

Genome-wide association study identifies multiple susceptibility loci for pancreatic cancer

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Supplemental Table 1. Description of studies included in PanScan III

Study	No. of cases	No. of controls	Location	Source of cases	Study reference
STAGE 1: PanScan III GWAS					
<i>Stage 1 Cohort Studies</i>					
Agricultural Health Study (AHS)	27		USA	Linkage to state cancer registries.	Alavanja MC, et al. Cancer and noncancer risk to women in agriculture and pest control: the Agricultural Health Study. J Occup Med. 1994Nov;36(11):1247-50. [PMID: 7532217]
The Alpha-Tocopherol, Beta-Carotene Prevention Study (ATBC)	44	217	Finland	Linkage to Finnish Cancer registry	The alpha-tocopherol, beta-carotene lung cancer prevention study: design, methods, participant characteristics, and compliance. The ATBC Cancer Prevention Study Group. Ann Epidemiol. 1994 Jan;4(1):1-10. [PMID: 8205268]
Cancer Prevention Study (CPS-II)	158	214	USA	Identified through self-report on biannual questionnaires starting in 1997 or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Calle EE. et al. The American Cancer Society Cancer Prevention Study II Nutrition Cohort: rationale, study design, and baseline characteristics. Cancer. 2002;94:2490-501. [PMID:11900235]
European Prospective Investigation Into Cancer and Nutrition Study (EPIC)	174	263	Europe	Cancer registries in participating countries (Denmark, Italy, The Netherlands, Norway, Spain, Sweden and the UK) and through health insurance records, cancer and pathology registries, and active follow-up of study subjects and next of kin (France, Germany, and Greece)	Riboli E. et al. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. 1997;26(1):S6-14. [PMID:9126529] Riboli E. et al. European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr. Public Health Nutr 2002;5(6B):1113-24. [PMID:12639222]
Health Professionals Follow-up Study (HFPS)	25	84	USA	Identified through self-report on biannual questionnaires or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Rimm E. et al. Prospective study of alcohol consumption and risk of coronary disease in men. Lancet. Lancet 1991;338:464-8. [PMID: 1678444]

The Melbourne Collaborative Cohort Study (MCCS)	77	75	Australia	Linkage to national cancer registries.	Giles GG. et al. The Melbourne Collaborative Cohort Study. IARC Sci Publ. IARC Sci Publ 2002;156:69-70. [PMID: 12484128]
Multiethnic Cohort Study of Diet and Health (MEC)	28	200	USA	Linkage to the Hawaii Tumor Registry, the Cancer Surveillance Program of Los Angeles County, and the California State Cancer Registry	Kolonel LN et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am J Epidemiol. 2000 Feb 15;151(4):346-57. [PMID:10695593]
Nurse's Health Study (NHS)	29	437	USA	Identified through self-report on biannual questionnaires or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Colditz GA. et al. The Nurses' Health Study: lifestyle and health among women. Nat Rev Cancer. Nat Rev Cancer 2005;5:388-96. [PMID: 15864280]
Physicians Health Study (PHS)	15		USA	Identified through self-report on biannual questionnaires or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Manson JE et al. Aspirin in the primary prevention of angina pectoris in a randomized trial of United States physicians. <i>Am J Med.</i> 1990;89(6):772-776. [PMID:2252045]
Prostate, Lung, Colorectal, Ovarian Cancer Screening Trial (PLCO)	91	3042	USA	Self-report through annual questionnaires. Confirmed by pathology reports and medical records.	Hayes RB et al. Methods for etiologic and early marker investigations in the PLCO trial. Mutat Res. Mutat Res 2005;592:147-54. [PMID: 16054167]
Selenium and Vitamin E Cancer Prevention Trial (SELECT)	54		USA	Self-report through bi-annual clinic visits during the trial. Confirmed by pathology reports.	Lippman SM et al. Designing the Selenium and Vitamin E Cancer Prevention Trial (SELECT). J Natl Cancer Inst. 2005 Jan 19;97(2):94-102. [PMID: 15657339]
Vitamins and Lifestyle Study (VITAL)	48		USA	Linkage to the western Washington state SEER registry	White E et al. VITamins And Lifestyle cohort study: study design and characteristics of supplement users. Am J Epidemiol. 2004;159:83-93. [PMID:14693663]
Women's Health Initiative (WHI)	169	226	USA	Self-report through semi-annual clinic visits or annual	Anderson GL, et al. Implementation of the Women's Health Initiative study design. Ann Epidemiol. 2003

contact. Verified
through medical
records.

