Song et al., 2021
CPNE1	Tang et al., 2018	CRIM1	Jiang et al., 2021
POU5F1	Gou et al., 2017	SP1	Wang et al., 2020
LRP1	Legaki et al., 2020	VEGF-C	Ping et al., 2021
SGK3	Yao et al., 2018	Tra2 β	Liu et al., 2018
BIRC5	Zu et al., 2012	c-MET	Gao et al., 2015
TRIM29	Zhou et al., 2016	HIF1AN	Wu et al., 2018
c-MET	Gao et al., 2015	SGMS2	Pan et al., 2021

MAP3K2	Wang et al., 2021	NFIB	Lin et al., 2022
MEF2D	Wang et al., 2019	EphA4	Dong et al., 2018
EGR3	Zhang et al., 2019	E2F3	Song et al., 2021

miR-101-3p

FOXP4	Xue et al., 2022	RAB5A	Sheng et al., 2014
HIPK3	Tao et al, 2022	KIF2A	Zhao et al., 2020
WEE1	Sun et al., 2022 Chen et al., 2019	SRF	Wu et al., 2017
USP47	Park et al., 2022	BICC1	Wang et al., 2020
BIRC5	Meng et al., 2021	SOX9	Liu et al., 2017
EZH2	Dong et al., 2021 Wang et al., 2018 Li et al., 2019	FOXP1	Sun et al., 2018
MAPK1	Zhao et al., 2021	PDCD4	Zhao et al., 2019
KPNA2	Wang et al., 2021	TLR2	Dong et al., 2015
DUSP1	Xin et al., 2021	APP	Barbato et al., 2019
SKP1	Zhang et al., 2021	RAC1	Lin et al., 2014
CUL4B	Gu et al., 2021 Zhang et al., 2019 Xie et al., 2021	IRF2BP2	Yao et al., 2019
MTOR	Gu et al., 2021	TRIB1	Niespolo et al., 2020
Notch1	Jiang et al., 2021	CMIP	Zhang et al., 2017
EIF4G2	Wang et al., 2021	CCN4	Pommier et al., 2021
VEGFA	Guo et al., 2021	MCL-1	Cui et al., 2018 Zhu et al., 2017
CLDN1	Du et al., 2021	COX2	Ma et al., 2016
TET2	Chen et al., 2020	ATP5B	Zheng et al., 2014
BICC1	Wang et al., 2020	CDH5	Cao et al., 2019
C/EBP α	Zhao et al., 2020	CPEB1	Xiaoping et al., 2013
KLF6	Zhao et al., 2020	ZEB2	Lin et al., 2019
STC1	An et al., 2020 Yuan et al., 2021	PIM1	Liu et al., 2015
KRAS	Ding et al., 2020	ATG4D	Frankel et al., 2011
PTGS2	Wei et al., 2020	RAB5A	Frankel et al., 2011
HDAC9	Sun et al., 2020	STMN1	Frankel et al., 2011 Zhu et al., 2018
RAP2B	Zhou et al., 2020	C-MET	Zhu et al., 2017
TRIM44	Li et al., 2019	HGF	Liu et al., 2020

ATX	Wang et al., 2019	NLK	Shen et al., 2014
MED19	Zhang et al., 2019	CFTR	Hassan et al., 2012
ZEB1	Fan et al., 2019	BICC1	Wang et al., 2020
Beclin-1	Sun et al., 2019	CXCR7	Yang et al., 2019
AMPK	Cao et al., 2019	MKP-1	Qiu et al., 2020
VEGF-C	Liu et al., 2019 Li et al., 2019	KDM1A	Huang et al., 2019
RAP1B	Zhou et al., 2020	KPNB1	Liu et al., 2019
		SOCS5	Zhang et al., 2020
CREB1	Yang et al., 2019	MEK1	Huang et al., 2019
HMGA2	Jiang et al., 2016	ANXA2	Bao et al., 2017
SOX4	Tavazoie et al., 2008	Nrf2	Dong et al., 2019
PTPRN2	Tavazoie et al., 2008	USP22	Zhao et al., 2016
MERTK	Tavazoie et al., 2008	FOXO1	Wang et al., 2017
TNC	Tavazoie et al., 2008	ABCC1	Shao et al., 2021
TIGAR	Xu et al., 2017	Jak2	Wang et al., 2014
CXCL12	Zhang et al., 2015	RAP1A	Chen et al., 2020
FOS	Liang et al 2014	TGF- β 1	Wang et al., 2021
FZD4	Chen et al., 2019	RUNX1	Wang et al., 2015
ROCK2	Ye et al., 2016	PTGER4	Chandramouli et al., 2012

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TABLE S3

Levels of CFTR protein content in Calu-3 cells treated with PNA-a145, PNA-a101, and PNA-a335 administrated singularly or in combination

Treatment	CFTR (Fold average)	Standard Deviation (SD)
PNA-a145	1.94	0.19
PNA-a101	1.96	0.07
PNA-a335	1.57	0.14
PNA-a145 + PNA-a101	9.33	0.99
PNA-a145 + PNA-a335	4.95	0.26
PNA-a101 + PNA-a335	1.93	0.20