

Supplementary Table 1. Overview of study samples and genotyping platforms.

Dataset	Sample Size		Genotyping Platform	GWAS	Stage
	Case	Control			
PanScan I and II	3,525	3,642	Illumina HumanHap550 Infinium II, Human 610-Quad	STAGE I	
Female	1,684	1,757			
Male	1,841	1,885			
Cohort Studies	1,394	1,459			
Case-Control studies	2,131	2,183			
PanScan III	1,582	5,203	OmniExpress, Omni1M, Omni2.5 and Omni5M	STAGE I	
Female	801	1,337			
Male	781	3,866			
Cohort Studies	939	4,758			
Case-Control studies	643	445			
PanC4	3,933	3,651	Illumina OmniExpressExome	STAGE I	
Female	1,653	1,613			
Male	2,280	2,038			
Cohort Studies	0	0			
Case-Control studies	3,933	3,651			
PANDoRA	2,737	4,752	TaqMan	Replication	
Female	1,197	2,157			
Male	1,522	2,523			
Missing gender	18	72			
Cohort Studies	0	0			
Case-Control studies	2,737	4,752			
TOTAL Cohort	2,333	6,217			
TOTAL Case-control	9,444	11,031			
TOTAL	11,777	17,248			

Cases and control subjects included in the final analysis are listed. Genotype quality control is detailed in the Materials and Methods section.

Supplementary Table 2: Previously Reported Pancreatic Cancer Susceptibility Loci

Chr ^a SNP Position ^b Gene	Effect Allele (Minor)/ Reference Allele	Statistic	PANSCAN I&II	PANSCAN III	PANC4	All GWAS	PANDoRA	GWAS + PANDORA
1q32.1 rs2816938 199,985,368 <i>NR5A2</i>	A/T	Maf ^c cases;controls	0.25; 0.22	0.25; 0.23	0.27; 0.23			
		Info ^d	1	1	1			
		OR(CI)	1.25(1.17-1.33)	1.19(1.08 -1.30)	1.19(1.12 -1.27)	1.21(1.17-1.26)		
		p-value	1.81x10 ⁻⁸	2.33x10 ⁻³	2.80x10 ⁻⁶	3.36x10 ⁻¹⁵		
		Heterogeneity ^e				6.48x10 ⁻¹		
1q32.1 rs3790844 200,007,432 <i>NR5A2</i>	G/A	maf cases;controls	0.20; 0.24	0.20; 0.24	0.20; 0.23			
		info	g	g	g			
		OR(CI)	0.77(0.70-0.85)	0.86(0.74-0.97)	0.83(0.76 -0.91)	0.81(0.76-0.86)		
		p-value	2.16x10 ⁻¹⁰	7.62x10 ⁻³	6.87x10 ⁻⁶	7.62x10 ⁻¹⁶		
		heterogeneity				2.60x10 ⁻¹		
2p13.3 rs1486134 67,639,769 <i>ETAA1(2236bp 3')</i>	G/T	maf cases;controls	0.30; 0.28	0.29; 0.28	0.30; 0.28		0.29; 0.27	
		info	g	g	g		g	
		OR(CI)	1.10(1.03-1.17)	1.11(1.00 -1.21)	1.14(1.07 -1.21)	1.12(1.07-1.16)	1.16(1.06-1.27)	1.13(1.09-1.17)
		p-value	8.04x10 ⁻³	5.90x10 ⁻²	1.88x10 ⁻⁴	9.80x10 ⁻⁷	9.42x10 ⁻⁴	4.61x10 ⁻⁹
		heterogeneity				7.53x10 ⁻¹	3.32x10 ⁻²	1.04x10 ⁻¹
3q29 rs9854771 189,508,471 <i>TP63</i>	A/G	maf cases;controls	0.34; 0.37	0.34; 0.36	0.33; 0.36		0.34; 0.36	
		info	1	g	1			
		OR(CI)	0.87(0.81-0.93)	0.96(0.87 -1.06)	0.88(0.82 -0.94)	0.89(0.85-0.93)	0.93(0.86-1.01)	0.90(0.86-0.94)
		p-value	7.98x10 ⁻⁵	4.00x10 ⁻¹	1.28x10 ⁻⁴	1.14x10 ⁻⁷	1.01x10 ⁻¹	4.54x10 ⁻⁸
		heterogeneity				2.44x10 ⁻¹	8.15x10 ⁻¹	6.50x10 ⁻¹
5p15.33 rs2736098 1,294,086 <i>TERT</i>	T/C	maf cases;controls	0.26; 0.28	0.22; 0.27	0.24 0.27		0.22; 0.20	
		info	0.84	g	0.92		g	
		OR(CI)	0.85(0.77-0.93)	0.78(0.67-0.89)	0.83(0.75 -0.91)	0.83(0.78-0.88)	0.89(0.79-0.99)	0.84(0.79-0.88)
		p-value	6.11x10 ⁻⁵	1.28x10 ⁻⁵	1.95x10 ⁻⁶	5.80x10 ⁻¹⁴	1.68x10 ⁻²	6.86x10 ⁻¹⁵
		heterogeneity				5.19x10 ⁻¹		4.18x10 ⁻¹
5p15.33 rs35226131	T/C	maf cases;controls	0.02; 0.03	0.02; 0.03	0.02; 0.03			

1,295,373 <i>TERT, CLPTM1L</i>		info	0.77	0.84	0.98			
		OR(CI)	0.61(0.35-0.87)	0.66(0.35 -0.97)	0.71(0.51 -0.91)	0.67(0.53-0.81)		
		p-value	2.15x10 ⁻⁴	9.05x10 ⁻³	6.82x10 ⁻⁴	2.19x10 ⁻⁸		
		heterogeneity				6.95x10 ⁻¹		
5p15.33 rs401681 1,322,087 <i>CLPTM1L</i>	T/C	maf cases;controls	0.49; 0.45	0.49; 0.45	0.49; 0.44			
		info	g	0.996	g			
		OR(CI)	1.19(1.12-1.25)	1.20(1.11 -1.30)	1.19(1.13 -1.25)	1.19(1.15-1.23)		
		p-value	3.53x10 ⁻⁷	1.27x10 ⁻⁴	9.15x10 ⁻⁸	9.32x10 ⁻¹⁷		
		heterogeneity				9.73x10 ⁻¹		
7p13 rs17688601 40,866,663 <i>SUGCT</i>	A/C	maf cases;controls	0.24; 0.27	0.25; 0.27	0.25; 0.27		0.25; 0.28	
		info	g	g	g		g	
		OR(CI)	0.85(0.78-0.92)	0.92(0.81-1.02)	0.88(0.82-0.95)	0.88(0.83-0.93)	0.91(0.83-1)	0.88(0.84-0.93)
		p-value	4.14x10 ⁻⁵	1.14x10 ⁻¹	1.13x10 ⁻³	8.23x10 ⁻⁸	3.93x10 ⁻²	1.11x10 ⁻⁸
		heterogeneity				5.63x10 ⁻¹	7.25x10 ⁻²	1.70x10 ⁻¹
7q32.3 rs6971499 130,680,521 <i>LINC-PINT</i>	C/T	maf cases;controls	0.12;0.14	0.13; 0.16	0.13; 0.16		0.12; 0.15	
		info	0.95	g	g			
		OR(CI)	0.83(0.73-0.92)	0.79(0.66 -0.93)	0.82(0.73 -0.91)	0.82(0.76-0.88)	0.80(0.67-0.92)	0.81(0.76-0.87)
		p-value	1.52x10 ⁻⁴	7.12x10 ⁻⁴	2.32x10 ⁻⁵	4.32x10 ⁻¹¹	3.82x10 ⁻⁴	7.41x10 ⁻¹⁴
		heterogeneity				8.79x10 ⁻¹		9.43x10 ⁻¹
8q24.21 rs10094872 128,719,884 <i>MYC</i>	T/A	maf cases;controls	0.40; 0.36	0.39; 0.36	0.38; 0.36			
		info	0.94	0.96	0.97			
		OR(CI)	1.17(1.10-1.24)	1.18(1.08 -1.28)	1.11(1.04 -1.18)	1.14(1.10-1.19)		
		p-value	1.28x10 ⁻⁵	9.83x10 ⁻⁴	3.25x10 ⁻³	1.19x10 ⁻⁹		
		heterogeneity				4.55x10 ⁻¹		
8q24.21 rs1561927 129,568,078 <i>MIR1208</i>	C/T	maf cases;controls	0.25; 0.28	0.25; 0.27	0.24; 0.26		0.26; 0.28	
		info	g	g	g		g	
		OR(CI)	0.86(0.79-0.94)	0.87(0.76 -0.98)	0.92(0.84 -0.99)	0.89(0.84-0.93)	0.91(0.81-0.99)	0.89(0.85-0.93)
		p-value	1.06x10 ⁻⁴	1.06x10 ⁻²	2.74x10 ⁻²	6.18x10 ⁻⁷	3.69x10 ⁻²	7.09x10 ⁻⁸
		heterogeneity				4.54x10 ⁻¹		6.25x10 ⁻¹
9q34 rs505922	C/T	maf cases;controls	0.39; 0.35	0.41; 0.35	0.40; 0.35			
		info	1	1	g			

