**Supplementary table. *KAL1* mutations in Kallmann syndrome**

| Exon | Nucleotide change | Aminoacid change | Protein domain | References |
|---|---|---|---|---|
| 1 | 3G>A | M1? | | Albuisson et al., 2005; Montenegro et al., 2013 |
| - | 67-92del | Frameshift | Cysteine-rich region | C. Dodé, unpublished |
| - | 90_100dup11 | Frameshift | - | Montenegro et al., 2013 |
| - | 92_102dup11 | Frameshift | - | Gu et al., 1998 |
| - | 95_105dup11 | Frameshift | - | Söderlund et al., 2002 |
| - | 100_101del | Frameshift | - | Sato et al., 2004 |
| - | 113C>A | S38X | - | Sykiotis et al., 2010 |
| - | 132delC | Frameshift | - | C. Dodé, unpublished |
| - | 161T>G | L54R | - | Sykiotis et al., 2010 |
| - | 169C>T | Q57X | - | C. Dodé, unpublished |
| - | 196C>T | Q66X | - | Izumi et al., 2001 |
| Intron 1 | IVS1+1G>T | | | Albuisson et al., 2005 |
| - | IVS1+1G>C | | | C. Dodé, unpublished |
| 2 | 224_225insC | Frameshift | - | Ribeiro et al., 2007 |
| | 224del | Frameshift | | C. Dodé, unpublished |
| 3 | 262_269del | Frameshift | - | Sato et al., 2004 |
| - | 268T>G | C90G | - | C. Dodé, unpublished |
| - | 279_280del | Frameshift | - | Ma et al., 2011 |
| 4 | 322del | Frameshift | - | Sykiotis et al., 2010 |
| - | 400T>G | C134G | WAP | Jap et al., 2011 |
| | 428T>C | F143S | - | C. Dodé, unpublished |
| - | 487T>C | C163R | - | Jap et al., 2011 |
| - | 488G>A | C163Y | - | Sato et al., 2004 |
| - | 490T>C | C164R | - | C. Dodé, unpublished |
| - | 490_492del | C164del | - | Bhagavath et al., 2007 |
| - | 514T>C | C172R | - | Oliveira et al., 2001 |
| Intron 4 | IVS4+1G>T | | | Sato et al., 2004 |
| 5 | 570dupA | Frameshift | FnIII(1) | Albuisson et al., 2005 |
| - | 571C>T | R191X | - | Oliveira et al., 2001; Sato et al., 2004; Albuisson et al., 2005; Trarbach et al., 2005 |
| - | 610_611del | Frameshift | - | Reardon, 2007 |
| - | 649T>G | Y217D | - | C. Dodé, unpublished |
| - | 697del | Frameshift | - | C. Dodé, unpublished |
| - | 711G>A | W237X | - | Hardelin et al., 1993a |
| - | 714_715del | Frameshift | - | Sato et al., 2004 |
| Intron 5 | IVS5-1G>T | | | O'Neill et al., 1998 |
| 6 | 769C>T | R257X | - | Hardelin et al., 1993a; Bhagavath et al., 2007; Montenegro et al., 2013 |
| - | 773G>A | W258X | - | Hardelin et al., 1993a |
| - | 773del | Frameshift | - | C. Dodé, unpublished |
| - | 784C>T | R262X | - | Söderlund et al., 2002; Albuisson et al., 2005 |
| - | 785G>C | R262P | - | Albuisson et al., 2005 |
| - | 788T>G | V263G | - | Loidi et al., 2005 |
| - | 801T>A | N267K | - | Hardelin et al., 1993a |
| - | 831del | Frameshift | - | Hardelin et al., 1993a |
| Intron 6 | IVS6-1G>A | | | Izumi et al., 2001 |
| 7 | 911A>G | N304S | FnIII(2) | Versiani et al., 2007 |
| - | 958G>T | E320X | - | Albuisson et al., 2005 |
| - | 984C>G | Y328X | - | Georgopoulos et al., 1997 |
| - | 1015A[3] | Frameshift | - | Hardelin et al., 1993a |
| - | 1016_1017insGTCA | Frameshift | - | C. Dodé, unpublished |
| Intron 7 | IVS7+1G>T | | | Trarbach et al., 2006 |
| 8 | 1187C>T | S396L | FnIII(2)-(3) linker | Dodé et al., 2006 |
| - | 1201_1207, IVS8+1+2del | Frameshift | - | Georgopoulos et al., 1997 |
| 9 | 1257_1270del | Frameshift | FnIII(3) | Izumi et al., 2001 |

