

**Supplementary Table S1. Detailed clinical information on R1070 patients with references.**

Abbreviations: n.a.—data not available; ref—patient referred to specified country; pers comm=personal communication with collaborator; diag=diagnosis; b=year of birth; dis=disease; FEV=forced expiratory volume; FVC=forced vital capacity; obstr lung dis=obstructive lung disease; def=deficiency; MI=meconium ileus; y=years; CFRD=Cystic Fibrosis-related diabetes; CBAVD=congenital bilateral absence of the vas deferens; CAVD=congenital absence of the vas deferens; PA=Pseudomonas aeruginosa; \* insufficient data to include patient; \*\* patient reported in Mickle *et al.*, 2000.

## A) Patients bearing R1070Q

patient ID #	genotype (allele 1 / allele 2)	diagnosis (as per reference)	sex of patient	lung function and disease	pancreatic status	sweat chloride levels	other traits and conditions	country of origin	references for patient data
#1	R1070Q / E822X	classic CF	female	mild disease	insufficient	97.5 mmol/L	b=1993, 1y (diag)	Greece	Tzetis M pers comm 2006, Canadian Database 2007
#2	R1070Q / 2789+5G>A	nonclassic CF	n.a.	n.a.	sufficient	n.a.	pancreatitis, b=1992	Greece	Tzetis M pers comm 2006
#3	R1070Q / S549N	CBAVD	male	n.a.	n.a.	n.a.	n.a.	Pakistan and Asia	Osborne 1993**
#4	R1070Q / D1152H	CBAVD	male	bronchiectasis	n.a.	56 mmol/L	7t/7t, 37y (diag)	France	Bienvenu 1997, Feldmann 2003**
#5	R1070Q / F1337V	CBAVD	male	n.a.	n.a.	n.a.	n.a.	Holland	Scheffer, Canadian Database 2007
#6*	R1070Q / n.a.	nonclassic CF	n.a.	n.a.	n.a.	n.a.	n.a.	Italy	Audrezet 1993**
#7*	R1070Q / n.a.	CF	n.a.	n.a.	insufficient	n.a.	n.a.	Bulgaria	Mercier 1993, Mercier 1994, Savov 1994, Estivill 1997**
#8*	R1070Q / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	Bulgaria	Mercier 1993, 1994, Savov 1994, Estivill 1997**
#9*	R1070Q / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	Albania	Mercier 1993, Mercier 1994**
#10*	R1070Q / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	Romania	Mercier 1993, Mercier 1994**
#11*	R1070Q / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	Bulgaria	Savov 1994, Estivill 1997**
#12*	R1070Q / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	Bulgaria	Savov 1994, Estivill 1997**
#13*	R1070Q / n.a.	CBAVD	male	n.a.	n.a.	n.a.	n.a.	Iran (Spain ref.)	Casals T pers comm 2006