136,149,229 <i>ABO</i>		OR(CI)	1.21(1.14-1.28)	1.37(1.27 -1.48)	1.28(1.21 -1.34)	1.27(1.22-1.31)		
		p-value	4.78x10 ⁻⁸	4.56x10 ⁻¹⁰	1.00x10 ⁻¹²	7.35x10 ⁻²⁷		
		heterogeneity				1.13x10 ⁻¹		
13q12.2 rs9581943 28,493,997 <i>PDX1-AS1-PDX1</i>	A/G	maf cases;controls	0.43;0.41	0.44; 0.40	0.43; 0.39		0.44; 0.41	
		info	1	g	g			
		OR(CI)	1.12(1.06-1.19)	1.22(1.13 -1.32)	1.17(1.11 -1.24)	1.16(1.12-1.21)	1.12(1.03-1.20)	1.15(1.12-1.19)
		p-value	6.31x10 ⁻⁴	3.10x10 ⁻⁵	1.17x10 ⁻⁶	1.21x10 ⁻¹²	8.82x10 ⁻³	5.12x10 ⁻¹⁴
		heterogeneity				3.37x10 ⁻¹		4.19x10 ⁻¹
13q22.1 rs9543325 73,916,628 <i>KLF5 and KLF12</i>	C/T	maf cases;controls	0.44; 0.37	0.43; 0.38	0.43; 0.37			
		info	g	g	g			
		OR(CI)	1.26(1.19 -1.33)	1.19(1.09 -1.28)	1.24(1.17 -1.30)	1.24(1.19-1.28)		
		p-value	2.87x10 ⁻¹¹	5.10x10 ⁻⁴	1.91x10 ⁻¹⁰	1.22x10 ⁻²²		
		heterogeneity				6.04x10 ⁻¹		
16q23.1 rs7190458 75,263,661 <i>BCAR1</i>	A/G	maf cases;controls	0.06; 0.05	0.06; 0.04	0.06; 0.04		0.05; 0.04	
		info	0.74	g	g			
		OR(CI)	1.33(1.16-1.50)	1.65(1.43 -1.86)	1.27(1.12 -1.41)	1.36(1.26 -1.46)	1.34(1.13-1.54)	1.36(1.27-1.44)
		p-value	9.38x10 ⁻⁴	4.69x10 ⁻⁶	1.39x10 ⁻³	7.09x10 ⁻¹⁰	5.07x10 ⁻³	1.29x10 ⁻¹¹
		heterogeneity				1.27x10 ⁻¹		2.46x10 ⁻¹
17q25.1 rs7214041 70,401,476 <i>LINC00673</i>	T/C	maf cases;controls	0.13; 0.12	0.13; 0.11	0.14; 0.11		0.14; 0.12	
		info	0.96	g	g			
		OR(CI)	1.16(1.05-1.28)	1.27(1.10 -1.47)	1.32(1.20 -1.46)	1.25(1.18-1.31)	1.25(1.11-1.41)	1.25(1.19-1.30)
		p-value	4.04x10 ⁻³	1.39x10 ⁻³	1.29x10 ⁻⁸	6.58x10 ⁻¹²	3.37x10 ⁻⁴	9.49x10 ⁻¹⁵
		heterogeneity				1.59x10 ⁻¹	3.69x10 ⁻¹	3.36x10 ⁻¹
22q12.1 rs16986825 29,300,306 <i>ZNRF3</i>	T/C	maf cases;controls	0.17; 0.15	0.18; 0.15	0.17; 0.15		0.20; 0.18	
		info	1	g	g			
		OR(CI)	1.16(1.07-1.25)	1.22(1.09 -1.35)	1.13(1.04 -1.22)	1.16(1.10-1.21)	1.14(1.04-1.25)	1.15(1.10 -1.20)
		p-value	1.61x10 ⁻³	2.02x10 ⁻³	5.24x10 ⁻³	2.93x10 ⁻⁷	1.27x10 ⁻²	1.21x10 ⁻⁸
		heterogeneity				6.13x10 ⁻¹		7.97x10 ⁻¹

a. Cytogenetic regions according to NCBI Human Genome Build 37

b. SNP position according to NCBI Human Genome Build 37

c. Minor allele frequency

d. Quality of imputation metric. See online methods for more detail. If a SNP is genotyped and not imputed, a 'g' is reported

e. P-value from test of heterogeneity

Supplementary Table 3: Additional Suggestive Pancreatic Cancer Susceptibility Loci

Chr ^a SNP Position ^b Gene	Effect Allele (Minor)/ Referenc e Allele	Statistic	PANSCAN I&II	PANSCAN III	PANC4	All GWAS ^c	PANDoRA	GWAS + PANDORA ^d
1p13.1 rs351365 113046395 <i>WNT2B</i>	T/C	maf cases;controls	0.24; 0.25	0.23; 0.25	0.23; 0.26		0.23; 0.25	
		info	0.91	g	g		g	
		OR (CI)	0.93 (0.83 -1.21)	0.94 (0.81 -1.01)	0.86 (0.79 -0.94)	0.90 (0.85 -0.95)	0.92 (0.83 -1.01)	0.90 (0.86 - 0.95)
		p-value	6.66x10 ⁻²	2.39x10 ⁻¹	1.11x10 ⁻⁴	3.00x10 ⁻⁵	8.02x10 ⁻²	6.32x10 ⁻⁶
		heterogeneity				3.21x10 ⁻¹	3.97x10 ⁻¹	4.81x10 ⁻¹
9q31.3 rs10991043 106797388 <i>SMC2</i> (59153bp on 5')	C/T	maf cases;controls	0.38; 0.37	0.39; 0.37	0.40; 0.36		0.36; 0.36	
		info	g	g	g		g	
		OR (CI)	1.08 (1.01 -1.15)	1.02 (0.93 -1.13)	1.20 (1.13 -1.29)	1.12 (1.07-1.16)	1 (0.92 - 1.08)	1.09 (1.05 - 1.13)
		p-value	3.33x10 ⁻²	6.64x10 ⁻¹	3.08x10 ⁻⁸	3.53x10 ⁻⁷	9.19x10 ⁻¹	6.97x10 ⁻⁶
		heterogeneity				8.91x10 ⁻³	3.02x10 ⁻¹	6.57x10 ⁻³
12q24.31 rs1182933 121,454,622 <i>HNF1A</i>	T/C	maf cases;controls	0.33; 0.30	0.31; 0.30	0.32; 0.30		0.35; 0.33	
		info	0.99	g	g		g	
		OR (CI)	1.15 (1.08 - 1.22)	1.09 (0.98-1.19)	1.08 (1.01-1.15)	1.11(1.06-1.15)	1.12 (1.03 - 1.20)	1.11 (1.07 - 1.15)
		p-value	1.23x10 ⁻⁴	1.15x10 ⁻¹	3.97x10 ⁻²	9.54x10 ⁻⁶	1.15x10 ⁻²	3.49x10 ⁻⁷
		heterogeneity				3.94x10 ⁻¹		5.95x10 ⁻¹
20q13.11 rs6073450 43086648 <i>PKIG/HNF4A</i> (73788 bp on 5')	A/G	maf cases;controls	0.40; 0.38	0.39; 0.38	0.40; 0.37		0.41; 0.40	
		info	g	g	g		g	
		OR (CI)	1.08 (1.01 -1.16)	1.05 (0.95 -1.15)	1.13 (1.05 -1.21)	1.09 (1.05-1.14)	1.09 (1- 1.18)	1.09 (1.05 - 1.13)
		p-value	1.90x10 ⁻²	3.53x10 ⁻¹	4.07x10 ⁻⁴	3.40x10 ⁻⁵	4.92x10 ⁻²	4.55x10 ⁻⁶
		heterogeneity				4.32x10 ⁻¹	9.03x10 ⁻¹	9.14x10 ⁻¹

a. Cytogenetic regions according to NCBI Human Genome Build 37

b. SNP position according to NCBI Human Genome Build 37

c. Minor allele frequency

d. Quality of imputation metric. See online methods for more detail. If snp is genotyped and not imputed, a 'g' is reported

e. P-value from test of heterogeneity of the Stage 1 studies (PanScan I & II, PanScan III and PanC4) and Stage2 (PanScan I & II, PanScan III, PanC4 and PANDoRA)

