|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pain | Chr | SNP | OR (95% CI) | SE | P | Minor Allele | MAF | Gene |
| CP | Constant | 1\* | rs7417320 | 1.54 (1.26, 1.9) | 0.11 | 3.69E-05 | G | 0.47 | *MAD2L2* |
| 3 | rs1154373 | 0.64 (0.52, 0.78) | 0.11 | 1.40E-05 | G | 0.38 | *GRM7* |
| 3 | rs3804883 | 1.58 (1.27, 1.98) | 0.11 | 5.69E-05 | G | 0.34 | *GRM7* |
| 5 | rs1895360 | 7.96 (3.03, 20.95) | 0.49 | 2.64E-05 | T | 0.04 | *PPP2R2B* |
| 5 | rs465409 | 6.32 (2.57, 15.58) | 0.46 | 6.16E-05 | A | 0.04 | *PPP2R2B* |
| 6 | rs4454135 | 1.58 (1.28, 1.95) | 0.11 | 2.31E-05 | C | 0.42 | Upstream *TNFRSF21* |
| 6 | rs803406 | 0.62 (0.49, 0.79) | 0.12 | 6.99E-05 | T | 0.24 | *PLEKHG1* |
| 8 | rs62480128 | 2.21 (1.54, 3.17) | 0.19 | 1.77E-05 | G | 0.13 | *CSMD1* |
| 9 | rs2761694 | 0.65 (0.52, 0.8) | 0.11 | 7.87E-05 | C | 0.33 | *PTPRD* |
| Constant-severe | 1\* | rs3767300 | 0.66 (0.54, 0.81) | 0.11 | 7.14E-05 | C | 0.41 | *MAD2L2* |
| 5 | rs1895360 | 8.17 (3.32, 20.1) | 0.46 | 4.83E-06 | T | 0.045 | *PPP2R2B* |
| 5 | rs465409 | 5.64 (2.51, 12.7) | 0.41 | 2.95E-05 | A | 0.044 | *PPP2R2B* |
| 6 | rs803406 | 0.6 (0.47, 0.76) | 0.12 | 3.10E-05 | T | 0.23 | *PLEKHG1* |
| 8 | rs62480128 | 2.37 (1.66, 3.39) | 0.18 | 2.03E-06 | G | 0.14 | *CSMD1* |
| 16 | rs6500947 | 1.63 (1.3, 2.06) | 0.12 | 3.09E-05 | G | 0.32 | *RBFOX1* |
| Severe | 5 | rs331201 | 2.24 (1.5, 3.34) | 0.21 | 8.98E-05 | T | 0.11 | Downstream *CDH10* |
| 7\* | rs4397289 | 1.57 (1.26, 1.95) | 0.11 | 6.55E-05 | G | 0.4 | *THSD7A* |
| 7 | rs4129040 | 0.62 (0.49, 0.79) | 0.12 | 8.76E-05 | G | 0.23 | *DPP6* |
| 8\* | rs7463086 | 0.63 (0.51, 0.77) | 0.11 | 1.02E-05 | G | 0.35 | *ERICH1-AS1* |
| 11 | rs7479307 | 0.41 (0.27, 0.62) | 0.21 | 2.13E-05 | T | 0.046 | *GRM5* |
| 16 | rs7202500 | 2.62 (1.66, 4.15) | 0.24 | 3.99E-05 | T | 0.095 | *RBFOX1* |
| 20\* | rs75501185 | 0.4 (0.26, 0.62) | 0.22 | 3.20E-05 | A | 0.045 | *SALL4* |
| RAP+ CP | Constant | 1 | rs41332551 | 2.33 (1.53, 3.54) | 0.21 | 7.29E-05 | T | 0.055 | *C1orf94* |
| 4 | rs2870322 | 0.54 (0.39, 0.73) | 0.16 | 9.40E-05 | C | 0.06 | *CCSER1* |
| 5 | rs1895360 | 3.77 (1.95, 7.28) | 0.34 | 8.24E-05 | T | 0.031 | *PPP2R2B* |
| 5 | rs2011893 | 0.25 (0.12, 0.49) | 0.36 | 7.82E-05 | G | 0.012 | *TENM2* |
| 6 | rs4129326 | 1.4 (1.19, 1.65) | 0.083 | 5.26E-05 | T | 0.44 | Upstream *TNFRSF21* |
| 6 | rs803411 | 0.68 (0.56, 0.82) | 0.095 | 4.04E-05 | T | 0.24 | *PLEKHG1* |
| 9 | rs77948918 | 0.62 (0.49, 0.78) | 0.12 | 5.64E-05 | C | 0.11 | *PTPRD* |
| 9 | rs7858684 | 0.69 (0.58, 0.83) | 0.089 | 4.17E-05 | T | 0.28 | *PTPRD* |
| 9 | rs191106810 | 0.55 (0.41, 0.74) | 0.15 | 9.55E-05 | A | 0.067 | *GABBR2* |
| 12 | rs759764 | 1.48 (1.22, 1.79) | 0.098 | 7.24E-05 | C | 0.27 | *ANKS1B* |
| Constant-severe | 1 | rs41332551 | 2.32 (1.54, 3.51) | 0.21 | 6.44E-05 | T | 0.058 | Upstream *TNFRSF21* |
| 2\* | rs17635425 | 2.32 (1.54, 3.51) | 0.21 | 6.13E-05 | C | 0.061 | *CNNM3* |
| 5 | rs10079739 | 1.41 (1.19, 1.67) | 0.087 | 7.51E-05 | C | 0.42 | *HCN1* |
| 5 | rs1895360 | 4.28 (2.2, 8.31) | 0.34 | 1.77E-05 | T | 0.034 | *PPP2R2B* |
| 7 | rs757323 | 1.4 (1.18, 1.66) | 0.086 | 9.76E-05 | G | 0.53 | Downstream *COBL* |
| 12 | rs759764 | 1.5 (1.23, 1.83) | 0.01 | 4.73E-05 | C | 0.27 | *ANKS1B* |
| 18 | rs77567232 | 3.35 (1.83, 6.13) | 0.31 | 9.09E-05 | T | 0.034 | *DCC* |
| 18 | rs4801075 | 2.77 (1.71, 4.49) | 0.25 | 3.52E-05 | T | 0.047 | *LINC-ROR* |
| 18 | rs181903213 | 4.69 (2.21, 9.96) | 0.38 | 5.82E-05 | T | 0.027 | *WDR7* |
| Severe | 2 | rs139971969 | 2.66 (1.63, 4.35) | 0.25 | 9.90E-05 | C | 0.052 | *EFHD1* |
| 4 | rs12646702 | 0.71 (0.6, 0.84) | 0.084 | 5.58E-05 | A | 0.45 | *SMAD1* |
| 7 | rs10270255 | 0.69 (0.58, 0.82) | 0.09 | 2.71E-05 | A | 0.26 | *THSD7A* |
| 7 | rs757323 | 1.48 (1.25, 1.75) | 0.085 | 3.58E-06 | G | 0.52 | Downstream *COBL* |
| 8\* | rs12550299 | 0.63 (0.5, 0.79) | 0.12 | 9.86E-05 | C | 0.12 | *MCPH1* |
| 11\* | rs7125204 | 1.5 (1.25, 1.8) | 0.093 | 1.26E-05 | G | 0.32 | *ELP4* |
| 16 | rs67176054 | 2.45 (1.7, 3.53) | 0.19 | 1.53E-06 | A | 0.09 | *RBFOX1* |
| 16 | rs34009260 | 2.19 (1.56, 3.08) | 0.17 | 5.96E-06 | A | 0.098 | *RBFOX1* |
| 16 | rs74011978 | 0.17 (0.073, 0.4) | 0.43 | 4.16E-05 | G | 0.0047 | *RBFOX1* |