## B) Patients bearing R1070Q+S466X

patient ID #	genotype (allele 1 / allele 2)	diagnosis (as per reference)	sex of patient	lung function and disease	pancreatic status	sweat chloride levels	other traits and conditions	country of origin	references for patient data
#1*	R1070Q+S466X / n.a.	CF	n.a.	n.a.	sufficient	n.a.	n.a.	Bulgaria	Mercier 1993, Mercier 1994, Savov 1994, Estivill 1997, Wang 2002**
#2	R1070Q+S466X / R1070Q+S466X	classic CF	n.a.	FEV=79%, FVC=74%	insufficient	99.3 mEq/l	liver cirrhosis, PA (9y), birth (diag), b=1981	Greece	Tzetis M pers comm 2006
#3	R1070Q+S466X / N1303K	classic CF	n.a.	n.a.	insufficient	n.a.	liver cirrhosis, MI, birth (diag), 1997-98	Greece	Tzetis M pers comm 2006
#4	R1070Q+S466X / F508del	classic CF	n.a.	mild disease	insufficient	133 mEq/l	PA (<1y), <1y (diag), b=1998	Greece	Tzetis M pers comm 2006
#5	R1070Q+S466X / F508del	classic CF	n.a.	mild disease	insufficient	87.7 mEq/l	PA (1y), <1y (diag), b=1994	Greece	Tzetis M pers comm 2006
#6	R1070Q+S466X / F508del	classic CF	male	FEV=84%, FVC=98%	insufficient	104 no units	b=1986, 1y (diag), CFRD, cirrhosis/liver dis (transplant)	USA	CFF Registry 2005
#7	R1070Q+S466X / 621+1G>T	classic CF	n.a.	n.a.	insufficient	98.4 mEq/l	<1y (diag), b=1996	Greece	Tzetis M pers comm 2006
#8	R1070Q+S466X / 711+3A>G	classic CF	n.a.	n.a.	insufficient	73.8 mEq/l	<1y (diag), b=1999	Greece	Tzetis M pers comm 2006
#9	R1070Q+S466X / F508del	classic CF	n.a.	mild disease	insufficient	100.4 mEq/l	PA (8y), b=1992	Greece	Tzetis M pers comm 2006
#10*	R1070Q+S466X / n.a.	CF	n.a.	n.a.	n.a.	n.a.	n.a.	France	Ferec C pers comm 2006
#11	R1070Q+S466X / F508del	classic CF	female	obstr lung dis; cough	insufficient	93-96 mmol/L	b=1997, 3 mo. (diag), PA, electrolyte def	Serbia-Montenegro	Radivojevic 2004, pers comm 2007
#12	R1070Q+S466X / F508del	classic CF	female	obstr lung dis; cough	insufficient	91-103 mmol/L	b=1997, 10 mo. (diag), electrolyte def	Serbia-Montenegro	Radivojevic 2004, pers comm 2007
#13	R1070Q+S466X / F508del	classic CF	n.a.	n.a.	n.a.	100 mEq/l	steatorrhea, b=1995	Greece	Tzetis M pers comm 2007

## C) Patients bearing R1070W and F508del

patient ID #	genotype (allele 1 / allele 2)	diagnosis (as per reference)	sex of patient	lung function and disease	pancreatic status	sweat chloride levels	other traits and conditions	country of origin	references for patient data
#1	R1070W / F508del	CBAVD	male	n.a.	n.a.	36 mEq/l	tg10t9/tg10t7, 32y (2000)	France	Jezequel 1995, Jezequel 2000, Claustres 2000**
#2	R1070W / F508del	CBAVD	male	n.a.	n.a.	n.a.	tg10t9/tg10t7, 36y (2000)	France	Jezequel 1995, Jezequel 2000, Claustres 2000**
#3*	R1070W / F508del	CBAVD	male	n.a.	n.a.	n.a.	n.a.	France	Claustres 2000
#4*	R1070W / F508del	CF	male	n.a.	n.a.	n.a.	CBAVD	France	Claustres 2000
#5*	R1070W / F508del	CF	male	n.a.	n.a.	n.a.	CBAVD	France	Claustres 2000
#6	R1070W / F508del	nonclassic CF	n.a.	n.a.	n.a.	30.5 mmol/L	0.4y (diag), neonatal hypertrypsinemia	France	Feldmann 2000
#7	R1070W / F508del	nonclassic CF	female	slight bronchiectasis	no disease	45 mmol/L	subfertile (diag as adult), 40y (1996)	France	Gervais 1996**
#8	R1070W / F508del	CBAVD	male	no disease	no disease	n.a.	n.a.	France	Gervais 1996**
#9	R1070W / F508del	CBAVD	male	no disease	no disease	n.a.	n.a.	France	Gervais 1996**
#10	R1070W / F508del	CBAVD	male	no disease	sufficient (6y)	14-17 mmol/L	0.25y (diag)	USA	Groman 2002
#11	R1070W / F508del	CAVD	male	bronchiectasis	n.a.	30 mmol/L	Young's syndrome (CF-like)	France	LeLannou 1995**
#12	R1070W / F508del	CAVD	male	bronchiectasis	n.a.	n.a.	Young's syndrome (CF-like)	France	LeLannou 1995**
#13	R1070W / F508del	CBAVD	male	n.a.	pancreatitis	n.a.	b=1966	France	Bienvenu T pers comm 2006
#14	R1070W / F508del	nonclassic CF	female	FEV=87%, FVC=53%	sufficient	<60 mmol/L	18y (diag, bronchitis), A.fumigatus, 40y(2006)	France	Bienvenu T pers comm 2006
#15	R1070W / F508del	nonclassic CF	n.a.	n.a.	n.a.	40 mmol/L	birth (diag)	France	Ferec 1995**
#16	R1070W+1102-7t / F508del	nonclassic CF	female	FEV=70%, FVC=72%	insufficient	28 no units	b=1958, diag=2003, CFRD, pregnancy (1), nasal polyps	USA	CFF Registry 2005
#17	R1070W+1102-7t / F508del	nonclassic CF	female	FEV=78%, FVC=100%	sufficient	20 no units	b=1962, diag=2003, depression	USA	CFF Registry 2005
#18	R1070W / F508del	nonclassic CF	male	FEV=85%, FVC=104%	insufficient	36 no units	b=1959, diag=1963	USA	CFF Registry 2005
#19	R1070W / F508del	nonclassic CF	female	mild disease	insufficient	22 no units	b=2000, diag=2003	USA	CFF Registry 2005

