

Supplementary table. *FGFR1* and *FGF8* mutations in Kallmann syndrome

Exon	Nucleotide change	Aminoacid change	Protein domain	References
<i>FGFR1</i>				
2	12G>A	W4X	Signal peptide	C. Dodé, unpublished
-	47C>G	A16G	-	C. Dodé, unpublished
3	142G>A	G48S	Ig1	Trarbach et al., 2006
-	208G>C	G70R	-	C. Dodé, unpublished
-	231C>G	N77K	-	Dodé et al., 2007
-	232C>G	R78C	-	Pitteloud et al., 2006b
-	246_247del [‡]	Frameshift	-	C. Dodé, unpublished
-	289G>A [‡]	G97S	-	C. Dodé, unpublished
-	290G>A	G97D	-	Dodé et al., 2003
-	296A>G	Y99C	-	Dodé et al., 2003; Raivio et al., 2009
-	302G>T [‡]	C101F	-	Dodé et al., 2007
-	303G>A	C101X	-	C. Dodé, unpublished
-	303C[3]	Frameshift	-	Dodé et al., 2003
-	304G>A	V102I	-	Albuisson et al., 2005; Pitteloud et al., 2006b
-	320C>A	S107X	-	Sato et al., 2004
-	320C>T	S107L	-	Sykoti et al., 2010
-	326dupG [‡]	Frameshift	-	C. Dodé, unpublished
-	327del	Frameshift	-	C. Dodé, unpublished
-	347T>G [‡]	V116G	-	C. Dodé, unpublished
-	350A>G	N117S	-	Raivio et al., 2009
4	386A>C	D129A	Acidic box	Albuisson et al., 2005
-	407C>A	S136X	-	C. Dodé, unpublished
-	412G>T	E138X	-	C. Dodé, unpublished
-	416A>G	K139R	-	C. Dodé, unpublished
-	418G>A	E140X	-	C. Dodé, unpublished
-	424_427del	Frameshift	-	C. Dodé, unpublished
5	482T>C	M161T	Ig2	C. Dodé, unpublished
-	499G>T*	A167S	-	Dodé et al., 2003; Thurman et al., 2012
6	535G>C [‡]	C178S	-	Zenaty et al., 2006
-	591C>A	F197L	-	Sykoti et al., 2010
-	625C>T	R209C	-	C. Dodé, unpublished
-	650T>C	M217T	-	C. Dodé, unpublished
-	672C>G	D224E	-	C. Dodé, unpublished
-	670G>C	D224H	-	Pitteloud et al., 2006b
-	682T>G	Y228D	-	Raivio et al., 2009
-	709G>A	G237S	-	Pitteloud et al., 2006a
-	710G>A	G237D	-	Pitteloud et al., 2006b
-	716T>C	I239T	-	Raivio et al., 2009; Chan et al., 2009
-	734T>C	L245P	-	Trarbach et al., 2006
7	748C>T	R250W	Ig2-Ig3 linker	Trarbach et al., 2006; Dodé et al., 2007
-	749G>A	R250Q	-	Falardeau et al., 2008
-	760C>T	R254W	-	Koika et al., 2013; C. Dodé, unpublished
-	761G>A	R254Q	-	Pitteloud et al., 2006b
-	809G>A	G270D	Ig3	Dodé et al., 2007
-	817G>A [‡]	V273M	-	Albuisson et al., 2005; Pitteloud et al., 2006b
-	821A>G	E274G	-	Pitteloud et al., 2006b
-	830G>A	C277Y	-	Dodé et al., 2003
-	841_846del	S281-D282del	-	Bailleul-Forestier et al., 2010
-	848C>G	P283R	-	Dodé et al., 2007
-	854C>G	P285R	-	Sykoti et al., 2010
-	858_866del	Frameshift	-	C. Dodé, unpublished