Oct;13(9 Suppl):S5-17.
[PMID: 14575938]

Total stage 1 cohort studies	939	4,758			
<i>Stage 1 Case series or case-control studies</i>					
Gastrointestinal Cancer Clinic of Dana-Farber Cancer Institute Study (DFCI-GCC)	360		USA	Pathologically-confirmed cases sequentially identified from an outpatient gastrointestinal cancer clinic	
PANcreatic Disease ReseArch (PANDoRA) consortium, Heidelberg	194		Germany	Confirmed cases from Heidelberg University Hospital	Campa D et al. Genetic susceptibility to pancreatic cancer and its functional characterisation: the PANcreatic Disease ReseArch (PANDoRA) consortium. Dig Liver Dis. 2013 Feb;45(2):95-9. [PMID: 23206934]
PANKRAS-II	89	445	Spain	Hospital-based, confirmed by oncologist review	Porta M et al; PANKRAS II Study Group. Timing of blood extraction in epidemiologic and proteomic studies: results and proposals from the PANKRAS II Study. Eur J Epidemiol. 2007;22(9):577-88. Epub 2007 Jul 18. Erratum in: Eur J Epidemiol. 2008;23(1):77. [PMID: 17636417]
Total stage 1 case series or case-control studies	643	445			
TOTAL STAGE 1 GWAS	1,582	5,203			

STAGE 2: PanScan I and II GWAS

Stage 2 Cohort studies

The Alpha-Tocopherol, Beta-Carotene Prevention Study (ATBC)	194	206	Finland	Linkage to Finnish Cancer registry	The alpha-tocopherol, beta-carotene lung cancer prevention study: design, methods, participant characteristics, and compliance. The ATBC Cancer Prevention Study Group. Ann Epidemiol. 1994 Jan;4(1):1-10. [PMID: 8205268]
Give Us a Clue to Cancer and Heart Disease Study (CLUEII)	67	70	Washington County MD, USA	Washington County Cancer Registry, Maryland State Cancer Registry	Gallicchio, L. et al. Single nucleotide polymorphisms in inflammation-related genes and mortality in a community-based cohort in Washington County, Maryland. Am J Epidemiol. 2008 Apr 1;167(7):807-13. [PMID: 18263601]
Cancer Prevention Study (CPS II)	115	115	USA	Identified through self-report on biannual questionnaires	Calle EE. et al. The American Cancer Society Cancer Prevention Study II Nutrition Cohort: rationale, study design, and baseline

				starting in 1997 or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	characteristics. <i>Cancer</i> . <i>Cancer</i> 2002;94:2490-501. [PMID:11900235]
European Prospective Investigation Into Cancer and Nutrition Study (EPIC)	418	432	Europe	Cancer registries in participating countries (Denmark, Italy, The Netherlands, Norway, Spain, Sweden and the UK) and through health insurance records, cancer and pathology registries, and active follow-up of study subjects and next of kin (France, Germany, and Greece)	Riboli E. et al. The EPIC Project: rationale and study design. <i>European Prospective Investigation into Cancer and Nutrition. Int J Epidemiol. Int J of Epidemiol</i> 1997;26(1):S6-14. [PMID:9126529] Riboli E. et al. <i>European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. Public Health Nutr. Public Health Nutr</i> 2002;5(6B):1113-24. [PMID:12639222]
Health Professionals Follow-up Study (HPFS)	52	49	USA	Identified through self-report on biannual questionnaires or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Rimm E. et al. Prospective study of alcohol consumption and risk of coronary disease in men. <i>Lancet. Lancet</i> 1991;338:464-8. [PMID: 1678444]
Nurse's Health Study (NHS)	81	83	USA	Identified through self-report on biannual questionnaires or through linkage with the National Death Index. Verified by medical records or linkage to state cancer registries.	Colditz GA. et al. The Nurses' Health Study: lifestyle and health among women. <i>Nat Rev Cancer. Nat Rev Cancer</i> 2005;5:388-96. [PMID: 15864280]
The New York University Women's Health Study (NYU-WHS)	10	11	USA	Self-report through questionnaires every 2-4 years, confirmed by medical and pathology records; and linkages to tumor registries of NY, NJ and Florida and NDI	Zeleniuch-Jacquotte A, et al. Postmenopausal levels of sex hormones and risk of breast carcinoma in situ: results of a prospective study. <i>Int J Cancer.</i> 2005 Mar 20;114(2):323-7. [PMID:15540225]
Physicians Health Study (PHS)	46	53	USA	Identified through self-report on biannual questionnaires or through linkage	Manson JE et al. Aspirin in the primary prevention of angina pectoris in a randomized trial of United States physicians. <i>Am J Med.</i> 1990;89(6):772-776.