**Table S4. Lead SNPS.** GWAS Catalog (1) gene association results for lead SNPs for each group of pancreatitis and pain from NAPS2 data. \*SNP has an eQTL as reported in GTEx (2).

CP, chronic pancreatitis; RAP, recurrent acute pancreatitis; Chr, chromosome; SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence intervals; SE, standard error; MAF, minor allele frequency.

|  |  |  |  |
| --- | --- | --- | --- |
| SNP | Gene(s) | eQTL Tissue(s) | Link |
| rs7417320 | *MAD2L2* | Testis  | <https://www.gtexportal.org/home/snp/rs7417320>  |
| *FBXO6* | Muscle-Skeletal |
| Artery-Aorta |
| Whole Blood |
| Heart-Left Ventricle |
| Artery-Coronary |
| Heart-Atrial Appendage |
| Artery-Tibial |
| rs3767300 | *MAD2L2* | Testis | <https://www.gtexportal.org/home/snp/rs3767300>  |
| Heart-Left Ventricle |
| *FBXO6* | Muscle-Skeletal |
| Artery-Aorta |
| Heart-Atrial Appendage |
| Artery-Tibial |
| Heart-Left Ventricle |
| Whole Blood |
| Artery-Coronary |
| Esophagus-Mucosa |
| Adipose-Subcutaneous |
| Skin-Sun Exposed(Lower leg) |
| rs4397289 | *THSD7A* | Brain-Cerebellum | <https://www.gtexportal.org/home/snp/rs4397289>  |
| *VWDE* | Cells-Cultured fibroblasts |
| rs7463086 | *ERICH1* | Whole Blood | <https://www.gtexportal.org/home/snp/rs7463086>  |
| rs75501185 | *SALL4* | Thyroid | <https://www.gtexportal.org/home/snp/rs75501185>  |
| Nerve-Tibial |
| Pancreas |
| rs17635425 | *LMAN2L* | Skin-Sun Exposed(Lower leg) | <https://www.gtexportal.org/home/snp/rs17635425>  |
| Skin-Not Sun Exposed(Suprapubic) |
| Muscle-Skeletal |
| *CIAO1* | Testis |
| *ADRA2B* | Skin-Sun Exposed(Lower leg) |
| rs12550299 | *MCPH1* | Nerve-Tibial | <https://www.gtexportal.org/home/snp/rs12550299>  |
| Colon-Sigmoid |
| Brain-Cerebellum |
| Brain-Cerebellar Hemisphere |
| Esophagus-Muscularis |
| Brain-Caudate(Basal ganglia) |

**Table S5.** eQTL loci for lead SNPs as reported from GTEx (2).

SNP, single nucleotide polymorphism; eQTL, expression quantitative trait loci.

References

1. Buniello A, MacArthur JAL, Cerezo M, Harris LW, Hayhurst J, Malangone C, et al. The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics 2019. Nucleic Acids Res. 2019;47(D1):D1005-D12. PMID: 30445434.

2. Lonsdale J, Thomas J, Salvatore M, Phillips R, Lo E, Shad S, et al. The Genotype-Tissue Expression (GTEx) project. Nature Genetics. 2013 2013/06/01;45(6):580-5.