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:

Chen JM, Mercier B, Audrezet MP, Ferec C. (2000) **Mutational analysis of the human pancreatic secretory trypsin inhibitor (*PSTI*) gene in hereditary and sporadic chronic pancreatitis.** J Med Genet 37, 67-69
1 family with unspecified number of affected and 3 unaffected; counted as 1 affected
Variant was described at the protein level as N11S

Witt H, Luck W, Hennies HC, Classen M, Kage A, Lass U, Landt O, Becker M. (2000) **Mutations in the gene encoding the serine protease inhibitor, Kazal type 1 are associated with chronic pancreatitis.** Nat Genet 25, 213-216
18 affected (6 homozygous)

Pfützer RH, Barmada MM, Brunskill AP, Finch R, Hart PS, Neoptolemos J, Furey WF, Whitcomb DC. (2000) **SPINK1/PSTI polymorphisms act as disease modifiers in familial and idiopathic chronic pancreatitis.** Gastroenterology 119, 615-623
29 affected (7 homozygous), 3 unaffected

Chen JM, Mercier B, Audrezet MP, Raguenes O, Quere I, Ferec C. (2001) **Mutations of the pancreatic secretory trypsin inhibitor (PSTI) gene in idiopathic chronic pancreatitis.** Gastroenterology 120, 1061-1064
17 affected (5 homozygous), 3 unaffected

Noone PG, Zhou Z, Silverman LM, Jowell PS, Knowles MR, Cohn JA. (2001) **Cystic fibrosis gene mutations and pancreatitis risk: relation to epithelial ion transport and trypsin inhibitor gene mutations.** Gastroenterology 121, 1310-1319
9 affected (1 homozygous)

Plendl H, Siebert R, Steinemann D, Grote W. (2001) **High frequency of the N34S mutation in the SPINK1 gene in chronic pancreatitis detected by a new PCR-RFLP assay.** Am J Med Genet 100, 252-253
6 affected (1 homozygous)

Kaneko K, Nagasaki Y, Furukawa T, Mizutamari H, Sato A, Masamune A, Shimosegawa T, Horii A. (2001) **Analysis of the human pancreatic secretory trypsin inhibitor (*PSTI*) gene mutations in Japanese patients with chronic pancreatitis.** J Hum Genet 46, 293-297
3 affected

Ockenga J, Dörk T, Stuhrmann M. (2001) **Low prevalence of *SPINK1* gene mutations in adult patients with chronic idiopathic pancreatitis.** J Med Genet 38, 243-244
1 affected (homozygous)

Kuwata K, Hirota M, Sugita H, Kai M, Hayashi N, Nakamura M, Matsuura T, Adachi N, Nishimori I, Ogawa M. (2001) **Genetic mutations in exons 3 and 4 of the pancreatic secretory trypsin inhibitor in patients with pancreatitis.** J Gastroenterol 36, 612-618
1 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

Rossi L, Pfützer RH, Parvin S, Ali L, Sattar S, Kahn AK, Gyr N, Whitcomb DC. (2001) **SPINK1/PSTI mutations are associated with tropical pancreatitis in Bangladesh. A preliminary report.** Pancreatology 1, 242-245
5 affected; all included in Schneider et al. (2002); not counted

Witt H, Luck W, Becker M, Böhmig M, Kage A, Truninger K, Ammann RW, O'Reilly D, Kingsnorth A, Schulz HU, Halangk W, Kielstein V, Knoefel WT, Teich N, Keim V. (2001) **Mutation in the SPINK1 trypsin inhibitor gene, alcohol use, and chronic pancreatitis.** JAMA 285, 2716-2717
16 affected, 5 unaffected

Chandak GR, Idris MM, Reddy DN, Bhaskar S, Sriram PV, Singh L. (2002) **Mutations in the pancreatic secretory trypsin inhibitor gene (*PSTI/SPINK1*) rather than the cationic trypsinogen gene (*PRSS1*) are significantly associated with tropical calcific pancreatitis.** J Med Genet 39, 347-351
31 affected (8 homozygous), 3 unaffected

Drenth JP, te Morsche R, Jansen JB. (2002) **Mutations in serine protease inhibitor Kazal type 1 are strongly associated with chronic pancreatitis.** Gut 50, 687-692
13 affected (2 homozygous), 2 unaffected

Schneider A, Suman A, Rossi L, Barmada MM, Beglinger C, Parvin S, Sattar S, Ali L, Khan AK, Gyr N, Whitcomb DC. (2002) ***SPINK1/PSTI* mutations are associated with tropical pancreatitis and type II diabetes mellitus in Bangladesh.** Gastroenterology 123, 1026-1030
21 affected (1 homozygous), 1 unaffected; 5 affected overlaps with Rossi et al. (2001); all counted

Truninger K, Witt H, Köck J, Kage A, Seifert B, Ammann RW, Blum HE, Becker M. (2002) **Mutations of the serine protease inhibitor, Kazal type 1 gene, in patients with idiopathic chronic pancreatitis.** Am J Gastroenterol 97, 1133-1137
6 affected (1 homozygous), 4 unaffected

Threadgold J, Greenhalf W, Ellis I, Howes N, Lerch MM, Simon P, Jansen J, Charnley R, Laugier R, Frulloni L, Oláh A, Delhaye M, Ihse I, Schaffalitzky de Muckadell OB, Andrén-Sandberg A, Imrie CW, Martinek J, Gress TM, Mountford R, Whitcomb D, Neoptolemos JP. (2002) T**he N34S mutation of SPINK1 (PSTI) is associated with a familial pattern of idiopathic chronic pancreatitis but does not cause the disease.** Gut 50, 675-681
21 affected (2 homozygous)

Gaia E, Salacone P, Gallo M, Promis GG, Brusco A, Bancone C, Carlo A. (2002) **Germline mutations in *CFTR* and *PSTI* genes in chronic pancreatitis patients.** Dig Dis Sci 47, 2416-2421
3 affected

Hassan Z, Mohan V, Ali L, Allotey R, Barakat K, Faruque MO, Deepa R, McDermott MF, Jackson AE, Cassell P, Curtis D, Gelding SV, Vijayaravaghan S, Gyr N, Whitcomb DC, Khan AK, Hitman GA. (2002) ***SPINK1* is a susceptibility gene for fibrocalculous pancreatic diabetes in subjects from the Indian subcontinent.** Am J Hum Genet 71, 964-968
146 affected (20 homozygous), 40 unaffected (2 homozygous)
Figure 1 shows the 2 unaffected homozygous family members

