

***SPINK1* c.-215G>A**

Variant is in linkage with variant c.194+2T>C

Citations:

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

2 affected (homozygous)

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 (3 homozygous), 1 heterozygous also carried p.N34S

Shimosegawa T, Kume K, Masamune A. (2006) ***SPINK1* gene mutations and pancreatitis in Japan.** *J Gastroenterol Hepatol* 21 Suppl 3, S47-51

10 affected (3 homozygous); may overlap with Kume et al. (2005), counted as 1 heterozygous affected

Kume K, Masamune A, Kikuta K, Shimosegawa T. (2006) **[-215G>A; IVS3+2T>C] mutation in the *SPINK1* gene causes exon 3 skipping and loss of the trypsin binding site.** *Gut* 55, 1214

2 affected (1 homozygous), 1 unaffected

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

3 affected

Allele specific PCR was used to verify linkage with c.194+2T>C

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

1 affected (homozygous)

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

1 affected, likely overlap with Kume et al. (2006); did not count

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

9 affected (4 homozygous); overlap with Shimosegawa et al. (2006); counted as 1 homozygous affected

Boulling A, Witt H, Chandak GR, Masson E, Paliwal S, Bhaskar S, Reddy DN, Cooper DN, Chen JM, Férec C. (2011) **Assessing the pathological relevance of *SPINK1* promoter variants.** *Eur J Hum Genet* 19, 1066-1073

9 affected, 1 unaffected; 1 affected may overlap with Witt et al. (2000) where linked variant was detected; 8 affected counted

Ota Y, Masamune A, Inui K, Kume K, Shimosegawa T, Kikuyama M. (2010) **Phenotypic variability of the homozygous IVS3+2T>C mutation in the serine protease inhibitor Kazal type 1 (*SPINK1*) gene in patients with chronic pancreatitis.** *Tohoku J Exp Med* 221, 197-201
4 affected (3 homozygous); 1 unaffected heterozygous daughter of an affected homozygote

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
14 affected, 1 unaffected

Hegy 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

Functional studies:

Boulling A, Witt H, Chandak GR, Masson E, Paliwal S, Bhaskar S, Reddy DN, Cooper DN, Chen JM, Férec C. (2011) **Assessing the pathological relevance of *SPINK1* promoter variants.** *Eur J Hum Genet* 19, 1066-1073

Derikx MH, Geisz A, Kereszturi É, Sahin-Tóth M. (2015) **Functional significance of *SPINK1* promoter variants in chronic pancreatitis.** *Am J Physiol Gastrointest Liver Physiol* 308, G779-784

Hegy 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