				with the National Death Index. Verified by medical records or linkage to state cancer registries.	[PMID:2252045]
Prostate, Lung, Colorectal, Ovarian Cancer Screening Trial (PLCO)	180	201	USA	Self-report through annual questionnaires. Confirmed by pathology reports and medical records.	Hayes RB et al. Methods for etiologic and early marker investigations in the PLCO trial. Mutat Res. 2005;592:147-54. [PMID: 16054167]
Women's Health Initiative (WHI)	206	208	USA	Self-report through semi-annual clinic visits or annual contact. Verified through medical records.	Anderson GL, et al. Implementation of the Women's Health Initiative study design. Ann Epidemiol. 2003 Oct;13(9 Suppl):S5-17. [PMID: 14575938]
Womens' Heath Study (WHS)	25	31	USA	Self report or death follow-up.	Rexrode KM, et al. Baseline characteristics of participants in the Women's Health Study. J Womens Health Gend Based Med. 2000 Jan-Feb;9(1):19-27. [PMID: 10718501] Wolpin BM, et al. Hyperglycemia, insulin resistance, impaired pancreatic β -cell function, and risk of pancreatic cancer. J Natl Cancer Inst. 2013 Jul 17;105(14):1027-35. [PMID: PMC3714020]
Total stage 2 cohort studies	1,394	1,459			
Stage 2 Case-Control studies					
Johns Hopkins Hospital	178	175	USA	JHU Clinic Controls spouse (in-Law) of pancreatic cancer patient, no history pancreatic cancer	
Mayo Clinic Molecular Epidemiology Case-Control Study	635	617	Upper Mid-West: Minn., Iowa, Wisconsin, USA	Clinic Controls General Medical Evaluation (primary care) patients, no personal history of cancer (except non-melanoma of skin)	McWilliams RR, et al. Polymorphisms in DNA repair genes, smoking, and pancreatic adenocarcinoma risk. Cancer Res. 2008 Jun 15;68(12):4928-35. [PMID: PMC2652067]
Memorial Sloan Kettering	126	134	NYC, USA	Clinic Controls spouses of patients; visitors accompanying patients, no personal history of cancer (except non-melanoma of skin)	Olson SH, et al. Allergies, variants in IL-4 and IL-4R alpha genes, and risk of pancreatic cancer. Cancer Detect Prev. 2007;31(5):345-51. [PMID: 18031948]
MD Anderson	256	266	Texas, USA	Hospital Controls friends and spouses of non-pancreatic cancer	Hassan MM, et al. Risk factors for pancreatic cancer:case-control study. Am J Gastroenterol. 2007

				patients at MDA, no personal history of cancer (except non-melanoma of skin)	Dec;102(12):2696-70. [PMID: PMC2423805]
PACIFIC Study	246	241	Seattle, WA and Northern California, USA	Group Health (Seattle Pufet Sound) and Kaiser Permanente	
Toronto	278	259	Ontario (cases) Greater Toronto (controls), Canada	Population-based cancer registry Controls Ontario population-based case control study of colorectal cancer, ARCTIC	Eppel A, et al. Allergies are associated with reduced pancreas cancer risk: A population-based case-control study in Ontario, Canada. Int J Cancer. 2007 Nov 15;121(10):2241-5. [PMID: 17582608]
UCSF	206	212	San Francisco Bay Area, USA	Population-based cancer registry/ Controls random digit-dial within six SF Bay Area counties, no history pancreatic cancer	Duell EJ, et al. Detecting pathway-based gene-gene and gene-environment interactions in pancreatic cancer. Cancer Epidemiol Biomarkers Prev. 2008 Jun;17(6):1470-9. [PMID: 18559563]
Yale	206	279	Connecticut, USA	Population-based cancer registry Controls block list-directed Random digit-dial, no personal history of cancer (except non-melanoma of skin)	Risch HA. Etiology of pancreatic cancer, with a hypothesis concerning the role of N-nitroso compounds and excess gastric acidity. J Natl Cancer Inst. 2003 Jul2;95(13):948-60. [PMID: 12837831]
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Total stage 2 case-control studies	2,131	2,183			
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TOTAL STAGE 2 GWAS	3,525	3,642			
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STAGE 3: REPLICATION					
PANDoRA	2000	4797	Europe	Clinic based caes from 15 basic and/or clinical research groups, across six European countries	Campa D et al. Genetic susceptibility to pancreatic cancer and its functional characterisation: the PANcreatic Disease Research (PANDoRA) consortium. Dig Liver Dis. 2013 Feb;45(2):95-9. [PMID: 23206934]
Cancer and Leukemia Group B (CALGB) study 80303	307		USA	Phase III multi-institution clinical trial of bevacizumab and gemcitabine. Cases histologically confirmed. Cancer not amenable to curative surgery.	Innocenti Fet al. A genome-wide association study of overall survival in pancreatic cancer patients treated with gemcitabine in CALGB 80303. Clin Cancer Res. 2012 Jan 15;18(2):577-84. [PMC3412624]
PLCO		755	USA	Self-report through annual questionnaires. Confirmed by pathology reports and medical records.	Hayes RB et al. Methods for etiologic and early marker investigations in the PLCO trial. Mutat Res. Mutat Res 2005;592:147-54. [PMID: 16054167]