Audrézet MP, Chen JM, Le Maréchal C, Ruszniewski P, Robaszkiewicz M, Raguénès O, Quéré I, Scotet V, Férec C. (2002) **Determination of the relative contribution of three genes-the cystic fibrosis transmembrane conductance regulator gene, the cationic trypsinogen gene, and the pancreatic secretory trypsin inhibitor gene-to the etiology of idiopathic chronic pancreatitis.** Eur J Hum Genet 10, 100-106
4 affected (1 homozygous)

Bhatia E, Choudhuri G, Sikora SS, Landt O, Kage A, Becker M, Witt H. (2002) **Tropical calcific pancreatitis: strong association with *SPINK1* trypsin inhibitor mutations.** Gastroenterology 123, 1020-1025
37 affected (11 homozygous), 7 unaffected (1 homozygous)

Teich N, Schulz HU, Witt H, Böhmig M, Keim V. (2003) **N34S, a pancreatitis associated SPINK1 mutation, is not associated with sporadic pancreatic cancer.** Pancreatology 3, 67-68
10 unaffected; including 2 with pancreatic cancer

Keim V, Witt H, Bauer N, Bodeker H, Rosendahl J, Teich N, Mossner J. (2003) T**he course of genetically determined chronic pancreatitis**. JOP 4, 146-154
59 affected (11 homozygous); 18 affected (6 homozygous) likely overlap with Witt et al. (2000); 41 affected (5 homozygous) counted

Felderbauer P, Hoffmann P, Einwächter H, Bulut K, Ansorge N, Schmitz F, Schmidt WE. (2003) **A novel mutation of the calcium sensing receptor gene is associated with chronic pancreatitis in a family with heterozygous SPINK1 mutations.** BMC Gastroenterol 3, 34
1 family with 1 affected and 3 unaffected; 1 affected and 1 unaffected also carried *CASR* c.518T>C (p.L173P)

Bhatia E, Balasubramanium K, Rajeswari J, Kordonouri O, Witt H, Landt O, Simon P, Lerch MM (2003) **Absence of association between *SPINK1* trypsin inhibitor mutations and Type 1 or 2 diabetes mellitus in India and Germany.** Diabetologia 46, 1710-1711
23 unaffected (3 homozygous); including 11 with diabetes (3 homozygous)

Gomez-Lira M, Bonamini D, Castellani C, Unis L, Cavallini G, Assael BM, Pignatti PF. (2003) **Mutations in the *SPINK1* gene in idiopathic pancreatitis Italian patients.** Eur J Hum Genet 11, 543-546
3 affected (1 homozygous), 1 heterozygous also carried *CFTR* p.L997F

Perri F, Piepoli A, Stanziale P, Merla A, Zelante L, Andriulli A. (2003) **Mutation analysis of the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene, the cationic trypsinogen (*PRSS1*) gene, and the serine protease inhibitor, Kazal type 1 (*SPINK1*) gene in patients with alcoholic chronic pancreatitis.** Eur J Hum Genet 11, 687-692

1 affected

Schneider A, Pfützer RH, Barmada MM, Slivka A, Martin J, Whitcomb DC. (2003) **Limited contribution of the SPINK1 N34S mutation to the risk and severity of alcoholic chronic pancreatitis: a report from the United States.** Dig Dis Sci 48, 1110-1115
6 affected, 3 unaffected; likely overlap with Pfützer et al. (2000); 2 affected counted

Matsubayashi H, Fukushima N, Sato N, Brune K, Canto M, Yeo CJ, Hruban RH, Kern SE, Goggins M. (2003) **Polymorphisms of *SPINK1* N34S and CFTR in patients with sporadic and familial pancreatic cancer.** Cancer Biol Ther 2, 652-655
5 affected, 7 unaffected (4 with pancreatic cancer and 3 with cholecystitis)

Weiss FU, Simon P, Witt H, Mayerle J, Hlouschek V, Zimmer KP, Schnekenburger J, Domschke W, Neoptolemos JP, Lerch MM. (2003) ***SPINK1* mutations and phenotypic expression in patients with pancreatitis associated with trypsinogen mutations.** J Med Genet 40, e40
5 affected, 2 unaffected; all carried *PRSS1* p.R122H

Kuwata K, Hirota M, Nishimori I, Otsuki M, Ogawa M. (2003) **Mutational analysis of the pancreatic secretory trypsin inhibitor gene in familial and juvenile pancreatitis in Japan.** J Gastroenterol 38, 365-370
7 affected (2 homozygous); 1 homozygous and 1 heterozygous who also carried p.R67C were reported in 2001; 5 affected counted (1 homozygous)

Hirota M, Kuwata K, Ohmuraya M, Ogawa M. (2003) **From acute to chronic pancreatitis: the role of mutations in the pancreatic secretory trypsin inhibitor gene.** JOP 4, 83-88
9 affected, likely overlap with Kuwata et al. (2001, 2003); homozygotes not specified; not counted

Felley C, Morris MA, Wonkam A, Hirschel B, Flepp M, Wolf K, Furrer H, Battegay M, Bernasconi E, Telenti A, Frossard JL. (2004) **The role of CFTR and SPINK-1 mutations in pancreatic disorders in HIV-positive patients: a case-control study.** AIDS 18, 1521-1527
2 affected (also HIV positive), 2 unaffected

Gundling F, Reitmeier F, Tannapfel A, Schutz A, Weber A, Ussmuller J, Keim V, Mossner J, Teich N. (2004) **Chronic parotitis: not another SPINKosis.** Dig Dis 22, 292-295
5 unaffected including 2 with chronic parotitis

Chandak GR, Idris MM, Reddy DN, Mani KR, Bhaskar S, Rao GV, Singh L. (2004) **Absence of PRSS1 mutations and association of SPINK1 trypsin inhibitor mutations in hereditary and non-hereditary chronic pancreatitis.** Gut 53, 723-728
75 affected (15 homozygous), 8 unaffected, possible overlap with Chandak et al. (2002); 44 affected (7 homozygous) and 5 unaffected counted

Masamune A, Mizutamari H, Kume K, Asakura T, Satoh K, Shimosegawa T. (2004) **Hereditary pancreatitis as the premalignant disease: a Japanese case of pancreatic cancer involving the SPINK1 gene mutation N34S.** Pancreas 28, 305-310
1 family with 2 affected (homozygous, 1 also with pancreatic cancer) and 5 unaffected

