

***SPINK1* c.163C>T p.P55S**

rs111966833

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 affected, 2 unaffected

Variant was described at the protein level as P32S

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

1 unaffected

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

2 affected; also carried p.N34S; 2 unaffected

Perri F, Piepoli A, Andriulli A. (2002) **On the role of *CFTR*, *PSSR1* and *PST1/SPINK1* in idiopathic chronic pancreatitis.** Eur J Hum Genet 211, 107

1 affected

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 (*PRSSI*) are significantly associated with tropical calcific pancreatitis.** J Med Genet 39, 347-351

2 affected; 1 also carried p.N34S, 1 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

2 affected; 1 also carried p.N34S

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

1 affected, 2 unaffected

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

1 family with 2 affected and 2 unaffected

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**

(PRSSI) 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; 2 unaffected; with alcoholic liver disease

Schneider A, Pfützner 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

2 affected, 1 also carried p.N34S, 2 unaffected; likely overlap with Pfützner et al. (2000); 1 affected counted

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

2 affected, 3 unaffected, possible overlap with Chandak et al. (2002); 1 affected and 2 unaffected counted

Le Maréchal C, Chen JM, Le Gall C, Plessis G, Chipponi J, Chuzhanova NA, Raguénès O, Férec C. (2004) **Two novel severe mutations in the pancreatic secretory trypsin inhibitor gene (SPINK1) cause familial and/or hereditary pancreatitis.** Hum Mutat 23, 205

1 affected; also carried c.87+1G>A

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

3 affected; 1 also carried p.N34S; 2 unaffected; possible overlap with Pfützner et al. (2000) and Schneider et al. (2003); 1 affected counted

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

1 affected

Lempinen M, Paju A, Kempainen 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

1 affected, 6 unaffected

Tukiainen E, Kylänpää ML, Kempainen 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

3 affected with acute pancreatitis, 6 unaffected, same controls as in Lempinen et al. (2005); 3 affected counted

Valmu L, Paju A, Lempinen M, Kempainen 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

3 affected; likely overlap with Lempinen et al. (2005) and/or Tukiainen et al. (2005); did not count

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

1 affected, 2 unaffected

Text and Table 4 contradict; text values were counted

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

1 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 Hepatol 20, 726-731

4 affected, 4 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

5 affected, 5 unaffected (1 homozygous)

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

1 affected (homozygous)

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

1 affected

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

4 affected; 2 also carried p.N34S; likely overlap with Pfützner et al. (2000) and/or Schneider et al. (2003, 2004); 1 affected counted

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

1 affected

Jørgensen 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

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 *PRSSI* variants in chronic pancreatitis: is the role of mutated *CFTR* overestimated?** Gut 62, 582-592

4 affected, 16 unaffected

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

1 affected; also carried *PRSSI* p.D100H

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 *PRSSI*, *SPINK1*, *CTRC* and *CFTR* genes in 253 young French patients.** PLoS One 8, e73522

3 affected, 1 also carried c.87+1G>A, likely overlap with Le Maréchal et al. (2004) and possibly Chen et al. (2000); 1 affected counted

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

1 unaffected

Schubert S, Traub F, Brakensiek K, von Kopylow K, Marohn B, Maelzer M, Gaedcke J, Kreipe H, Stuhmann M. (2014) ***CFTR*, *SPINK1*, *PRSSI*, and *CTRC* mutations are not associated with pancreatic cancer in German patients.** Pancreas 43, 1078-1082

1 unaffected

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

1 affected, 1 unaffected

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

2 affected, 2 unaffected (calculated from percentage given in Discussion)

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]

3 affected, 2 unaffected

Gaitch N, Hubert D, Gameiro C, Burgel PR, Houriez F, Martinez B, Honoré I, Chapron J, Kanaan R, Dusser D, Girodon E, Bienvenu T. (2016) **CFTR and/or pancreatitis susceptibility genes mutations as risk factors of pancreatitis in cystic fibrosis patients?** *Pancreatology* 16, 515-522

1 unaffected (CF patient)

Described in text only; not listed in Table

Sofia VM, Da Sacco L, Surace C, Tomaiuolo AC, Genovese S, Grotta S, Gnazzo M, Petrocchi S, Ciocca L, Alghisi F, Montemitto E, Martemucci L, Elce A, Lucidi V, Castaldo G, Angioni A. (2016) **Extensive molecular analysis suggested the strong genetic heterogeneity of idiopathic chronic pancreatitis.** *Mol Med* 2016 May 26. [Epub ahead of print]

2 affected

Functional studies:

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