Supplementary Table 4: Additional Loci selected for replication genotyping in the PANDORA population ($P < 1 \times 10^{-6}$)

Chr ^a SNP Position ^b Gene	Effect Allele (Minor)/ Reference Allele	Statistic	PANSCAN I/II 3,525 cases 3,642 controls	PANSCAN III 1,582 cases 5,203 controls	PANC4 3,933 cases 3,651 Controls	ALL GWAS 9,040 cases 12,496 controls	PANDoRA 2,737 cases 4,752 controls	GWAS + PANDoRa 11,777 cases 17,248 controls
2q24.1 rs12478462 153,654,720 <i>ARL6IP6</i>	G/T	maf ^c cases;controls	0.25; 0.23	0.26; 0.24	0.24; 0.22		0.23; 0.24	
		info ^d	1.0	g	g		g	
		OR (CI)	1.11 (1.03-1.20)	1.19 (1.07-1.33)	1.14(1.05-1.23)	1.14 (1.08-1.19)	0.98 (0.89- 1.07)	1.10 (1.05-1.14)
		p-value	9.52x10 ⁻³	1.80x10 ⁻³	9.89x10 ⁻⁴	3.03x10 ⁻⁷	5.91x10 ⁻¹	2.04x10 ⁻⁵
		Heterogeneity p-value ^e				5.83x10 ⁻¹		2.39x10 ⁻²
4q31.21 rs6537481 148,396,094 <i>EDNRA</i>	G/A	maf cases;controls	0.23; 0.24	0.24; 0.25	0.23; 0.25		0.26; 0.26	
		info	0.99	0.97	0.97	-	g	
		OR (CI)	0.89 (0.83 -0.97)	0.88 (0.79-0.98)	0.86 (0.79-0.92)	0.88 (0.83 -0.92)	1.01 (0.92-1.10)	0.90(0.87-0.94)
		p-value	5.15x10 ⁻³	2.54x10 ⁻²	6.69x10 ⁻⁵	1.15x10 ⁻⁷	9.12x10 ⁻¹	3.81x10 ⁻⁶
		Heterogeneity p-value				7.37x10 ⁻¹		6.10x10 ⁻²
9q31.3 rs2417487 106,887,581 <i>SMC2</i>	A/G	maf cases;controls	0.46; 0.43	0.46; 0.44	0.47; 0.44		0.45; 0.43	
		info	0.99	0.99	0.99		g	
		OR (CI)	1.10 (1.04 – 1.21)	1.05 (0.95 – 1.13)	1.14 (1.08-1.19)	1.11 (1.07-1.15)	1.03 (0.96-1.10)	1.09 (1.05-1.12)
		p-value	2.04x10 ⁻³	3.43x10 ⁻¹	6.72x10 ⁻⁶	1.49x10 ⁻⁷	3.79x10 ⁻¹	5.70x10 ⁻⁷
		Heterogeneity p-value				2.15x10 ⁻¹		9.19x10 ⁻²
16q24.1 rs7200646 86,335,351 <i>LINC01081/ LINC00917</i>	C/T	maf cases;controls	0.37:0.34	0.36:0.34	0.36:0.34		0.35:0.35	
		info	g	g	g		g	
		OR (CI)	1.13 (1.06-1.20)	1.14(1.04-1.24)	1.11 (1.04-1.18)	1.12 (1.07-1.17)	1 (0.92-1.08)	1.09 (1.05 – 1.13)
		p-value	6.32x10 ⁻⁴	9.64x10 ⁻³	2.02x10 ⁻³	1.39x10 ⁻⁷	9.31x10 ⁻¹	4.21x10 ⁻⁶
		Heterogeneity p-value				9.14x10 ⁻¹		8.01x10 ⁻²
17q21.1 rs77038344 38,644,214 <i>IGFBP4/TNS4</i>	T/C	maf cases;controls	0.09; 0.08	0.10; 0.08	0.09; 0.08		0.09;0.10	
		info	0.89	0.95	0.97	-	g	
		OR (CI)	1.18 (1.04-1.34)	1.30 (1.10 - 1.54)	1.19 (1.06-1.34)	1.17 (1.11 -1.24)	0.92 (0.81-1.05)	1.13 (1.06 - 1.19)

		p-value	8.88×10^{-3}	2.48×10^{-3}	2.89×10^{-3}	9.50×10^{-7}	2.01×10^{-1}	3.73×10^{-4}
		Heterogeneity p-value				6.52×10^{-1}		3.11×10^{-3}
22q11.1 rs450960 1831630 <i>MICAL3</i>	T/C	maf cases;controls	0.31; 0.29	0.33; 0.30	0.31; 0.30		0.29; 0.30	
		info	1.0	1.0	1.0	-		
		OR (CI)	1.10 (1.02-1.18)	1.27 (1.15 – 1.41)	1.08 (1.00-1.15)	1.11 (1.07 -1.15)	0.96 (0.89 -1.04)	1.08 (1.04-1.11)
		p-value	1.11×10^{-2}	4.68×10^{-6}	3.75×10^{-2}	7.71×10^{-7}	3.47×10^{-1}	1.40×10^{-4}
		Heterogeneity p-value				2.59×10^{-2}		4.16×10^{-4}

a. Cytogenetic regions according to NCBI Human Genome Build 37

b. SNP position according to NCBI Human Genome Build 37

c. Minor allele frequency

d. Quality of imputation metric. See online methods for more detail. If snp is genotyped and not imputed, a 'g' is reported

e. P-value from test of heterogeneity

Supplementary Table 5. Polygenic Risk Scores.

PRS percentile	OR (95% CI)	P-value	N	# cases (%)
<10%	0.40 (0.38-0.55)	$<2 \times 10^{-16}$	757	258 (34%)
10-20%	0.57 (0.47-0.68)	3.28×10^{-10}	756	294 (39%)
20-40%	0.78 (0.68-0.90)	7.27×10^{-4}	1513	708 (47%)
40-60%	1	-----	1513	801 (53%)
60-80%	1.18 (1.02-1.36)	2.59×10^{-2}	1513	862 (57%)
80-90%	1.40 (1.17-1.67)	2.06×10^{-4}	757	463 (61%)
>90%	2.20 (1.83-2.65)	$<2 \times 10^{-16}$	757	539 (71%)

Polygenic Risk Scores (PRS) were calculated in the PanC4 population.

Supplementary Table 6. Association results for Chinese and Japanese pancreatic cancer risk loci in participants of European descent in PanScan I, II, III and PanC4