-	891del	Frameshift	-	C. Dodé, unpublished
-	936G>A	K312K (splice site)	-	Dodé et al., 2003
8A	1070C>T	T357I	-	Miura et al., 2010
8B	961_962del	Frameshift	-	C. Dodé, unpublished
-	961_964del [‡]	Frameshift	-	C. Dodé, unpublished
-	967G>T	E324X	-	Dodé et al., 2007
-	995C>G	S332C	-	Dodé et al., 2007
-	1004A>T	D335V	-	C. Dodé, unpublished
-	1016A>G	Y339C	-	Pitteloud et al., 2006b
-	1018A>G	T340A	-	C. Dodé, unpublished
-	1019C>T	T340M	-	C. Dodé, unpublished
-	1023C>G	C341W	-	Bailleul-Forestier et al., 2010
-	1025T>C	L342S	-	Pitteloud et al., 2007
-	1028C>T	A343V	-	Trarbach et al., 2006
-	1037C>G	S346C	-	Pitteloud et al., 2006b
-	1038dupT	Frameshift	-	Sykiotis et al., 2010
-	1038T[3]	Frameshift	-	C. Dodé, unpublished
-	1042G>A	G348R	-	Bailleul-Forestier et al., 2010; C. Dodé, unpublished
9	1081G>C	A361P	Juxtamembrane	Dodé et al., 2007
-	1088_1089insAG	Frameshift	-	C. Dodé, unpublished
-	1093_1094del	Frameshift	-	Albuisson et al., 2005
-	1097C>T	P366L	-	Trarbach et al., 2006
-	1151C>A [‡]	A384D	Transmembrane	C. Dodé, unpublished
-	1279G>T	V427L	Juxtamembrane	Sykiotis et al., 2010
10	1286T>A	V429E	-	Sykiotis et al., 2010
-	1317_1318del [‡]	Frameshift	-	Sato et al., 2006; Dodé et al., 2007
-	1368G>T	M456I	-	C. Dodé, unpublished
-	1377_1378insA	Frameshift	-	Novo et al., 2012
-	1383T[3]	Frameshift	-	C. Dodé, unpublished
-	1409G>T	R470L	-	Pitteloud et al., 2007
-	1424G>A	R475Q	-	C. Dodé, unpublished
Intron 11	IVS11-2A>G			Sykiotis et al., 2010
12	1561G>A	A520T	Tyrosine kinase	Albuisson et al., 2005
-	1612A>G	I538V	-	Pitteloud et al., 2006b
Intron 12	IVS12-2A>G			C. Dodé, unpublished
13	1755C>A	Y585X	-	Pitteloud et al., 2006b
-	1810G>A	A604T	-	Sarfati et al., 2010
-	1819G>A	V607M	-	Dodé et al., 2003
-	1825C>T	R609X	-	Riley et al., 2007
-	1837dupT	Frameshift	-	Albuisson et al., 2005
-	1852_1853del	Frameshift	-	Trarbach et al., 2006
-	1854G>T	K618N	-	Raivio et al., 2009
14	1862A>G [‡]	H621R	-	Dodé et al., 2007
-	1864C>T	R622X	-	Dodé et al., 2003; Pitteloud et al., 2005; Xu et al., 2007
-	1864C>G [‡]	R622G	-	Zenaty et al., 2006
-	1865G>A	R622Q	-	Zenaty et al., 2006
-	1907_1908del	Frameshift	-	C. Dodé, unpublished
-	1970_1971del	Frameshift	-	Dodé et al., 2003
Intron 14	IVS14+1G>A			Dallago et al., 2007; Dodé et al., 2007
15	1981C>T	R661X	-	Dodé et al., 2007
-	1987C>T	P663S	-	C. Dodé, unpublished
-	1996T>A	W666R	-	Dodé et al., 2003
-	2011G>C	A671P	-	Raivio et al., 2009
-	2038C>T	Q680X	-	Pitteloud et al., 2006a
Intron 15	IVS15+1G>A			Dodé et al., 2003
16	2054C>T	S685F	-	Dodé et al., 2007
-	2059G>A	G687R	-	Sato et al., 2005;

