**SPINK1**  c.101A>G  p.N34S

Variant is in linkage with variants c.56-37T>C, c.87+268A>G, c.195-606G>A, and c.195-66_65insTTTT

Citations:


1 family with unspecified number of affected and 3 unaffected; counted as 1 affected

Variant was described at the protein level as N11S


18 affected (6 homozygous)


29 affected (7 homozygous), 3 unaffected


17 affected (5 homozygous), 3 unaffected


9 affected (1 homozygous)


6 affected (1 homozygous)


3 affected


1 affected (homozygous)

I family with 2 affected (1 homozygous) and 3 unaffected (1 homozygous); all heterozygous also carry p.R67C

Table 1 contradicts pedigree and lists 1 family member (#16) as idiopathic


5 affected; all included in Schneider et al. (2002); not counted


16 affected, 5 unaffected


31 affected (8 homozygous), 3 unaffected


13 affected (2 homozygous), 2 unaffected


21 affected (1 homozygous), 1 unaffected; 5 affected overlaps with Rossi et al. (2001); all counted


6 affected (1 homozygous), 4 unaffected


21 affected (2 homozygous)


3 affected

146 affected (20 homozygous), 40 unaffected (2 homozygous)

Figure 1 shows the 2 unaffected homozygous family members


4 affected (1 homozygous)


37 affected (11 homozygous), 7 unaffected (1 homozygous)


10 unaffected; including 2 with pancreatic cancer


59 affected (11 homozygous); 18 affected (6 homozygous) likely overlap with Witt et al. (2000); 41 affected (5 homozygous) counted


1 family with 1 affected and 3 unaffected; 1 affected and 1 unaffected also carried CASR c.518T>C (p.L173P)


23 unaffected (3 homozygous); including 11 with diabetes (3 homozygous)


3 affected (1 homozygous), 1 heterozygous also carried CFTR p.L997F

1 affected

6 affected, 3 unaffected; likely overlap with Pfützer et al. (2000); 2 affected counted

5 affected, 7 unaffected (4 with pancreatic cancer and 3 with cholecystitis)

5 affected, 2 unaffected; all carried PRSS1 p.R122H

7 affected (2 homozygous): 1 homozygous and 1 heterozygous who also carried p.R67C were reported in 2001; 5 affected counted (1 homozygous)

9 affected, likely overlap with Kuwata et al. (2001, 2003); homozygotes not specified; not counted

2 affected (also HIV positive), 2 unaffected

5 unaffected including 2 with chronic parotitis

75 affected (15 homozygous), 8 unaffected, possible overlap with Chandak et al. (2002); 44 affected (7 homozygous) and 5 unaffected counted

1 family with 2 affected (homozygous, 1 also with pancreatic cancer) and 5 unaffected
I family with 1 affected (pregnant) and 1 unaffected, plus 1 affected sister with heterozygous c.*32C>T but no p.N34S

5 affected; 1 also carried p.P55S, 3 unaffected, likely overlap with previous papers from same group; not counted

1 affected

1 affected

8 affected

14 affected (1 homozygous), 19 unaffected including 7 with pancreatic cancer

29 affected (1 homozygous), 12 unaffected, controls overlap with Lempinen et al. (2005); only affected counted

37 unaffected, includes 22 with diabetes

9 affected (1 homozygous), 1 unaffected
7 affected (1 homozygous), 1 unaffected; likely overlap Lempinen et al. (2005) and/or Tukiainen et al. (2005); not counted

Keiles S, Kammesheidt A. (2006) **Identification of CFTR, PRSS1, and SPINK1 mutations in 381 patients with pancreatitis.** Pancreas 33, 221-227
22 affected

11 affected (1 homozygous), 1 unaffected; possible overlap with Kume et al. (2005); 2 affected heterozygous counted

4 affected, 2 unaffected
Text and Table 4 contradict; text value was counted

134 affected; likely overlap with Chandak et al. (2002, 2004); homozygotes not specified; 59 affected counted as heterozygous