Chr	GWAS study	SNP Position	Genotype category ^a	Info ^b	Reference allele	Effect allele	Subjects		Stage	Effect allele frequency		Allelic OR ^c (95% CI)	P ^d	P _{het} ^e
							Controls	Cases		Controls	Cases			
5p13.1	Chinese	rs2255280 39394989	i i i	0.776 0.782 0.796	C	A	3642	3525	PanScan I+II	0.9946	0.9935	0.77 (0.60-0.99)	0.299	
							5203	1582	PanScan III	0.9930	0.9935	1.16 (0.83-1.62)	0.664	
							3651	3933	PanC4	0.9944	0.9944	1.03 (0.81-1.32)	0.905	
									Combined			1.06 (0.91-1.24)	0.713	
10q26.11	Chinese	rs12413624 120278944	i i i	1.000 0.999 0.998	T	A	3642	3525	PanScan I+II	0.4386	0.4330	0.98 (0.95-1.02)	0.636	
							5203	1582	PanScan III	0.4369	0.4283	0.93 (0.89-0.98)	0.162	
							3651	3933	PanC4	0.4314	0.4289	0.99 (0.96-1.03)	0.833	
									Combined			0.98 (0.96-1.00)	0.294	
21q22.3	Chinese	rs1547374 43778895	g g g	1.000 1.000 1.000	A	G	3642	3525	PanScan I+II	0.3118	0.3128	1.00 (0.96-1.03)	0.956	
							5203	1582	PanScan III	0.3133	0.3404	1.14 (1.08-1.20)	0.012	
							3651	3933	PanC4	0.3114	0.3229	1.03 (1.00-1.07)	0.363	
									Combined			1.04 (1.02-1.06)	0.098	
21q21.3	Chinese	rs372883 30717737	i i g	0.999 1.000 1.000	T	C	3642	3525	PanScan I+II	0.4787	0.4818	1.01 (0.98-1.05)	0.714	
							5203	1582	PanScan III	0.4893	0.4959	1.06 (1.01-1.11)	0.241	
							3651	3933	PanC4	0.4984	0.4830	0.94 (0.90-0.97)	0.041	
									Combined			0.99 (0.97-1.01)	0.568	
22q13.32	Chinese	rs5768709 48929569	i i i	0.930 0.977 0.980	A	G	3642	3525	PanScan I+II	0.3894	0.3927	1.01 (0.97-1.04)	0.842	
							5203	1582	PanScan III	0.4010	0.4059	1.01 (0.96-1.06)	0.839	
							3651	3933	PanC4	0.4031	0.3909	0.94 (0.91-0.97)	0.079	
									Combined			0.98 (0.96-1.00)	0.356	
6p25.3	Japanese	rs9502893 1340189	g g g	1.000 1.000 1.000	C	T	3642	3525	PanScan I+II	0.5501	0.5434	0.97 (0.94-1.00)	0.392	
							5203	1582	PanScan III	0.5643	0.5382	0.86 (0.82-0.91)	0.002	
							3651	3933	PanC4	0.5592	0.5493	0.96 (0.93-1.00)	0.249	
									Combined			0.94 (0.92-0.97)	0.009	
7q36.2	Japanese	rs6464375 153625843	g i g	1.000 0.999 1.000	C	T	3642	3525	PanScan I+II	0.0555	0.0570	1.04 (0.97-1.12)	0.582	
							5203	1582	PanScan III	0.0583	0.0603	1.02 (0.92-1.13)	0.864	
							3651	3933	PanC4	0.0594	0.0600	1.01 (0.95-1.09)	0.833	
									Combined			1.02 (0.98-1.07)	0.580	
12p11.21	Japanese	rs708224 32436409	g i g	1.000 0.998 1.000	A	G	3642	3525	PanScan I+II	0.5927	0.5767	0.93 (0.9-0.97)	0.050	
							5203	1582	PanScan III	0.5761	0.5644	0.93 (0.89-0.98)	0.142	
							3651	3933	PanC4	0.5818	0.5908	1.04 (1-1.07)	0.261	
									Combined			0.98 (0.96-1.00)	0.257	

Results from unconditional logistic regression for SNPs marking published Chinese and Japanese pancreatic cancer susceptibility loci in participants of European descent from PanScan I-III and PanC4. A total of 9,040 pancreatic cancer patients and 12,496 control subjects with GWAS genotype and imputation data available were included. ^aGenotype category: g=genotyped, i=imputed. ^bInfo: imputation information content/accuracy score. ^cFor PanScan I+II, the analysis was adjusted for age, sex, study, arm and significant principal components; for PanScan III, the analysis was adjusted for age, sex, geographic region, and significant principal components; for PanC4, the analysis was adjusted for age, sex, study and significant principal components. ^d1 d.f. score test. ^eP value for test of heterogeneity. Chr: chromosome and band of reported locus.

Supplemental Table 7. DEPICT enrichment analysis showing tissues where genes from associated loci are highly expressed.

MeSH first level term	MeSH term	MeSH second level term	<i>P</i> -value*
Epithelial Cells	A11.436	Cells	5.06E-05
Hepatocytes	A11.436.348	Cells	9.18E-05
Gastrointestinal Tract	A03.556	Digestive System	4.23E-04
Intestines	A03.556.124	Digestive System	6.56E-04
Rectum	A03.556.124.526.767	Digestive System	7.14E-04
Lower Gastrointestinal Tract	A03.556.249	Digestive System	9.99E-04
Intestine Large	A03.556.249.249	Digestive System	1.06E-03
Colon	A03.556.249.249.356	Digestive System	1.12E-03
Intestine Small	A03.556.124.684	Digestive System	3.00E-03
Colon Sigmoid	A03.556.249.249.356.668	Digestive System	3.25E-03
Cecum	A03.556.249.249.209	Digestive System	3.65E-03
Salivary Glands	A03.556.500.760	Digestive System	4.37E-03
Ileum	A03.556.249.124	Digestive System	4.77E-03
Intestinal Mucosa	A03.556.124.369	Digestive System	4.81E-03
Parotid Gland	A03.556.500.760.464	Digestive System	6.77E-03
Upper Gastrointestinal Tract	A03.556.875	Digestive System	7.10E-03
Urinary Bladder	A05.810.890	Urogenital System	3.30E-03
Cervix Uteri	A05.360.319.679.256	Urogenital System	3.99E-03

DEPICT enrichment analysis was performed for GWAS significant pancreatic cancer risk loci from this publication and four other publications from pancreatic cancer GWAS in European populations (references 18-22). Shown are MeSH tissues where enrichment for pancreatic cancer risk loci was significant at FDR<0.05. The *P* value for the "pancreas" MESH term was 0.013 and was not significant after correction for multiple testing. Note that no genes or SNP-gene pairs were significant in DEPICT analysis at FDR<0.05 (data not shown). *Nominal *P*-values for DEPICT analysis for associations with FDR<0.05. MeSH: Medical Subject Headings from PubMed.

Supplementary Table 8. Pathway enrichment analysis using KEGG, GO Molecular Function and GO Biological Process annotation.

NGR	TNGR	NG	TNG	Hyp	Hyp*	Annotations
24	34208	5	48	1.83E-10	5.48E-09	(KEGG) 04950: Maturity onset diabetes of the young
NGR	TNGR	NG	TNG	Hyp	Hyp*	Annotations
898	34208	9	48	3.81E-06	3.12E-04	GO:0003700: sequence-specific DNA binding transcription factor activity (MF)
541	34208	7	48	1.00E-05	4.10E-04	GO:0043565: sequence-specific DNA binding (MF)
1785	34208	11	48	2.86E-05	7.81E-04	GO:0003677: DNA binding (MF)
163	34208	4	48	8.21E-05	1.68E-03	GO:0044212: transcription regulatory region DNA binding (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0004458: D-lactate dehydrogenase (cytochrome) activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0003721: telomeric template RNA reverse transcriptase activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0003964: RNA-directed DNA polymerase activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0047277: globoside alpha-N-acetylgalactosaminyltransferase activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0004380: glycoprotein-fucosylgalactoside alpha-N-acetylgalactosaminyltransferase activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0004381: fucosylgalactoside 3-alpha-galactosyltransferase activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:00030548: acetylcholine receptor regulator activity (MF)
1	34208	1	48	1.40E-03	7.67E-03	GO:0031208: POZ domain binding (MF)
24	34208	2	48	5.22E-04	8.56E-03	GO:0070491: repressing transcription factor binding (MF)
NGR	TNGR	NG	TNG	Hyp	Hyp*	Annotations
21	34208	3	48	3.39E-06	4.18E-04	GO:0034644: cellular response to UV (BP)
2	34208	2	48	1.93E-06	4.76E-04	GO:0035565: regulation of pronephros size (BP)
27	34208	3	48	7.41E-06	6.10E-04	GO:0030073: insulin secretion (BP)
578	34208	7	48	1.53E-05	9.46E-04	GO:0045944: positive regulation of transcription from RNA polymerase II promoter (BP)
6	34208	2	48	2.88E-05	1.02E-03	GO:0060261: positive regulation of transcription initiation from RNA polymerase II promoter (BP)
121	34208	4	48	2.57E-05	1.06E-03	GO:0031018: endocrine pancreas development (BP)
416	34208	6	48	2.49E-05	1.23E-03	GO:0000122: negative regulation of transcription from RNA polymerase II promoter (BP)
468	34208	6	48	4.79E-05	1.48E-03	GO:0045893: positive regulation of transcription, DNA-dependent (BP)
12	34208	2	48	1.26E-04	3.46E-03	GO:0030111: regulation of Wnt receptor signaling pathway (BP)
84	34208	3	48	2.28E-04	5.63E-03	GO:0007389: pattern specification process (BP)
20	34208	2	48	3.60E-04	8.09E-03	GO:0001824: blastocyst development (BP)
102	34208	3	48	4.04E-04	8.31E-03	GO:0009887: organ morphogenesis (BP)

Pathway enrichment analysis was performed for genes located within +/- 100 kb of each of the novel risk loci as well as for loci published previously by our PanScan and PanC4 GWAS. NGR: Number of annotated genes in the reference list; TNGR: total number of genes in the reference list; NG: number of annotated genes in the input list; TNG: Total number of genes in the input list; Hyp: hypergeometric *P*-value; Hyp*: FDR corrected hypergeometric *P*-value. A corrected (Hyp*) *P* value of 0.01 was used as a cutoff.