				Sykiotis et al., 2010; C. Dodé, unpublished
-	2069T>G	L690P	-	Bailleul-Forestier et al., 2010
-	2074G>A	E692K	-	C. Dodé, unpublished
-	2077A>T	I693F	-	Dodé et al., 2007
-	2099C>T	P700L	-	Sykiotis et al., 2010
-	2107G>C	G703R	-	Pitteloud et al., 2006b
-	2107G>A	G703S	-	Pitteloud et al., 2006b
-	2156T>G	M719R	-	Dodé et al., 2003
-	2164C>T	P722S	-	Trarbach et al., 2006
-	2165C>A+2172C>G	P722H+N724K	-	Pitteloud et al., 2006a
17	2190C>G	Y730X	-	Albuisson et al., 2005
-	2203del [‡]	Frameshift	-	C. Dodé, unpublished
-	2233C>T	P745S	-	Sato et al., 2004; Sykiotis et al., 2010
17&18	2292G>T+2302G>T	Q764H+D768Y	-	Falardeau et al., 2008
18	2302G>C	D768H	C-terminal region	Sykiotis et al., 2010
-	2314C>T	P772S	-	Dodé et al., 2003, 2007
-	2383G>A	V795I	-	Trarbach et al., 2006
-	2399C>T	P800L	-	C. Dodé, unpublished
-	2464C>T	R822C	C-terminal residue	Dodé et al., 2007
Balanced translocation: breakpoint between exons 2 and 3				Kim et al., 2005
Whole gene deletion + contiguous gene syndrome				Dodé et al., 2003
<i>FGF8</i>				
1B	40C>A	H14N	Signal peptide	Falardeau et al., 2008
-	68A>T	Q23L	-	Sykiotis et al., 2010
1C	77C>T	P26L	Alternatively spliced N-terminal region	Falardeau et al., 2008
-	76_93dup	P26_A31dup	-	C. Dodé, unpublished
-	86_103del	G29_R34del	-	C. Dodé, unpublished
-	118T>C*	F40L	-	Falardeau et al., 2008
1D	229C>T	R77C	-	C. Dodé, unpublished
-	298A>G	K100E	FGF constant region	Falardeau et al., 2008
2	379C>G	R127G	-	Falardeau et al., 2008
-	379C>T	R127X	-	Trarbach et al., 2010
-	385C>T	R129X	-	Trarbach et al., 2010
-	506C>T	A169V	-	C. Dodé, unpublished
3	686C>T	T229M	-	Falardeau et al., 2008

About 70% of the mutations of *FGFR1* and *FGF8* are missense mutations. All the known mutations of these genes have been detected in the heterozygous state, with the exception of the amino-acid substitutions A167S in *FGFR1* and F40L in *FGF8* (Dodé et al., 2003; Falardeau et al., 2008). The R250Q, N117S, R470L, A604T, K618N, P745S, and Q764H+D768Y mutations of *FGFR1* have been found together with a K100E monoallelic mutation of *FGF8*, Q106R/L83V or Q106R/R262Q biallelic mutations of *GNRHR*, a R85L monoallelic mutation of *PROKR2*, a R262Q monoallelic mutation of *GNRHR*, a Q23L monoallelic mutation of *FGF8*, and a F40L biallelic mutation of *FGF8*, respectively (Falardeau et al., 2008; Pitteloud et al., 2007; Raivio et al., 2009; Sarfati et al., 2010; Sykiotis et al., 2010). In addition, the I239T mutation of *FGFR1* has been found together with a R31C monoallelic mutation of *GNRH1*, with or without a S202G monoallelic mutation of *PROKR2* (Chan et al., 2009).

* Biallelic mutation.

‡ *De novo* mutation.

Abbreviations: Ig1 to Ig3, immunoglobulin-like domains (1) to (3).

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