Inoue N, Ito T, Akashi T, Kawabe K, Oono T, Gibo J, Arita Y, Nawata H, Funakoshi A. (2004) **Acute pancreatitis in the early stages of pregnancy associated with a PSTI gene mutation.** Pancreas 29, 242-243
1 family with 1 affected (pregnant) and 1 unaffected, plus 1 affected sister with heterozygous c.*32C>T but no p.N34S

Schneider A, Barmada MM, Slivka A, Martin JA, Whitcomb DC. (2004) **Clinical characterization of patients with idiopathic chronic pancreatitis and *SPINK1* mutations.** Scand J Gastroenterol 39, 903-904
5 affected; 1 also carried p.P55S, 3 unaffected, likely overlap with previous papers from same group; not counted

Lee KH, Ryu JK, Yoon WJ, Lee JK, Kim YT, Yoon YB. (2005) **Mutation analysis of SPINK1 and CFTR gene in Korean patients with alcoholic chronic pancreatitis.** Dig Dis Sci 50, 1852-185
1 affected

Kühn AC, Teich N, Caca K, Limbach A, Hirsch W. (2005) **Chronic pancreatitis with pancreaticolithiasis and pseudocyst in a 5-year-old boy with homozygous SPINK1 mutation.** Pediatr Radiol 35, 902-905
1 affected

Weiss FU, Simon P, Bogdanova N, Mayerle J, Dworniczak B, Horst J, Lerch MM. (2005) **Complete cystic fibrosis transmembrane conductance regulator gene sequencing in patients with idiopathic chronic pancreatitis and controls.** Gut 54, 1456-1460
8 affected

Lempinen M, Paju A, Kemppainen E, Smura T, Kylänpää ML, Nevanlinna H, Stenman J, Stenman UH. (2005) **Mutations N34S and P55S of the SPINK1 gene in patients with chronic pancreatitis or pancreatic cancer and in healthy subjects: a report from Finland.** Scand J Gastroenterol 40, 225-230
14 affected (1 homozygous), 19 unaffected including 7 with pancreatic cancer

Tukiainen E, Kylänpää ML, Kemppainen E, Nevanlinna H, Paju A, Repo H, Stenman UH, Puolakkainen P. (2005) **Pancreatic secretory trypsin inhibitor (*SPINK1*) gene mutations in patients with acute pancreatitis.** Pancreas 30, 239-242
29 affected (1 homozygous), 12 unaffected, controls overlap with Lempinen et al. (2005); only affected counted

Schneider A, Lawrence EC, Barmada MM, Norris JM, Hamman RF, Marshall JA, Ferrell RE, Whitcomb DC. (2005) **The SPINK1 N34S mutation is not associated with Type 2 diabetes mellitus in a population of the USA.** Diabet Med 22, 744-748
37 unaffected, includes 22 with diabetes

Kume K, Masamune A, Mizutamari H, Kaneko K, Kikuta K, Satoh M, Satoh K, Kimura K, Suzuki N, Nagasaki Y, Horii A, Shimosegawa T. (2005) **Mutations in the serine protease inhibitor Kazal Type 1 (*SPINK1*) gene in Japanese patients with pancreatitis.** Pancreatology 5, 354-360
9 affected (1 homozygous), 1 unaffected

Valmu L, Paju A, Lempinen M, Kemppainen E, Stenman UH. (2006) **Application of proteomic technology in identifying pancreatic secretory trypsin inhibitor variants in urine of patients with pancreatitis.** Clin Chem 52, 73-81
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

Shimosegawa T, Kume K, Masamune A. (2006) ***SPINK1* gene mutations and pancreatitis in Japan.** J Gastroenterol Hepatol 21 Suppl 3, S47-51
11 affected (1 homozygous), 1 unaffected; possible overlap with Kume et al. (2005); 2 affected heterozygous counted

Piepoli A, Gentile A, Valvano MR, Barana D, Oliani C, Cotugno R, Quitadamo M, Andriulli A, Perri F. (2006) **Lack of association between *UGT1A7, UGT1A9, ARP, SPINK1* and *CFTR* gene polymorphisms and pancreatic cancer in Italian patients.** World J Gastroenterol 12, 6343-6348
4 affected, 2 unaffected
Text and Table 4 contradict; text value was counted

Mahurkar S, Idris MM, Reddy DN, Bhaskar S, Rao GV, Thomas V, Singh L, Chandak GR. (2006) **Association of cathepsin B gene polymorphisms with tropical calcific pancreatitis.** Gut 55, 1270-1275
134 affected; likely overlap with Chandak et al. (2002, 2004); homozygotes not specified; 59 affected counted as heterozygous

Bhaskar S, Reddy DN, Mahurkar S, Rao GV, Singh L, Chandak GR. (2006) **Lack of significant association of an insertion/deletion polymorphism in the angiotensin converting enzyme (*ACE*) gene with tropical calcific pancreatitis**. BMC Gastroenterol 6, 42
52 affected, 3 unaffected, likely overlap with Chandak et al. (2002, 2004) and Mahurkar et al. (2006); homozygotes not specified; not counted

Felderbauer P, Klein W, Bulut K, Ansorge N, Dekomien G, Werner I, Epplen JT, Schmitz F, Schmidt WE. (2006) **Mutations in the calcium-sensing receptor: a new genetic risk factor for chronic pancreatitis?** Scand J Gastroenterol 41, 343-348
66 affected (7 homozygous), 38 unaffected

Sobczyńska-Tomaszewska A, Bak D, Oralewska B, Oracz G, Norek A, Czerska K, Mazurczak T, Teisseyre M, Socha J, Zagulski M, Bal J. (2006) **Analysis of *CFTR, SPINK1, PRSS1* and *AAT* mutations in children with acute or chronic pancreatitis.** J Pediatr Gastroenterol Nutr 43, 299-306
14 affected (2 homozygous)

Kalinin VN, Kaifi JT, Schwarzenbach H, Sergeyev AS, Link BC, Bogoevski D, Vashist Y, Izbicki JR, Yekebas EF. (2006) **Association of rare *SPINK1* gene mutation with another base substitution in chronic pancreatitis patients.** World J Gastroenterol 12, 5352-5356
10 affected

Masamune A, Kume K, Takagi Y, Kikuta K, Satoh K, Satoh A, Shimosegawa T. (2007) **N34S mutation in the *SPINK1* gene is not associated with alternative splicing.** Pancreas 34, 423-428
2 affected (homozygous)

Masamune A, Kume K, Shimosegawa T. (2007) **Differential roles of the *SPINK1* gene mutations in alcoholic and nonalcoholic chronic pancreatitis.** J Gastroenterol 42 Suppl 17, 135-140
11 affected (1 homozygous), 1 unaffected; likely overlap with Shimosegawa et al. (2006); not counted