Supplementary Table 9: Expression QTL (eQTL) findings for novel pancreatic cancer risk loci. Genes in a 1MB region centered on the marker SNPs at each locus were assessed in GTEx pancreatic tissue samples.

Chr1p36.33: eQTLs for rs13303010						
Gene Symbol	Gencode Id	SNP	P-value	Effect Size*	T-Statistic	Standard Error
KLHL17	ENSG00000187961.9	rs13303010	2.10E-05	-0.42	4.4	0.094
NOCL2	ENSG00000188976.6	rs13303010	0.0010	0.39	-3.4	0.12
SAMD11	ENSG00000187634.6	rs13303010	0.02	-0.26	2.3	0.11
DVLI	ENSG00000107404.13	rs13303010	0.04	-0.14	2.1	0.07
<i>ANKRD65</i>	ENSG00000235098.4	rs13303010	0.05	-0.35	2	0.18
<i>PUSL1</i>	ENSG00000169972.7	rs13303010	0.08	0.17	-1.8	0.097
<i>ATAD3C</i>	ENSG00000215915.5	rs13303010	0.08	-0.28	1.8	0.16
<i>AGRN</i>	ENSG00000188157.9	rs13303010	0.13	0.14	-1.5	0.094
<i>RNF223</i>	ENSG00000237330.2	rs13303010	0.25	-0.2	1.2	0.17
<i>CCNL2</i>	ENSG00000221978.7	rs13303010	0.26	0.087	-1.1	0.077
<i>ISG15</i>	ENSG00000187608.5	rs13303010	0.34	-0.15	0.95	0.15
<i>VWAI</i>	ENSG00000179403.10	rs13303010	0.38	-0.1	0.88	0.12
<i>TTL10</i>	ENSG00000162571.9	rs13303010	0.40	-0.14	0.85	0.16
<i>C1orf159</i>	ENSG00000131591.13	rs13303010	0.47	-0.073	0.73	0.1
<i>ACAP3</i>	ENSG00000131584.14	rs13303010	0.48	-0.061	0.7	0.086
<i>PLEKHN1</i>	ENSG00000187583.6	rs13303010	0.49	-0.072	0.69	0.1
<i>UBE2J2</i>	ENSG00000160087.16	rs13303010	0.49	0.072	-0.69	0.1
<i>TAS1R3</i>	ENSG00000169962.4	rs13303010	0.50	-0.12	0.67	0.18
<i>MIR429</i>	ENSG00000198976.1	rs13303010	0.56	-0.1	0.58	0.18
<i>B3GALT6</i>	ENSG00000176022.3	rs13303010	0.60	0.069	-0.52	0.13
<i>SCN1D</i>	ENSG00000162572.15	rs13303010	0.65	0.054	-0.45	0.12
<i>MRPL20</i>	ENSG00000242485.1	rs13303010	0.67	-0.051	0.43	0.12
<i>LINC00115</i>	ENSG00000225880.4	rs13303010	0.79	0.038	-0.27	0.14
<i>TNFRSF18</i>	ENSG00000186891.9	rs13303010	0.84	0.037	-0.2	0.18
<i>FAM87B</i>	ENSG00000177757.1	rs13303010	0.85	-0.038	0.19	0.2
<i>AURKAP1</i>	ENSG00000175756.9	rs13303010	0.89	-0.014	0.13	0.1
<i>HES4</i>	ENSG00000188290.6	rs13303010	0.92	-0.013	0.099	0.13
<i>TNFRSF4</i>	ENSG00000186827.6	rs13303010	0.95	0.011	-0.064	0.16
<i>MXRA8</i>	ENSG00000162576.12	rs13303010	0.99	-0.0012	0.011	0.11
<i>SDF4</i>	ENSG00000078808.12	rs13303010	1.00	-0.00081	0.0056	0.14

Additional RefSeq genes in the 1MB region were either not found in GTEx or not sufficiently expressed. *The direction of effect is listed for the risk increasing allele from the GWAS.

Chr8q21.11: eQTLs for rs2941471						
Gene Symbol	Gencode Id	SNP	P-value	Effect Size*	T-Statistic	Standard Error
HNFA4G	ENSG00000164749.7	rs2941471	0.038	0.15	2.1	0.073
<i>CASC9</i>	ENSG00000249395.2	rs2941471	0.88	-0.018	-0.16	0.12

Additional RefSeq genes in the 1MB region were either not found in GTEx or not sufficiently expressed. *The direction of effect is listed for the risk increasing allele from the GWAS.

Chr17q12: eQTLs for rs4795218						
Gene Symbol	Gencode Id	SNP	P-value	Effect Size	T-Statistic	Standard Error
<i>TBC1D3</i>	ENSG00000197681.8	rs4795218	0.09	0.27	1.7	0.16
<i>TADA2A</i>	ENSG00000108264.12	rs4795218	0.22	-0.17	-1.2	0.14
<i>SOC57</i>	ENSG00000174111.8	rs4795218	0.36	0.081	0.91	0.089
<i>MRPL45</i>	ENSG00000174100.5	rs4795218	0.43	-0.064	-0.8	0.079
<i>HNFB1B</i>	ENSG00000108753.8	rs4795218	0.44	0.09	0.77	0.12
<i>ACACA</i>	ENSG00000132142.15	rs4795218	0.48	-0.073	-0.71	0.1
<i>DUSP14</i>	ENSG00000161326.8	rs4795218	0.50	-0.072	-0.67	0.11
<i>SYNRG</i>	ENSG00000006114.11	rs4795218	0.57	-0.084	-0.57	0.15
<i>GPR179</i>	ENSG00000188888.7	rs4795218	0.60	0.079	0.52	0.15
<i>TBC1D3H</i>	ENSG00000242384.3	rs4795218	0.64	-0.079	-0.47	0.17
<i>TBC1D3F</i>	ENSG00000185128.11	rs4795218	0.66	-0.069	-0.44	0.16
<i>DDX52</i>	ENSG00000141141.10	rs4795218	0.78	0.035	0.28	0.12
<i>TBC1D3C</i>	ENSG00000234972.4	rs4795218	0.99	-0.0028	-0.017	0.17

Additional RefSeq genes in the 1MB region were either not found in GTEx or not sufficiently expressed.

chr18q21.32: eQTLs for rs1517037						
Gene Symbol	Gencode Id	SNP	P-value	Effect Size	T-Statistic	Standard Error
<i>CCBE1</i>	ENSG00000183287.9	rs1517037	0.59	-0.061	-0.55	0.11
<i>GRP</i>	ENSG00000134443.5	rs1517037	0.82	-0.034	-0.22	0.15
<i>LMAN1</i>	ENSG00000074695.5	rs1517037	0.96	-0.002	-0.044	0.045
<i>MALT1</i>	ENSG00000172175.8	rs1517037	0.2	-0.15	-1.3	0.11
<i>SEC11C</i>	ENSG00000166562.4	rs1517037	0.94	-0.0043	-0.074	0.058
<i>ZNF532</i>	ENSG00000074657.9	rs1517037	0.18	-0.14	-1.4	0.1

Additional RefSeq genes in the 1MB region were either not found in GTEx or not sufficiently expressed.

Chr7p12.3: eQTLs for rs73328514						
Gene Symbol	Gencode Id	SNP	P-value	Effect Size	T-Statistic	Standard Error
<i>TNS3</i>	ENSG00000136205.12	rs73328514	0.34	0.095	0.95	0.099

Additional RefSeq genes in the 1MB region were either not found in GTEx or not sufficiently expressed.