| | | | | |
|---|---|---|---|---|
| - | 1261C>T | Q421X | - | Hardelin et al., 1993a |
| - | 1267C>T | R423X | - | Hardelin et al., 1993a; Albuisson et al., 2005; Sarfati et al., 2010 |
| - | 1270C>T | R424X | - | Sato et al., 2004; Salenave et al., 2008; Jap et al., 2011; Ma et al., 2011 |
| 10 | 1369C>T | R457X | - | Oliveira et al., 2001; Albuisson et al., 2005 |
| - | 1385G>A | W462X | - | Montenegro et al., 2013 |
| - | 1392_1405del | Frameshift | - | Georgopoulos et al., 1997 |
| | 1424C>T | S475X | | Sykiotis et al., 2010 |
| - | 1433C>A | S478X | - | Versiani et al., 2007 |
| 11 | 1505_1518del | Frameshift | - | Versiani et al., 2007 |
| - | 1540G>A | E514K | - | Maya-Nunez et al., 1998; Georgopoulos et al., 2007 |
| - | 1540G>T | E514X | - | C. Dodé, unpublished |
| - | 1551C>G | F517L | - | Georgopoulos et al., 1997 |
| - | 1600_1601del | Frameshift | - | C. Dodé, unpublished |
| 12 | 1651_1654delinsAGCT | P551E552delinsSX | FnIII(4) | Albuisson et al., 2005 |
| - | 1698del | Frameshift | - | Quinton et al., 1996 |
| - | 1711T>A | W571R | - | Albuisson et al., 2005 |
| - | 1735_1738del | Frameshift | - | C. Dodé, unpublished |
| - | 1801del | Frameshift | - | Oliveira et al., 2001 |
| - | 1806del | Frameshift | - | Trarbach et al., 2005 |
| - | 1822C>T | Q608X | - | C. Dodé, unpublished |
| Intron 12 | IVS12-1G>A | | | Hardelin et al., 1993a |
| 13 | 1851T>G | Y617X | - | Salenave et al., 2008 |
| - | 1887_1888del | Frameshift | - | Sykiotis et al., 2010; Ma et al., 2011 |
| - | 1891C>T | R631X | - | Jansen et al., 2000; Sato et al., 2004 |
| - | 1903C>T | Q635X | - | C. Dodé, unpublished |
| - | 1978G>A | A660T | - | Georgopoulos et al., 2007 |
| 14 | 1997A>T + 2003G>A | K666M;R668H | C-terminal region | Bhagavath et al., 2007 |
| Deletion of exon 1 | | | Cysteine-rich | Quinton et al., 1996 |
| Deletion of exon 5 | | | FnIII(1) | Söderlund et al., 2002 |
| Deletion of exon 11 | | | FnIII(3) | Quinton et al., 1996 |
| Deletion of exon 1-2 | | | Cysteine-rich | Montenegro et al., 2013 |
| Deletion of exons 3-5 | | | Cysteine-rich to FnIII(1) | Maya-Nunez et al., 1998 |
| Deletion of exons 3-6 | | | - | Trarbach et al., 2006 |
| Deletion of exons 3-13 | | | Cysteine-rich to FnIII(4) | Massin et al., 2003 |
| Deletion of exons 3-14 | | | Cysteine-rich to C-terminal | Montenegro et al., 2013 |
| Deletion of exons 5-10 | | | FnIII(1-3) | Nagata et al., 2000; Trarbach et al., 2005 |
| Deletion of exons 5-14 | | | FnIII(1) to C-terminal | Montenegro et al., 2013 |
| Deletion of exons 13-14 | | | FnIII(4) to C-terminal | Bick et al., 1992; Bhagavath et al., 2007 |
| Whole gene deletion ± contiguous gene syndrome | | | | Ballabio & and Andria, 1992; Hardelin et al., 1993b; Oliveira et al., 2001; Pedersen-White et al., 2008; Salenave et al., 2008 |

- Most mutations of *KAL1* are nonsense mutations, frameshift mutations or intragenic deletions, all presumably leading to complete gene inactivation. The 80 different *KAL1* point mutations identified to date include only 19 missense mutations. The S396L and R423X mutations of *KAL1* have been found together with L173R monoallelic mutations of *PROKR2* (Dodé et al., 2006; Sarfati et al., 2010).

Abbreviations: WAP, whey acidic protein-like domain; FnIII(1) to FnIII(4), fibronectin-like type III repeats (1) to (4).

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