52 affected, 3 unaffected, likely overlap with Chandak et al. (2002, 2004) and Mahurkar et al. (2006); homozygotes not specified; not counted

66 affected (7 homozygous), 38 unaffected

14 affected (2 homozygous)

10 affected
2 affected (homozygous)

11 affected (1 homozygous), 1 unaffected; likely overlap with Shimosegawa et al. (2006); not counted

PaCa44 and PancTu-1 cell lines are heterozygous; not counted

1 family with 1 affected who also carried p.G48E and 1 unaffected

2 affected

2 unaffected

Aoun E, Slivka A, Papachristou DJ, Gleeson FC, Whitcomb DC, Papachristou GI. (2007) **Rapid evolution from the first episode of acute pancreatitis to chronic pancreatitis in human subjects.** JOP 8, 573-578
2 affected (1 homozygous)

48 affected, likely overlap with Chandak et al. (2002, 2004), Mahurkar et al. (2006) and Bhaskar et al. (2006); homozygotes not specified; not counted

Shimosegawa T, Kume K, Masamune A. (2008) **SPINK1, ADH2, and ALDH2 gene variants and alcoholic chronic pancreatitis in Japan.** J Gastroenterol Hepatol 23 Suppl 1, S82-S86
12 affected (2 homozygous), 2 unaffected; likely overlap with Shimosegawa et al. (2006); 1 affected (homozygous) counted
11 affected, mutation not specified; counted as heterozygous p.N34S

148 affected; likely overlap with Chandak et al. (2002, 2004), Mahurkar et al. (2006, 2007) and Bhaskar et al. (2006), homozygotes not specified; 14 affected counted as heterozygous

4 affected

3 unaffected; with hyperenzymemia

24 affected (1 homozygous), 18 unaffected

57 affected, 21 unaffected, possible overlap with Pfützer et al. (2000), homozygotes not specified; 28 affected and 18 unaffected counted as heterozygous

5 affected

6 affected, 6 unaffected

67 affected (13 homozygous), 10 unaffected

Oddly, homozygotes found only; no heterozygous carriers


Oddly, homozygotes found only; no heterozygous carriers


19 affected (6 also with pancreatic cancer), 5 unaffected (3 with pancreatic cancer)

Paper also describes family previously reported by Masamune et al. (2004)

Aoun E, Muddana V, Papachristou GI, Whitcomb DC. (2010) **SPINK1 N34S is strongly associated with recurrent acute pancreatitis but is not a risk factor for the first or sentinel acute pancreatitis event.** Am J Gastroenterol 105, 446-451

9 affected (3 homozygous), 19 unaffected, possible overlap with Pfützer et al. (2000) and Muddana et al. (2008); not counted


1 affected (with PanINs), also carried **CFTR 2789+5G>A and IVS-5T**

Maruyama K, Harada S, Yokoyama A, Mizukami S, Naruse S, Hirota M, Nishimori I, Otsuki M. (2010) **Association analyses of genetic polymorphisms of GSTM1, GSTT1, NQO1, NAT2, LPL, PRSS1, PSTI, and CFTR with chronic alcoholic pancreatitis in Japan.** Alcohol Clin Exp Res 34 Suppl 1, S34-S38

Unclear what, if anything, was found


2 affected


4 affected (1 homozygous)


48 affected (8 homozygous), 4 unaffected; possible overlap with Garg et al. (2009); 26 affected (4 homozygous) and 3 unaffected counted


3 affected

Unclear if overlaps with the two other Joergensen papers (2010); all counted
16 affected
Unclear if overlaps with the two other Joergensen papers (2010); all counted

9 affected (2 homozygous)
Unclear if overlaps with the two other Joergensen papers (2010); all counted

9 affected
Mutation not specified; counted as heterozygous p.N34S

29 affected (4 homozygous), 2 unaffected; possible overlap with Pfützer et al. (2000); Muddana et al. (2008); not counted

3 affected

1 affected

4 affected; with hyperparathyroidism, same subjects as in Felderbauer et al. (2008); not counted