8	7853491	0.71	0.89	16241443	C	A	0.84	0.46	0.4	0.61					Nrc3,Nkx2,Nkx3			3103.5 of GDFP
8	7853534	0.71	0.89	16257780	A	G	0.88	0.46	0.41	0.61					7 altered motifs			3103.5 of GDFP
8	7853586	0.71	0.89	16261149	G	A	0.88	0.46	0.4	0.61					Nkx3,Psalm1			3103.5 of GDFP
8	7853644	0.71	0.89	16263509	A	C	0.8	0.46	0.4	0.6				ENSR			7 altered motifs	3103.5 of GDFP
8	7853795	0.71	0.89	16264121	C	C	0.88	0.46	0.4	0.61								3103.5 of GDFP
8	7853797	0.71	0.89	16264121	A	G	0.88	0.46	0.4	0.61					Nkx2,Nkx3			3103.5 of GDFP
8	7853840	0.70	0.89	16271370	A	T	0.88	0.46	0.4	0.61					GATA3			3103.5 of GDFP

The numeric values in parentheses were calculated for diverging sites in protein structure. The resulting scores used change scores (CS) - Equations (5) as provided by SIFT to be interpreted. Rank 0 and 10 are "highly conserved/less likely altered" amino acids.

hMh132: rsl399918																				
17	5607499	0.77	0.98	111424921	G	A	0.06	0.13	0.14	0.21	1NG	5 sites	ENSR,IPSC,1,NG	PH2,GATA3			7 altered motifs	INSTR	intense	
17	5607799	1.00	1.00	14118169	G	A	0.04	0.23	0.32	0.22	7 sites	14 sites	9 sites	FNXAL,FXNA5,TCF4			8 altered motifs	INSTR	intense	
17	5607799	1.00	1.00	16119999	C	T	0.08	0.23	0.32	0.22	6 sites	13 sites	72 sites	16 altered motifs	CTCF,PU1,SDF1			7 altered motifs	INSTR	intense
17	5607961	0.97	1.00	141264144	A	C	0.09	0.21	0.34	0.23	JAY,STRM,1,NG	14 sites	MNS				4f	INSTR	intense	
17	5608538	1.00	1.00	14128270	G	A	0.08	0.23	0.31	0.23	9 sites	4 sites	ENSR,G1,ENSR				1 NR,YY1	INSTR	intense	
17	5607961	0.97	1.00	141264144	G	A	0.07	0.16	0.32	0.21	11 sites	4 sites	IPSC				4 altered motifs	INSTR	intense	
17	5608165	0.70	1.00	1412138469	G	C	0.02	0.16	0.32	0.19	4 sites	4 sites	IPSC	ZNF263			7 altered motifs	INSTR	intense	
17	5608207	0.76	0.94	141455811	A	C	0.03	0.16	0.32	0.22	ENSR,G1,PAN3						ZBTB24	INSTR	intense	

hMh132: rsl399927																					
18	5687628	0.87	0.98	142624144	G	A	0.13	0.22	0.17	0.18			ENSR,BS1,SKN1	BS1			GR,NBP1,YY1		110.5 of GDFP		
18	5687629	0.88	1.00	142624144	G	T	0.13	0.22	0.17	0.18			ENSR,BS1,SKN1				Hmg1,Mef2		110.5 of GDFP		
18	5687661	0.88	1.00	142624144	A	G	0.27	0.25	0.17	0.18			ENSR,BS1,SKN1				Pax5,2,Sp100		110.5 of GDFP		
18	5687682	0.88	1.00	142624144	T	C	0.13	0.22	0.17	0.18			ENSR,BS1						110.5 of GDFP		
18	5687717	0.88	1.00	142624144	G	A	0.13	0.22	0.17	0.18			ENSR,BS1				GATA3		100.5 of GDFP		
18	5687729	0.88	1.00	142624144	T	G	0.13	0.22	0.17	0.17			ENSR,BS1				GATA,Pu-1		100.5 of GDFP		
18	5687727	0.88	1.00	142624144	C	T	0.13	0.22	0.17	0.18			ENSR,BS1	IPSC					90.5 of GDFP		
18	5687793	0.88	1.00	142624144	C	T	0.13	0.22	0.17	0.18			ENSR,BS1				Mx1,PPAR		90.5 of GDFP		
18	5687897	0.88	1.00	142624144	A	AG	0.14	0.22	0.17	0.18			ENSR,BS1						4 altered motifs	90.5 of GDFP	
18	5687899	0.88	1.00	142624144	G	A	0.13	0.22	0.17	0.18			ENSR,BS1						7 altered motifs	90.5 of GDFP	
18	5687810	0.88	1.00	142624144	C	T	0.25	0.22	0.17	0.18							SRE,YY1,ZBTB24		90.5 of GDFP		
18	5687824	1.00	1.00	142624144	C	T	0.26	0.22	0.17	0.18										90.5 of GDFP	
18	5687862	0.88	1.00	142624144	G	A	0.16	0.22	0.17	0.18									7 altered motifs	90.5 of GDFP	
18	5687884	0.98	1.00	142624144	A	G	0.29	0.25	0.17	0.19									8 altered motifs	90.5 of GDFP	
18	5687941	0.98	1.00	142624144	A	G	0.29	0.25	0.17	0.19									8 altered motifs	90.5 of GDFP	
18	5687948	0.98	1.00	142624144	T	C	0.3	0.25	0.17	0.19									PRAB,SEF-1	90.5 of GDFP	
18	5687983	0.98	1.00	142624144	T	C	0.3	0.25	0.17	0.19									Pax5,TFE	90.5 of GDFP	
18	5687987	0.90	0.98	142624144	T	C	0.34	0.22	0.17	0.2			ESC						4f	70.5 of GDFP	
18	5888111	0.98	0.99	142624144	G	A	0.15	0.26	0.17	0.2									Stat3,Relb	70.5 of GDFP	
18	5888113	0.98	0.99	142624144	C	A	0.15	0.26	0.17	0.2									Relb	70.5 of GDFP	
18	5888177	0.88	0.99	142624144	T	C	0.34	0.24	0.17	0.19			BEN						7 altered motifs	70.5 of GDFP	
18	5888319	0.88	0.99	142624144	T	G	0.32	0.24	0.17	0.19			BEN	PAN3						7 altered motifs	70.5 of GDFP
18	5888320	0.88	0.99	142624144	T	G	0.32	0.24	0.17	0.19										10 altered motifs	70.5 of GDFP

Rank 0 on SIFT and 10000 data was used for this analysis. The most significant variant at each rank locus is highlighted in a light yellow color.

Supplementary Table 11. Change in probability of transcription factor binding site (TFBS) motif presence due to allelic changes at SNPs at the 1p36.33 risk locus.