Hucl T, Jesnowski R, Pfützer RH, Elsässer HP, Löhr M. (2007) ***SPINK1* variants in young-onset pancreatic cancer.** J Gastroenterol 42, 599
PaCa44 and PancTu-1 cell lines are heterozygous; not counted

Boulling A, Le Maréchal C, Trouvé P, Raguénès O, Chen JM, Férec C. (2007) **Functional analysis of pancreatitis-associated missense mutations in the pancreatic secretory trypsin inhibitor (*SPINK1*) gene.** Eur J Hum Genet 15, 936-942
1 family with 1 affected who also carried p.G48E and 1 unaffected

Tzetis M, Kaliakatsos M, Fotoulaki M, Papatheodorou A, Doudounakis S, Tsezou A, Makrythanasis P, Kanavakis E, Nousia-Arvanitakis S. (2007) **Contribution of the *CFTR* gene, the pancreatic secretory trypsin inhibitor gene (*SPINK1*) and the cationic trypsinogen gene (*PRSS1*) to the etiology of recurrent pancreatitis.** Clin Genet 71, 451-457
2 affected

Räty S, Piironen A, Babu M, Pelli H, Sand J, Uotila S, Nordback I, Herzig KH. (2007) **Screening for human cationic trypsinogen (PRSS1) and trypsinogen inhibitor gene (SPINK1) mutations in a Finnish family with hereditary pancreatitis.** Scand J Gastroenterol 42, 1000-1005
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)

Mahurkar S, Bhaskar S, Reddy DN, Rao GV, Chandak GR. (2007) **Comprehensive screening for *reg1α* gene rules out association with tropical calcific pancreatitis.** World J Gastroenterol 13, 5938-5943
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

Frulloni L, Scattolini C, Graziani R, Cavestro GM, Pravadelli C, Amodio A, Manfredi R, Scarpa A, Vantini I. (2008) **Clinical and radiological outcome of patients suffering from chronic pancreatitis associated with gene mutations.** Pancreas 37, 371-376
11 affected, mutation not specified; counted as heterozygous p.N34S

Mahurkar S, Bhaskar S, Reddy DN, Prakash S, Rao GV, Singh SP, Thomas V, Chandak GR. (2008) **TCF7L2 gene polymorphisms do not predict susceptibility to diabetes in tropical calcific pancreatitis but may interact with SPINK1 and CTSB mutations in predicting diabetes.** BMC Med Genet 9, 80
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

Felderbauer P, Karakas E, Fendrich V, Bulut K, Horn T, Lebert R, Holland-Letz T, Schmitz F, Bartsch D, Schmidt WE. (2008) **Pancreatitis risk in primary hyperparathyroidism: relation to mutations in the *SPINK1* trypsin inhibitor (N34S) and the cystic fibrosis gene.** Am J Gastroenterol 103, 368-374
4 affected

Gullo L, Laghi L, Migliori M, Lucrezio L, Bianchi P, Randolph AE, Mantovani V, Bastagli L, Pezzilli R, Malesci A. (2008) ***SPINK1* and *PRSS1* mutations in benign pancreatic hyperenzymemia.** Pancreas 37, 31-35
3 unaffected; with hyperenzymemia

O'Reilly DA, Witt H, Rahman SH, Schulz HU, Sargen K, Kage A, Cartmell MT, Landt O, Larvin M, Demaine AG, McMahon MJ, Becker M, Kingsnorth AN. (2008) **The *SPINK1* N34S variant is associated with acute pancreatitis.** Eur J Gastroenterol Hepatol20, 726-731
24 affected (1 homozygous), 18 unaffected

Muddana V, Lamb J, Greer JB, Elinoff B, Hawes RH, Cotton PB, Anderson MA, Brand RE, Slivka A, Whitcomb DC. (2008) **Association between *calcium sensing receptor* gene polymorphisms and chronic pancreatitis in a US population: role of *serine protease inhibitor Kazal 1type* and alcohol.** World J Gastroenterol 14, 4486-4491
57 affected, 21 unaffected, possible overlap with Pfützer et al. (2000), homozygotes not specified; 28 affected and 18 unaffected counted as heterozygous

Murugaian EE, Premkumar RM, Radhakrishnan L, Vallath B. (2008) **Novel mutations in the calcium sensing receptor gene in tropical chronic pancreatitis in India.** Scand J Gastroenterol 43, 117-121
5 affected

Bagul A, Pushpakom S, Balachander S, Newman WG, Siriwardena A. (2009) **The *SPINK1* N34S variant is associated with acute pancreatitis.** Eur J Gastroenterol Hepatol 21, 485
6 affected, 6 unaffected

Sundaresan S, Chacko A, Dutta AK, Bhatia E, Witt H, Te Morsche RH, Jansen JB, Drenth JP. (2009) **Divergent roles of *SPINK1* and *PRSS2* variants in tropical calcific pancreatitis.** Pancreatology 9, 145-149
67 affected (13 homozygous), 10 unaffected

Oruc N, Ozutemiz O, Berdeli A, Ersoz G, Gunsar F, Karasu Z, Ilter T, Batur Y, Akarca US. (2009) Common SPINK-1 mutations do not predispose to the development of non-alcoholic fatty liver disease. Ann Hepatol 8, 116-119
2 unaffected (homozygous); with fatty liver disease
Oddly, homozygotes found only; no heterozygous carriers

Rajesh G, Elango EM, Vidya V, Balakrishnan V. (2009) **Genotype-phenotype correlation in 9 patients with tropical pancreatitis and identified gene mutations.** Indian J Gastroenterol 28, 68-71
5 affected

Schmitt F, Le Henaff G, Piloquet H, Leclair MD, David A, Heloury Y, Podevin G. (2009) **Hereditary pancreatitis in children: surgical implications with special regard to genetic background.** J Pediatr Surg 44, 2078-2082
1 family with 2 affected (1 homozygous) and 1 unaffected

Mora J, Comas L, Ripoll E, Gonçalves P, Queraltó JM, González-Sastre F, Farré A. (2009) **Genetic mutations in a Spanish population with chronic pancreatitis.** Pancreatology 9, 644-651
6 affected

Oh HC, Kim MH, Choi KS, Moon SH, Park do H, Lee SS, Seo DW, Lee SK, Yoo HW, Kim GH. (2009) **Analysis of *PRSS1* and *SPINK1* mutations in Korean patients with idiopathic and familial pancreatitis.** Pancreas 38, 180-183
3 affected