97 affected (13 homozygous), 7 unaffected, likely overlap with Witt et al. (2000, 2001) and Truninger et al. (2002); 73 heterozygous (7 homozygous) affected counted
13 affected

8 affected, 2 unaffected

10 affected (5 homozygous), 3 unaffected (1 homozygous); study highly problematic; not counted

6 affected
Mutation not specified; counted as heterozygous p.N34S

12 affected (1 homozygous); likely overlap with prior papers from the Shimosegawa group; not counted

4 affected

2 affected, 2 unaffected

25 affected, mutations not specified, not counted

15 affected, 2 unaffected
3 affected

2 affected

1 family with 1 affected and 1 unaffected

107 affected (17 homozygous), 26 unaffected. Possible overlap with Witt et al. (2000); Keim et al. (2003) and Steiner et al. (2011); 10 affected (4 homozygous) counted; 19 unaffected counted

1 family with 1 affected and 1 unaffected

3 affected

1 affected

1 affected

8 affected

20 affected, likely overlap with previous Chandak papers, homozygotes not specified; not counted

14 affected (1 homozygous), 1 also carried CFTR p.F508del, 1 also carried CFTR p.L997F

38 affected (14 homozygous; 1 also carried homozygous p.R65Q); likely overlap with Chen et al. (2000, 2001); 16 affected (9 homozygous) counted

139 affected (18 homozygous); likely overlap with Rosendahl et al. (2013); 32 affected (1 homozygous) counted

1 affected

Masamune, 27 affected (3 homozygous), 2 unaffected; likely overlap with prior papers from the Shimosegawa group; 18 affected (1 homozygous) counted

3 affected, 1 unaffected

1 affected; also carried PRSSI p.R122C, 3 unaffected, 1 also carried PRSSI p.R122C

22 affected (1 homozygous), 4 unaffected
11 affected (2 homozygous), 1 unaffected

67 affected (5 homozygous), 3 unaffected

Tremblay K, Dubois-Bouchard C, Brisson D, Gaudet D. (2014) Association of *CTRC* and *SPINK1* gene variants with recurrent hospitalizations for pancreatitis or acute abdominal pain in lipoprotein lipase deficiency. Front Genet 5, 90
3 subjects; unclear if found in affected or unaffected subjects; counted as affected
Variant is indicated as G>A in Table 2

2 affected (1 homozygous), 5 unaffected (2 homozygous)

3 affected, 1 unaffected

3 affected

3 affected (1 homozygous); likely overlap with prior Whitcomb papers; not counted

12 affected, 1 unaffected
Unaffected control was calculated from percentage given in Discussion

6 affected, 1 unaffected
26 affected (5 homozygous), 1 unaffected

1 affected; heterozygosity not specified

1 affected (homozygous)

3 affected, 1 unaffected

Moran RA, Quesada-Vazquez N, Sinha A, de-Madaria E, Singh VK. (2016) High penetrance of the PRSS1 A16V mutation in a kindred with SPINK1 N34S and CFTR TG11-5T co-mutations. Pancreas 45, e2-4
3 affected (2 homozygous), 1 unaffected; 1 affected heterozygous and 1 homozygous and the 1 unaffected also carried PRSS1 p.A16V

168 affected (33 homozygous); likely overlap with prior Chandak papers; 38 affected (18 homozygous) counted

2 affected

5 affected, 1 unaffected

10 affected

3 affected


19 affected (1 homozygous)


1 affected; also had pancreatic cancer


16 affected; also had pancreatic cancer

Functional studies:


Boulling A, Chen JM, Callebaut I, Férec C. (2012) *Is the SPINK1 p.Asn34Ser missense mutation per se the true culprit within its associated haplotype?* WebmedCentral GENETICS 2012; 3, WMC003084

Marchbank T, Mahmood A, Playford RJ. (2013) *Pancreatic secretory trypsin inhibitor causes autocrine-mediated migration and invasion in bladder cancer and phosphorylates the EGF receptor, Akt2 and Akt3, and ERK1 and ERK2.* Am J Physiol Renal Physiol 305, F382-389