SNP Name	Transcription Factor Motif	P-value 1	P-value 2	Fold Change in P-value	up/down	Database
rs13303160	SMARCC1	1.1E-06	2.1E-04	197	down	HOCOMOCO
rs13303160	FOSL1	1.3E-06	2.6E-04	196	down	JASPAR
rs13303160	JUND	1.7E-05	1.6E-03	94	down	HOCOMOCO
rs13303160	BACH2	3.3E-06	3.0E-04	89	down	SwissRegulon
rs13303160	BATF	3.4E-05	2.9E-03	86	down	HOCOMOCO
rs13303160	FOSL2	7.1E-06	5.3E-04	74	down	JASPAR
rs13303160	JUNB	5.6E-06	3.8E-04	67	down	JASPAR
rs13303327	PURA	9.2E-05	1.5E-06	63	up	HOCOMOCO
rs13303160	FOSB	7.5E-06	3.6E-04	48	down	HOCOMOCO
rs13303160	PAX5	2.2E-04	1.0E-02	47	down	HOCOMOCO
rs13303160	FOS	1.2E-05	5.1E-04	43	down	HOCOMOCO
rs13303160	FOS, FOSB, FOSL1, JUNB, and JUND	2.2E-05	8.9E-04	41	down	SwissRegulon
rs10465242	GCM1	9.9E-03	2.4E-04	41	up	HT-SELEX
rs111748052*	BRCA1	2.1E-02	8.7E-01	41	down	JASPAR
rs7524174	PAX2	6.1E-05	2.4E-03	39	down	HOCOMOCO
rs3935066	MZFI	1.1E-04	4.1E-03	38	down	JASPAR
rs7524174	MAFG and NEF2L1	2.4E-04	9.2E-03	38	down	JASPAR
rs111748052*	OCT1	5.0E-01	1.3E-02	37	up	TRANSFAC
rs13303160	JUN	3.5E-05	1.3E-03	37	down	HOMER
rs4970445	HINFP	8.8E-05	3.1E-03	35	down	HT-SELEX
rs13303327	SPI1	1.0E-04	3.4E-03	34	down	JASPAR
rs10465242	HLTF	8.3E-05	2.7E-03	32	down	HOCOMOCO
rs4970445	PURA	1.9E-05	6.2E-04	32	down	HOCOMOCO
rs13303160	JUNB	7.1E-06	2.2E-04	31	down	HOCOMOCO
rs4970445	TCF4	1.4E-02	4.6E-04	30	up	HT-SELEX
rs7524174	THAP1	1.1E-03	3.8E-05	29	up	HOCOMOCO
rs13303160	JUND	2.4E-05	6.8E-04	28	down	JASPAR
rs4970445	KLF15	8.7E-05	3.2E-06	28	up	HOCOMOCO
rs7524174	NFE2L1	3.5E-04	9.2E-03	27	down	SwissRegulon
rs13303160	JUN	7.6E-05	2.0E-03	26	down	JASPAR
rs13303010	GFI1B	4.9E-05	1.3E-03	26	down	SwissRegulon
rs13303160	JUN	1.3E-05	3.4E-04	26	down	HOCOMOCO
rs13303327	YY1	5.9E-06	1.5E-04	25	down	HOCOMOCO
rs13303160	FOS	5.9E-05	1.5E-03	25	down	JASPAR
rs3935066	TBX1	1.8E-04	4.5E-03	25	down	HT-SELEX
rs13303327	EHF	1.1E-05	2.7E-04	24	down	HOCOMOCO
rs7524174	NFE2L2	1.7E-04	3.9E-03	24	down	JASPAR
rs13303160	FOSL2	1.6E-05	3.6E-04	23	down	SwissRegulon
rs4970445	ZNF354C	7.9E-03	3.5E-04	23	up	JASPAR
rs13303160	BATF and JUN	1.7E-04	3.9E-03	23	down	JASPAR
rs13303160	NFE2	5.4E-05	1.2E-03	22	down	SwissRegulon
rs13303327	TEAD1	3.8E-04	8.2E-03	22	down	HOCOMOCO
rs4970445	PKNOX2	5.0E-03	2.3E-04	22	up	HOCOMOCO
rs13303160	FOSL1	2.7E-05	5.6E-04	21	down	HOCOMOCO
rs13303327	ELF1	1.4E-04	2.9E-03	21	down	JASPAR
rs4970445	HINFP	1.0E-04	2.1E-03	20	down	JASPAR
rs4970445	ELF2	1.1E-04	2.2E-03	20	down	HOCOMOCO
rs3935066	ZNF219	1.5E-04	2.8E-03	19	down	HOCOMOCO
rs3935066	TBX2	1.4E-04	2.7E-03	19	down	HT-SELEX
rs4970445	HINFP	9.6E-05	1.8E-03	19	down	HOCOMOCO
rs3935066	GSC2	3.4E-04	6.1E-03	18	down	HOCOMOCO
rs7524174	ESRRA	3.6E-04	6.4E-03	18	down	HT-SELEX
rs3935066	ZEB1	4.9E-03	2.9E-04	17	up	JASPAR
rs4970445	EN1 and EN2	7.1E-03	4.2E-04	17	up	SwissRegulon
rs13303160	FOSL2	2.2E-05	3.6E-04	16	down	HOCOMOCO
rs10465242	ASCL2	4.3E-03	2.7E-04	16	up	HOCOMOCO
rs3935066	SREBF1	3.6E-04	5.5E-03	15	down	HOMER
rs10465242	NKX2-8	4.6E-04	7.0E-03	15	down	HOCOMOCO
rs3935066	ZNF148	1.6E-04	2.5E-03	15	down	HOCOMOCO
rs13303327	ZNF143	7.4E-03	4.8E-04	15	up	HOMER
rs13303327	ATO1H1	4.0E-04	6.0E-03	15	down	JASPAR
rs7524174	SREBF2	2.8E-04	4.1E-03	15	down	JASPAR
rs4970445	ZIC2	2.5E-03	1.7E-04	15	up	HOCOMOCO
rs13303160	NFE2L2	1.6E-05	2.3E-04	15	down	SwissRegulon
rs7524174	NFE2	2.2E-04	3.2E-03	15	down	HOCOMOCO
rs7524174	ESRRG	8.3E-05	1.2E-03	15	down	HT-SELEX

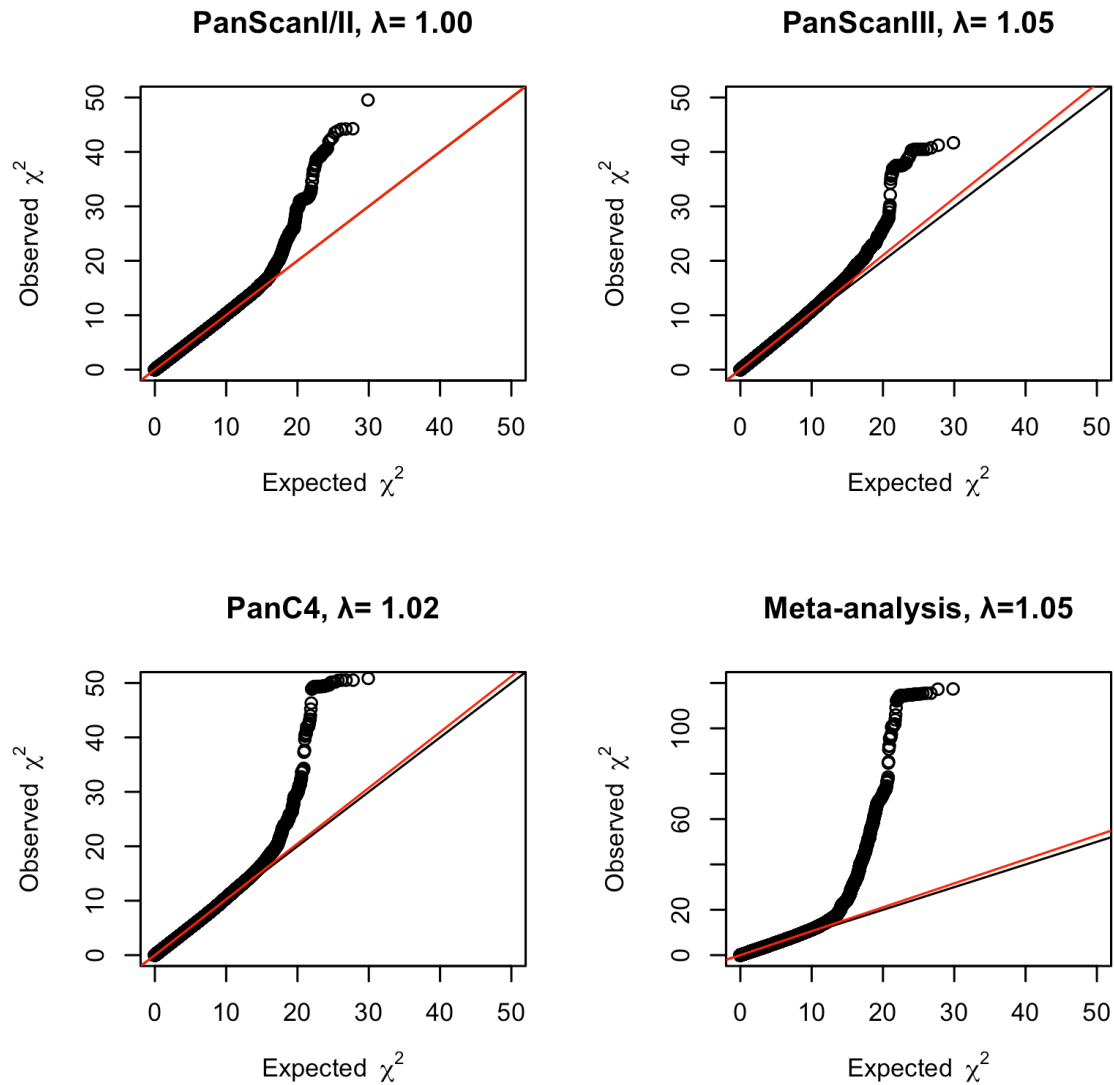
Probability 1 and Probability 2 correspond to the probability of the given TFBS motif with allele 1 or allele 2 of the specified SNP using PERFECTOS-APE analysis. The fold change represents the change in P-value for the TFBS motif.

* The probability and fold change were calculated by sTRAP (see Methods). Note that another indel, rs113491766, was also assessed by sTRAP but no differences above a fold change score of 15 were noted.