Derikx MH, Szmola R, te Morsche RH, Sunderasan S, Chacko A, Drenth JP. (2009) **Tropical calcific pancreatitis and its association with *CTRC* and *SPINK1* (p.N34S) variants.** Eur J Gastroenterol Hepatol 21, 889-894
47 affected (7 homozygous), 7 unaffected

Diaconu BL, Ciobanu L, Mocan T, Pfützer RH, Scafaru MP, Acalovschi M, Singer MV, Schneider A. (2009) **Investigation of the SPINK1 N34S mutation in Romanian patients with alcoholic chronic pancreatitis. A clinical analysis based on the criteria of the M-ANNHEIM classification.** J Gastrointestin Liver Dis 18, 143-150
5 affected, 1 unaffected

Groeneweg M, Poley JW, Dansen M, Brinkman JG, Escher JC, Nieuwenhuis EE. (2009) **Chronic hereditary pancreatitis in a girl with a serine protease inhibitor kazal type I (SPINK-1) gene mutation and a coxsackie type B5 infection.** Pediatr Infect Dis J 28, 169-170
1 affected; mutation not specified; counted as heterozygous p.N34S

Garg PK, Khajuria R, Kabra M, Shastri SS. (2009) **Association of *SPINK1* gene mutation and *CFTR* gene polymorphisms in patients with pancreas divisum presenting with idiopathic pancreatitis.** J Clin Gastroenterol 43, 848-852
22 affected (4 homozygous); 2 heterozygous and2 homozygous with pancreas divisum, 1 unaffected

Shimosegawa T, Kume K, Satoh K. (2009) **Chronic pancreatitis and pancreatic cancer: prediction and mechanism.** Clin Gastroenterol Hepatol 7 (11 Suppl), S23-S28
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

Rebours V, Couvelard A, Sauvanet A, Hammel P, Ruszniewski P, Lévy P. (2010) **Pancreatic intraepithelial neoplasia is associated with chronic pancreatitis due to serine protease inhibitor Kazal type 1 and cystic fibrosis transmembrane conductance regulator mutations.** Pancreas 39, 947-948
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

Sutton JM, Schmulewitz N, Sussman JJ, Smith M, Kurland JE, Brunner JE, Salehi M, Choe KA, Ahmad SA. (2010) **Total pancreatectomy and islet cell autotransplantation as a means of treating patients with genetically linked pancreatitis.** Surgery 148, 676-685
2 affected

Cavestro GM, Zuppardo RA, Bertolini S, Sereni G, Frulloni L, Okolicsanyi S, Calzolari C, Singh SK, Sianesi M, Del Rio P, Leandro G, Franzè A, Di Mario F. (2010) **Source Connections between genetics and clinical data: Role of MCP-1, CFTR, and SPINK-1 in the setting of acute, acute recurrent, and chronic pancreatitis.** Am J Gastroenterol 105, 199-206
4 affected (1 homozygous)

Midha S, Khajuria R, Shastri S, Kabra M, Garg PK. (2010) **Idiopathic chronic pancreatitis in India: phenotypic characterisation and strong genetic susceptibility due to *SPINK1* and *CFTR* gene mutations.** Gut 59, 800-807
48 affected (8 homozygous), 4 unaffected; possible overlap with Garg et al. (2009); 26 affected (4 homozygous) and 3 unaffected counted

Joergensen M, Brusgaard K, Crüger DG, Gerdes AM, Schaffalitzky de Muckadell OB. (2010) **Incidence, etiology and prognosis of first-time acute pancreatitis in young patients: a population-based cohort study.** Pancreatology 10, 453-461
3 affected
Unclear if overlaps with the two other Joergensen papers (2010); all counted

Joergensen M, Brusgaard K, Crüger DG, Gerdes AM, de Muckadell OB. (2010) **Incidence, prevalence, etiology, and prognosis of first-time chronic pancreatitis in young patients: a nationwide cohort study.** Dig Dis Sci 55, 2988-2998
16 affected
Unclear if overlaps with the two other Joergensen papers (2010); all counted

Joergensen MT, Brusgaard K, Crüger DG, Gerdes AM, Schaffalitzky de Muckadell OB. (2010) **Genetic, epidemiological, and clinical aspects of hereditary pancreatitis: a population-based cohort study in Denmark.** Am J Gastroenterol 105, 1876-1883
9 affected (2 homozygous)
Unclear if overlaps with the two other Joergensen papers (2010); all counted

Graziani R, Manfredi R, Cicero C, Contro A, Brandalise A, Tapparelli M, Frulloni L, Vantini I, Megibow A, Pozzi Mucelli R (2010) **Role of multislice computed tomography in the diagnosis of gene-mutation-associated pancreatitis (GMAP).** Radiol Med115, 875-888
9 affected
Mutation not specified; counted as heterozygous p.N34S

Schneider A, Larusch J, Sun X, Aloe A, Lamb J, Hawes R, Cotton P, Brand RE, Anderson MA, Money ME, Banks PA, Lewis MD, Baillie J, Sherman S, Disario J, Burton FR, Gardner TB, Amann ST, Gelrud A, George R, Rockacy MJ, Kassabian S, Martinson J, Slivka A, Yadav D, Oruc N, Barmada MM, Frizzell R, Whitcomb DC. (2011) **Combined bicarbonate conductance-impairing variants in *CFTR* and *SPINK1* variants are associated with chronic pancreatitis in patients without cystic fibrosis.** Gastroenterology 140, 162-171
29 affected (4 homozygous), 2 unaffected; possible overlap with Pfützer et al. (2000); Muddana et al. (2008); not counted

Lucidi V, Alghisi F, Dall'Oglio L, D'Apice MR, Monti L, De Angelis P, Gambardella S, Angioni A, Novelli G. (2011) **The etiology of acute recurrent pancreatitis in children: a challenge for pediatricians.** Pancreas 40, 517-521
3 affected

Lee YJ, Kim KM, Choi JH, Lee BH, Kim GH, Yoo HW. (2011) **High incidence of *PRSS1* and *SPINK1* mutations in Korean children with acute recurrent and chronic pancreatitis.** J Pediatr Gastroenterol Nutr 52, 478-481
1 affected

Felderbauer P, Karakas E, Fendrich V, Lebert R, Bartsch DK, Bulut K. (2011) **Multifactorial genesis of pancreatitis in primary hyperparathyroidism: evidence for "protective" (PRSS2) and "destructive" (CTRC) genetic factors.** Exp Clin Endocrinol Diabetes 119, 26-29
4 affected; with hyperparathyroidism, same subjects as in Felderbauer et al. (2008); not counted