## D) Patients bearing R1070W

patient ID #	genotype (allele 1 / allele 2)	diagnosis (as per reference)	sex of patient	lung function and disease	pancreatic status	sweat chloride levels	other traits and conditions	country of origin	references for patient data
#1	R1070W / 2869insG	CBAVD	male	rhinosinusitis	sufficient	110 mEq/l	7t/7t, 40y (1995), azoospermia	Spain	Casals 1995, Chillon 1995, Seibert 1996, Casals 2000**
#2	R1070W / 3272-26A+M470V	CBAVD	male	n.a.	n.a.	n.a.	tg10t7/tg11t7	Turkey	Dayagnac 2004
#3*	R1070W / n.a.	CBAVD	male	n.a.	n.a.	n.a.	tg11t7/tg10t7, 35y (2000)	France	Jezequel 2000
#4	R1070W / G542X	CUAVD	male	n.a.	n.a.	n.a.	tg10t9/tg11t7, allergy, 43y (2000)	France	Jezequel 2000
#5	R1070W / N1303K	nonclassic CF	female	recurrent infections	n.a.	intermed (2x)	4.5y (2005)	USA	McGinnis 2005
#6	R1070W / S1235R	CBAVD	male	n.a.	n.a.	60 mmol/L	33y (1998)	France	de la Taille 1998**
#7	R1070W / 5T-12TG	nonclassic CF	female	chronic bronchitis	n.a.	positive	growth deficit	Spain	Casals T pers comm 2006
#8	R1070W+R668C / K710X	classic	female	bronchiectasis	insufficient	positive	n.a.	Spain	Casals T pers comm 2006
#9	R1070W / D1152H	CBAVD	male	FEV=37%, FVC=46%, bronchiectasis	sufficient	<60 mmol/L	37y (diag), PA (40y), 49y (2006), osteoporosis	France	Bienvenu T pers comm 2006
#10*	R1070W / F191V	n.a.	n.a.	n.a.	n.a.	n.a.	n.a. (new entry; data pending)	USA	CFF Registry 2005

## E) Patients bearing R1070P

patient ID #	genotype (allele 1 / allele 2)	diagnosis (as per reference)	sex of patient	lung function and disease	pancreatic status	sweat chloride levels	other traits and conditions	country of origin	references for patient data
#1	R1070P / 2143delT	classic CF	male	mild obstructive disease	insufficient (>25y)	121 mmol/L	b=1969, 11y (diag), nasal polyps, FEV=71%, FVC=106%	USA (Polish)	Shrimpton 1997, Canadian Database 2007, CFF Registry 2005**
#2*	R1070P / F508del	CF	male	n.a.	n.a.	n.a.	n.a.	Northern Ireland	Doerk T, Canadian Database 2007**