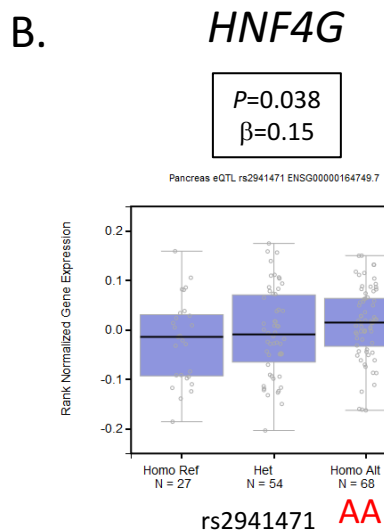
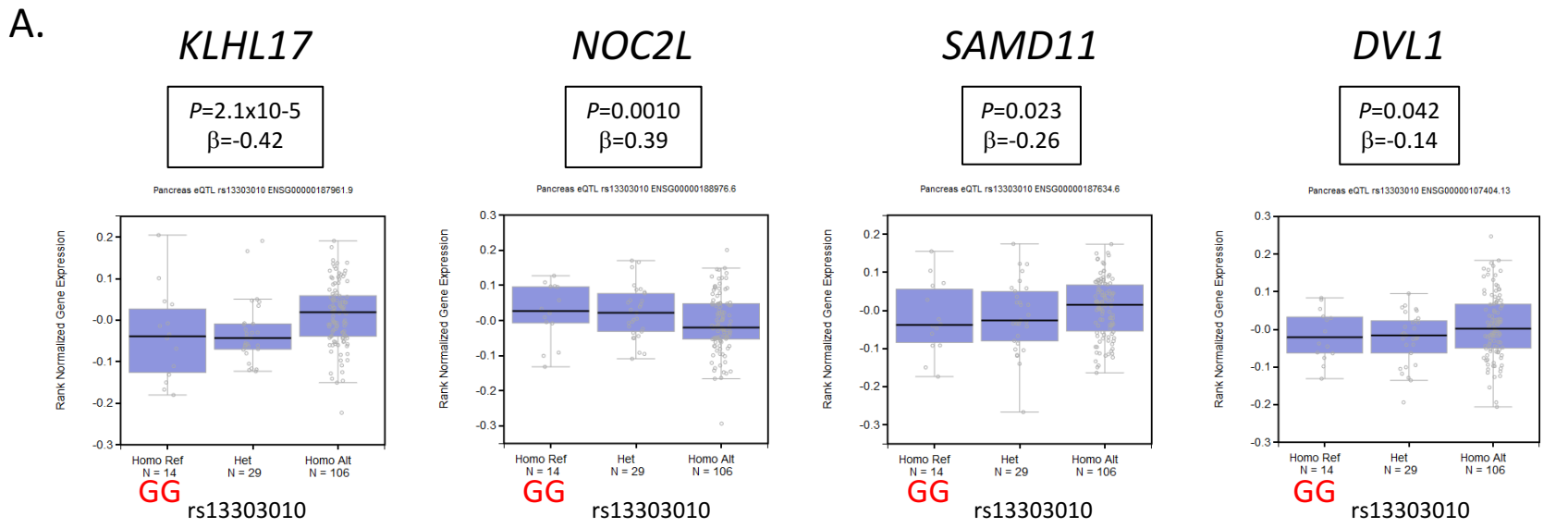
Supplementary Table 12. Differential gene expression in pancreatic tumors and histologically normal pancreatic tissue samples. Expression was assessed by mRNA-seq and compared in pancreatic tumors vs. histologically normal pancreatic tissue samples (TvN) and in pancreatic cell lines vs. histologically normal pancreatic tissue samples (CvN) for genes closest to reported variants on chromosomes 1p36.33 (*KLHL17*, *NOC2L*, *PLEKHN1*, *SAMD11* and *DVLI*), 8q21.11 (*HNF4G*), 17q12 (*HNF1B*) and 18q21.32 (*GRP*).

Gene Name	<i>KLHL17</i>	<i>NOC2L</i>	<i>PLEKHN1</i>	<i>SAMD11</i>	<i>DVLI</i>	<i>TNS3</i>	<i>HNF4G</i>	<i>HNF1B</i>	<i>GRP</i>
Entrez ID	339451	26155	84069	148398	1855	64759	3174	6928	2922
Normal 1	225.97	3660.06	28.71	587.03	4156.10	17699.93	1571.47	6237.08	356.51
Normal 2	273.89	4658.32	28.49	528.51	7315.98	22237.89	1743.46	4543.77	18.97
Normal 3	210.79	5909.00	22.12	871.09	7378.60	12606.85	1802.53	2803.25	1.16
Normal 4	563.04	5229.28	28.05	345.66	9502.26	21113.19	1978.71	4057.02	33.03
Normal 5	665.38	5353.50	26.48	206.24	10426.15	20124.43	1779.38	4293.38	10.14
Normal 6	915.91	5619.71	15.32	503.41	11117.67	22451.52	1367.77	7814.49	41.28
Normal 7	611.70	5172.29	156.63	1003.60	11257.82	26456.71	1402.82	7324.82	24.28
Normal 8	640.49	5030.28	36.14	745.72	11857.35	13787.15	549.33	1459.15	33.47
Normal 9	775.77	4815.84	0.10	632.31	10897.38	17744.63	1550.60	5904.95	66.12
Normal 10	322.31	5198.63	17.95	453.26	8587.31	17252.56	2044.12	2995.59	180.59
Tumor 1	583.56	6081.74	639.80	987.91	8825.92	11187.18	187.22	126.76	176.22
Tumor 2	227.66	2735.56	446.21	965.18	3073.61	14834.16	757.05	2662.97	287.69
Tumor 3	449.99	5622.10	623.81	564.39	3706.07	11838.02	1194.45	1023.96	362.12
Tumor 4	191.12	3964.56	120.28	1661.55	3529.93	10236.65	655.85	1347.16	545.46
Tumor 5	255.93	3611.40	128.60	1152.09	3647.30	19646.41	840.59	1676.55	236.45
Tumor 6	296.33	2934.45	260.18	1068.44	3666.85	17518.22	1384.42	1639.57	230.18
Tumor 7	159.31	2256.26	111.42	471.82	1767.52	13104.24	739.50	1392.81	150.64
Tumor 8	415.46	3262.21	334.37	678.51	3231.22	16676.89	989.86	2412.82	58.16
PANC-1	1895.65	21385.42	1112.92	3537.45	17241.69	55621.16	17.46	0.30	0.00
AsPC-1	375.03	8200.25	430.40	399.51	6118.31	8344.57	1763.78	0.12	0.00
BxPC-3	504.65	11016.30	664.76	472.14	5255.31	6447.52	305.91	2.50	0.00
CFPAC-1	718.15	11265.71	857.47	344.86	7538.27	11589.33	459.19	3033.01	0.00
SU8686	1202.52	16523.64	1143.64	584.81	11208.20	16336.15	345.72	547.98	0.00
MIAPaCa-2	805.96	22802.91	211.13	930.75	4925.21	21485.32	0.02	0.02	0.00
SW1990	1051.25	10028.07	1329.39	362.49	14119.23	11008.89	10.01	0.10	0.00
CAPAN-1	508.93	10711.86	430.83	433.39	4583.40	15843.78	190.49	1160.60	0.00
Hs766T	437.08	10898.64	59.27	356.77	5662.38	32046.28	0.00	9.08	0.00
Differential expression in pancreatic tumor samples as compared to histologically normal samples (TvN)									
logCPM	1.64	5.02	0.28	2.43	5.64	6.94	3.18	4.58	0.18
SignedFC	-1.72	-1.32	7.72	1.60	-2.47	-1.39	-1.79	-3.29	3.35
P-Value	0.105	0.083	1.81E-07	0.053	2.10E-05	0.110	0.005	5.54E-06	0.007
Differential expression in pancreatic tumor cell lines as compared to histologically normal samples (CvN)									
logCPM	2.67	6.50	1.91	2.72	6.33	7.47	2.99	4.40	NA
SignedFC	2.06	3.98	21.50	1.86	1.25	1.41	-3.32	-6.33	NA
P-Value	0.010	9.69E-10	3.98E-11	0.040	0.186	0.096	0.036	0.009	NA

Gene expression values are listed as adjusted counts per million (CPM) as per analysis in EdgeR. Normal samples were histologically normal tumor adjacent tissue samples. Signed fold changes were calculated in EdgeR. Tumor cellularity for tumor samples ranged from 60-90%. Data was generated as part of Hoskins et al. (2014) Carcinogenesis (PMID:25233928)⁵⁰.



Supplementary Figure 1. Quantile-quantile (Q-Q) plot of the association results in PanScan I+II (top left panel), PanScan III (top right panel), PanC4 (bottom left panel) and the meta-analysis of all three datasets (bottom right panel).



Supplementary Figure 2: Expression quantitative trait loci (eQTLs) for marker SNPs on chromosomes 1p36.33 (A.) and 8q21.11 (B.) in histologically normal pancreatic tissue samples from GTex (n=149). Expression QTLs were tested for the five GWAS significant risk loci. Nominally significant eQTLs are shown here. These were attempted for replication in the LTG and TCGA eQTL sample sets (Table 2 and Figure 2). Pancreatic cancer risk increasing alleles are indicated in red. The eQTL effect size is indicated for the GWAS risk increasing allele.