Steiner B, Rosendahl J, Witt H, Teich N, Keim V, Schulz HU, Pfützer R, Löhr M, Gress TM, Nickel R, Landt O, Koudova M, Macek M Jr, Farre A, Casals T, Desax MC, Gallati S, Gomez-Lira M, Audrezet MP, Férec C, des Georges M, Claustres M, Truninger K (2011) **Common *CFTR* haplotypes and susceptibility to chronic pancreatitis and congenital bilateral absence of the vas deferens.** Hum Mutat 32, 912-920
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

Sandhu B, Vitazka P, Ferreira-Gonzalez A, Pandya A, Vachhani R, Bouhaidar D, Zfass A, Sanyal A. (2011) **Presence of SPINK-1 variant alters the course of chronic pancreatitis.** J Gastroenterol Hepatol 26, 965-969
13 affected

Masamune A, Ariga H, Kume K, Kakuta Y, Satoh K, Satoh A, Shimosegawa T. (2011) **Genetic background is different between sentinel and recurrent acute pancreatitis.** J Gastroenterol Hepatol 26, 974-978
8 affected, 2 unaffected

Gasiorowska A, Talar-Wojnarowska R, Czupryniak L, Smolarz B, Romanowicz-Makowska H, Kulig A, Malecka-Panas E. (2011) **The prevalence of cationic trypsinogen (PRSS1) and serine protease inhibitor, Kazal type 1 (SPINK1) gene mutations in Polish patients with alcoholic and idiopathic chronic pancreatitis.** Dig Dis Sci 56, 894-901
10 affected (5 homozygous), 3 unaffected (1 homozygous); study highly problematic; not counted

Graziani R, Frulloni L, Cicero C, Manfredi R, Ambrosetti MC, Mautone S, Pozzi Mucelli R. (2012) **Bull's-eye pattern of pancreatic-duct stones on multidetector computed tomography and gene-mutation-associated pancreatitis (GMAP).** Radiol Med 117, 1275-1286
6 affected
Mutation not specified; counted as heterozygous p.N34S

Kume K, Masamune A, Ariga H, Hayashi S, Takikawa T, Miura S, Suzuki N, Kikuta K, Hamada S, Hirota M, Kanno A, Shimosegawa T. (2012) **Do genetic variants in the *SPINK1* gene affect the level of serum PSTI?** J Gastroenterol 47, 1267-1274
12 affected (1 homozygous); likely overlap with prior papers from the Shimosegawa group; not counted

Sultan M, Werlin S, Venkatasubramani N. (2012) **Genetic prevalence and characteristics in children with recurrent pancreatitis.** J Pediatr Gastroenterol Nutr 54, 645-650
4 affected

Jøergensen MT, Brusgaard K, Novovic S, Andersen AM, Hansen MB, Gerdes AM, de Muckadell OB. (2012) **Is the *SPINK1* variant p.N34S overrepresented in patients with acute pancreatitis?** Eur J Gastroenterol Hepatol 24, 309-315
2 affected, 2 unaffected

Bertin C, Pelletier AL, Vullierme MP, Bienvenu T, Rebours V, Hentic O, Maire F, Hammel P, Vilgrain V, Ruszniewski P, Lévy P. (2012) **Pancreas divisum is not a cause of pancreatitis by itself but acts as a partner of genetic mutations.** Am J Gastroenterol 107, 311-317
25 affected, mutations not specified, not counted

Cichoż-Lach H, Michalak M, Lis E, Wojcierowski J, Kowalik A, Słomka M, Korolczuk A. (2012) **The N34S mutation of the SPINK1 gene and alcoholic chronic pancreatitis.** Pol Arch Med Wewn 122, 277-283
15 affected, 2 unaffected

Sánchez-Ramírez CA, Flores-Martínez SE, García-Zapién AG, Montero-Cruz SA, Larrosa-Haro A, Sánchez-Corona J. (2012) **Screening of R122H and N29I mutations in the *PRSS1* gene and N34S mutation in the *SPINK1* gene in Mexican pediatric patients with acute and recurrent pancreatitis.** Pancreas 41, 707-711
3 affected

Minen F, De Cunto A, Martelossi S, Ventura A. (2012) **Acute and recurrent pancreatitis in children: exploring etiological factors.** Scand J Gastroenterol 47, 1501-1504
2 affected

Masson E, Hammel P, Garceau C, Bénech C, Quéméner-Redon S, Chen JM, Férec C. (2013) **Characterization of two deletions of the *CTRC* locus.** Mol Genet Metab 109, 296-300
1 family with 1 affected and 1 unaffected

Rosendahl J, Landt O, Bernadova J, Kovacs P, Teich N, Bödeker H, Keim V, Ruffert C, Mössner J, Kage A, Stumvoll M, Groneberg D, Krüger R, Luck W, Treiber M, Becker M, Witt H. (2013) ***CFTR, SPINK1, CTRC* and *PRSS1* variants in chronic pancreatitis: is the role of mutated *CFTR* overestimated?** Gut 62, 582-592
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

Awano H, Lee T, Yagi M, Masamune A, Kume K, Takeshima Y, Iijima K. (2013) **Childhood-onset hereditary pancreatitis with mutations in the CT gene and SPINK1 gene.** Pediatr Int 55, 646-649
1 family with 1 affected and 1 unaffected

Laje P, Adzick NS. (2013) **Modified Puestow procedure for the management of chronic pancreatitis in children.** J Pediatr Surg 48, 2271-2275
3 affected

Wilson GC, Sutton JM, Salehi M, Schmulewitz N, Smith MT, Kucera S, Choe KA, Brunner JE, Abbott DE, Sussman JJ, Ahmad SA. (2013) **Surgical outcomes after total pancreatectomy and islet cell autotransplantation in pediatric patients.** Surgery 154, 777-783
1 affected

Rho ES, Kim E, Koh H, Yoo HW, Lee BH, Kim GH. (2013) **Two cases of chronic pancreatitis associated with anomalous pancreaticobiliary ductal union and *SPINK1* mutation.** Korean J Pediatr 56, 227-230
1 affected

Ceppa EP, Pitt HA, Hunter JL, Leys CM, Zyromski NJ, Rescorla FJ, Sandrasegaran K, Fogel EL, McHenry LW, Watkins JL, Sherman S, Lehman GA. (2013) **Hereditary pancreatitis: endoscopic and surgical management.** J Gastrointest Surg 17, 847-856
8 affected

Paliwal S, Bhaskar S, Mani KR, Reddy DN, Rao GV, Singh SP, Thomas V, Chandak GR. (2013) **Comprehensive screening of chymotrypsin C (*CTRC*) gene in tropical calcific pancreatitis identifies novel variants.** Gut 62, 1602-1606

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

Hamoir C, Pepermans X, Piessevaux H, Jouret-Mourin A, Weynand B, Habyalimana JB, Leal T, Geubel A, Gigot JF, Deprez PH. (2013) **Clinical and morphological characteristics of sporadic genetically determined pancreatitis as compared to idiopathic pancreatitis: higher risk of pancreatic cancer in CFTR variants.** Digestion 87, 229-239
14 affected (1 homozygous), 1 also carried *CFTR* p.F508del, 1 also carried *CFTR* p.L997F

Masson E, Chen JM, Audrézet MP, Cooper DN, Férec C. (2013) **A conservative assessment of the major genetic causes of idiopathic chronic pancreatitis: data from a comprehensive analysis of *PRSS1, SPINK1, CTRC* and *CFTR* genes in 253 young French patients.** PLoS One 8, e73522
38 affected (14 homozygous; 1 also carried homozygous p.R65Q); likely overlap with Chen et al. (2000, 2001); 16 affected (9 homozygous) counted

Witt H, Beer S, Rosendahl J, Chen JM, Chandak GR, Masamune A, Bence M, Szmola R, Oracz G, Macek M Jr, Bhatia E, Steigenberger S, Lasher D, Bühler F, Delaporte C, Tebbing J, Ludwig M, Pilsak C, Saum K, Bugert P, Masson E, Paliwal S, Bhaskar S, Sobczynska-Tomaszewska A, Bak D, Balascak I, Choudhuri G, Nageshwar Reddy D, Rao GV, Thomas V, Kume K, Nakano E, Kakuta Y, Shimosegawa T, Durko L, Szabó A, Schnúr A, Hegyi P, Rakonczay Z Jr, Pfützer R, Schneider A, Groneberg DA, Braun M, Schmidt H, Witt U, Friess H, Algül H, Landt O, Schuelke M, Krüger R, Wiedenmann B, Schmidt F, Zimmer KP, Kovacs P, Stumvoll M, Blüher M, Müller T, Janecke A, Teich N, Grützmann R, Schulz HU, Mössner J, Keim V, Löhr M, Férec C, Sahin-Tóth M. (2013) **Variants in *CPA1* are strongly associated with early onset chronic pancreatitis.** Nat Genet 45, 1216-1220
139 affected (18 homozygous); likely overlap with Rosendahl et al. (2013); 32 affected (1 homozygous) counted

Walker NF, Warren OJ, Gawn L, Jiao LR. (2013) **The role of genetic testing in management of hereditary chronic pancreatitis.** JRSM Short Rep 4, 6
1 affected

Masamune A. (2014) **Genetics of pancreatitis: the 2014 update.** Tohoku J Exp Med 232, 69-77
Masamune, 27 affected (3 homozygous), 2 unaffected; likely overlap with prior papers from the Shimosegawa group; 18 affected (1 homozygous) counted

Martinez B, Heller M, Gaitch N, Hubert D, Burgel PR, Levy P, Girodon E, Bienvenu T. (2014) **p.Arg75Gln, a CFTR variant involved in the risk of CFTR-related disorders?** J Hum Genet 59, 206-210
3 affected, 1 unaffected

Sinha A, Cotsalas D, Akshintala VS, Afghani E, Singh VK.(2014) **Pedigree of a kindred with transheterozygous *PRSS1* R122C and *SPINK1* N34S mutations.** Pancreas 43, 974-976
1 affected; also carried *PRSS1* p.R122C, 3 unaffected, 1 also carried *PRSS1* p.R122C

Rai P, Sharma A, Gupta A, Aggarwal R. (2014) **Frequency of *SPINK1* N34S mutation in acute and recurrent acute pancreatitis.** J Hepatobiliary Pancreat Sci 21, 663-668
22 affected (1 homozygous), 4 unaffected

Schubert S, Traub F, Brakensiek K, von Kopylow K, Marohn B, Maelzer M, Gaedcke J, Kreipe H, Stuhrmann M. (2014) ***CFTR, SPINK1, PRSS1*, and *CTRC* mutations are not associated with pancreatic cancer in German patients.** Pancreas 243, 1078-1082
11 affected (2 homozygous), 1 unaffected

Singh S, Choudhuri G, Agarwal S. (2014) F**requency of CFTR, SPINK1, and cathepsin B gene mutation in North Indian population: connections between genetics and clinical data.** Scientific World Journal, 2014:763195
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

Pelaez-Luna M, Robles-Diaz G, Canizales-Quinteros S, Tusié-Luna MT. (2014) ***PRSS1* and *SPINK1* mutations in idiopathic chronic and recurrent acute pancreatitis.** World J Gastroenterol 20, 11788-11792
2 affected (1 homozygous), 5 unaffected (2 homozygous)

Martinez B, Heller M, Gaitch N, Hubert D, Burgel PR, Levy P, Girodon E, Bienvenu T. (2014) **p.Arg75Gln, a *CFTR* variant involved in the risk of *CFTR*-related disorders?** J Hum Genet 59, 206-210
3 affected, 1 unaffected

Wilson GC, Sutton JM, Smith MT, Schmulewitz N, Salehi M, Choe KA, Brunner JE, Abbott DE, Sussman JJ, Ahmad SA. (2015) **Total pancreatectomy with islet cell autotransplantation as the initial treatment for minimal-change chronic pancreatitis.** HPB (Oxford) 17, 232-238
3 affected

LaRusch J, Lozano-Leon A, Stello K, Moore A, Muddana V, O'Connell M, Diergaarde B, Yadav D, Whitcomb DC. (2015) **The common chymotrypsinogen C (*CTRC*) variant G60G (C.180T) increases risk of chronic pancreatitis but not recurrent acute pancreatitis in a North American population.** Clin Transl Gastroenterol 6, e68
3 affected (1 homozygous); likely overlap with prior Whitcomb papers; not counted

Koziel D, Gluszek S, Kowalik A, Chlopek M, Pieciak L. (2015) **Genetic mutations in *SPINK1, CFTR, CTRC* genes in acute pancreatitis.** BMC Gastroenterol 15, 70
12 affected, 1 unaffected
Unaffected control was calculated from percentage given in Discussion

Madro A, Ciesielka M, Celinski K, Slomka M, Czechowska G, Kurzepa J, Kaszelan-Szczerbinska B, Buszewicz G, Madro R. (2015) **The genetic predisposition and its impact on the diabetes mellitus development in patients with alcoholic chronic pancreatitis.** Gastroenterol Res Pract, 2015, 309156
6 affected, 1 unaffected

Poddar U, Yachha SK, Mathias A, Choudhuri G. (2015) **Genetic predisposition and its impact on natural history of idiopathic acute and acute recurrent pancreatitis in children.** Dig Liver Dis 47, 709-714
26 affected (5 homozygous), 1 unaffected

Ruiz-Navas P, Contreras-Ramirez M, Montero-Carvajalino AE, Castaño-Jaramillo LM, Orozco-Forero JP. (2015) **SPINK1 mutation in a pediatric patient with chronic pancreatitis: A case report.** Rev Gastroenterol Mex 80, 223-225
1 affected; heterozygosity not specified

Rygiel AM, Wojnicka-Stolarz M, Niepokój K, Oracz G, Bal J, Wertheim-Tysarowska K, Gutkowski K. (2015) **Chronic pancreatitis in a patient with the p.Ssn34Ser homozygous SPINK1 mutation--own experience.** Dev Period Med 19, 347-350
1 affected (homozygous)

Hegyi E, Geisz A, Sahin-Tóth M, Derikx M, Németh BC, Balázs A, Hritz I, Izbéki F, Halász A, Párniczky A, Takács T, Kelemen D, Sarlós P, Hegyi P, Czakó L. (2016) ***SPINK1*** **promoter variants in chronic pancreatitis.** Pancreas 45, 148-153
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

Paliwal S, Bhaskar S, Reddy DN, Rao GV, Thomas V, Singh SP, Chandak GR. (2016) **Association analysis of PRSS1-PRSS2 and CLDN2-MORC4 variants in nonalcoholic chronic pancreatitis using tropical calcific pancreatitis as model.** Pancreas 45, 1153-1157
168 affected (33 homozygous); likely overlap with prior Chandak papers; 38 affected (18 homozygous) counted

Oracz G, Kolodziejczyk E, Sobczynska-Tomaszewska A, Wejnarska K, Dadalski M, Grabarczyk AM, Kierkus J, Woynarowski M, Wertheim-Tysarowska K, Ryzko J, Bal J, Rygiel AM. (2016) **The clinical course of hereditary pancreatitis in children - A comprehensive analysis of 41 cases.** Pancreatology 16, 535-541
2 affected

da Costa MZ, Pires JG, Nasser PD, Ferreira CD, Teixeira AC, Paranaguá-Vezozzo DC, Guarita DR, Carrilho FJ, Ono SK. (2016) **Frequency of tabagism and N34S and P55S mutations of serine peptidase inhibitor, Kazal type 1 (*SPINK1*) and R254W mutation of chymotrypsin C (*CTRC*) in patients with chronic pancreatitis and controls.** Pancreas. 2016 May 21. [Epub ahead of print]
5 affected, 1 unaffected

Palermo JJ, Lin TK, Hornung L, Valencia CA, Mathur A, Jackson K, Fei L, Abu-El-Haija M. (2016) **Genophenotypic analysis of pediatric patients with acute recurrent and chronic pancreatitis.** Pancreas. 2016 May 19. [Epub ahead of print]
10 affected

Cho SM, Shin S, Lee KA. (2016) ***PRSS1, SPINK1, CFTR,* and *CTRC* pathogenic variants in Korean patients with idiopathic pancreatitis.** Ann Lab Med 36, 555-560
3 affected

Saito N, Suzuki M, Sakurai Y, Nakano S, Naritaka N, Minowa K, Sai JK, Shimizu T. (2016) **Genetic analysis of Japanese children with acute recurrent and chronic pancreatitis.** J Pediatr Gastroenterol Nutr 2016 Jun 21. [Epub ahead of print]
19 affected (1 homozygous)

Moran RA, Klapheke R, Jalaly NY, Makary MA, Hirose K, Goggins M, Wood L, Laheru DA, Lennon AM, Khashab MA, Singh VK. (2016) **Metastatic pancreatic adenocarcinoma associated with chronic calcific pancreatitis and a heterozygous SPINK1 N34S mutation.** Pancreatology 2016 Jun 21. [Epub ahead of print]
1 affected; also had pancreatic cancer

Midha S, Sreenivas V, Kabra M, Chattopadhyay TK, Joshi YK, Garg PK. **Genetically determined chronic pancreatitis but not alcoholic pancreatitis is a strong risk factor for pancreatic cancer.** Pancreas 2016 Aug 11. [Epub ahead of print]
16 affected; also had pancreatic cancer

Functional studies:

Kuwata K, Hirota M, Shimizu H, Nakae M, Nishihara S, Takimoto A, Mitsushima K, Kikuchi N, Endo K, Inoue M, Ogawa M. (2002) **Functional analysis of recombinant pancreatic secretory trypsin inhibitor protein with amino-acid substitution.** J Gastroenterol 37, 928-934

Hirota M, Kuwata K, Ohmuraya M, Ogawa M. (2003) **From acute to chronic pancreatitis: the role of mutations in the pancreatic secretory trypsin inhibitor gene.** JOP 4, 83-88

Valmu L, Paju A, Lempinen M, Kemppainen E, Stenman UH. (2006) **Application of proteomic technology in identifying pancreatic secretory trypsin inhibitor variants in urine of patients with pancreatitis.** Clin Chem 52, 73-81

Király O, Wartmann T, Sahin-Tóth M.(2007) **Missense mutations in pancreatic secretory trypsin inhibitor (SPINK1) cause intracellular retention and degradation.** Gut 56, 1433-1438

Boulling A, Le Maréchal C, Trouvé P, Raguénès O, Chen JM, Férec C. (2007) **Functional analysis of pancreatitis-associated missense mutations in the pancreatic secretory trypsin inhibitor (*SPINK1*) gene.** Eur J Hum Genet 15, 936-942

Masamune A, Kume K, Takagi Y, Kikuta K, Satoh K, Satoh A, Shimosegawa T. (2007) **N34S mutation in the *SPINK1* gene is not associated with alternative splicing.** Pancreas 34, 423-428

Kereszturi E, Király O, Sahin-Tóth M. (2009) **Minigene analysis of intronic variants in common *SPINK1* haplotypes associated with chronic pancreatitis.** Gut 58, 545-549

Kume K, Masamune A, Ariga H, Hayashi S, Takikawa T, Miura S, Suzuki N, Kikuta K, Hamada S, Hirota M, Kanno A, Shimosegawa T. (2012) **Do genetic variants in the *SPINK1* gene affect the level of serum PSTI?** J Gastroenterol 47, 1267-1274

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