Carotene and Retinol Efficacy Trial (CARET) and samples from studies with DNA that was inadequate for GWAS*	274	USA	Self-report to the Coordinating Center at the Hutchinson Cancer Center. Verified through pathology reports and medical records.	Thornquist MD et al. Statistical design and monitoring of the Carotene and Retinol Efficacy Trial (CARET). Control Clin Trials. 1993 Aug;14(4):308-24. [PMID: 8365195]
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TOTAL STAGE 3 REPLICATION	2,576	5,552
GRAND TOTAL STAGE 1, 2, 3	7,683	14,397

* Cases from studies without adequate DNA for participation in the GWAS were used in the replication stage. These cases were drawn from: AHS, ATBC, CPS-II, DFCI, EPIC, HPFS, MCCS, MEC, PHS, PLCO, VITAL, and WHI.

Supplementary Table 2. Stage 1 subjects genotyped, quality control exclusions, and subjects included in the European ancestry analysis

Study	Genotyped Subjects	Exclusions								Final subjects included in the analysis	Control subjects from previous scans in analysis
		High missing rate	Extreme heterozygosity	Gender discordance	Unexpected duplicates	Non EUR	Missing phenotype	PI exclude or relatedness check	Unexpected duplicates with PanScan I+II		
	Cases	Cases	Cases	Cases	Cases	Cases	Cases	Cases		Cases	Controls
ATBC	45	1								44	217
AgHealth	36	5				2			2	27	
CPSII	167					3			6	158	214
DFCI	405	11	1	2	1	25			5	360	
EPIC	177	2				1				174	263
HPFS	27		1			1				25	84
Heidelberg	205	4			1	3	2		1	194	
MCCS	78					1				77	75
MEC	29					1				28	200
NHS	31					2				29	437
PHSI	15									15	
PLCO	141	39				9			2	91	3042
SELECT	70	1				14			1	54	
SMWHS	109	1				108					
PANKRASII	93			3		1				89	445
VITAL	52	3				1				48	
WHI	214	11			1	27		2	4	169	226
Total	1894	78	2	5	3	199	2	2	21	1582	5203

Supplementary Table 3. Characteristics of stage 1 cases and controls included for GWAS

Study	Age category	Case		Case Total	Control		Control Total	Grand Total
		Female	Male		Female	Male		
AgHealth	51_60	2		2				2
	61_70	4	7	11				11
	71_80		9	9				9
	OVER_80	1	4	5				5
AgHealth Total		7	20	27				27
ATBC	LESS_51					1	1	1
	51_60		1	1		33	33	34
	61_70		7	7		94	94	101
	71_80		32	32		72	72	104
	OVER_80		4	4		17	17	21
ATBC Total			44	44		217	217	261
CPSII	51_60	1		1	17	5	22	23
	61_70	11	8	19	50	59	109	128
	71_80	37	49	86	38	41	79	165
	OVER_80	23	29	52	4		4	56
CPSII Total		72	86	158	109	105	214	372
DFCI	LESS_51	22	21	43				43
	51_60	41	56	97				97
	61_70	61	66	127				127
	71_80	41	37	78				78
	OVER_80	7	8	15				15
DFCI Total		172	188	360				360
EPIC	LESS_51	4	1	5	9	14	23	28
	51_60	15	11	26	44	38	82	108
	61_70	41	33	74	59	53	112	186
	71_80	41	21	62	30	12	42	104
	OVER_80	6	1	7	3	1	4	11
EPIC Total		107	67	174	145	118	263	437
Heidelberg	LESS_51	10	13	23				23
	51_60	25	26	51				51
	61_70	26	42	68				68
	71_80	21	27	48				48
	OVER_80	2	2	4				4
Heidelberg Total		84	110	194				194
HPFS	LESS_51					2	2	2
	51_60		1	1		12	12	13
	61_70		7	7		25	25	32

	71_80		8	8		37	37	45
	OVER_80		9	9		8	8	17
HPFS Total			25	25		84	84	109
MCCS	51_60	4	4	8	4	6	10	18
	61_70	12	10	22	13	14	27	49
	71_80	19	22	41	12	17	29	70
	OVER_80	3	3	6	7	2	9	15
MCCS Total		38	39	77	36	39	75	152
MEC	LESS_51	1		1	46		46	47
	51_60		2	2	71		71	73
	61_70	3	2	5	60		60	65
	71_80	5	4	9	23		23	32
	OVER_80	5	6	11				11
MEC Total		14	14	28	200		200	228
NHS	LESS_51				32		32	32
	51_60	1		1	142		142	143
	61_70	4		4	169		169	173
	71_80	16		16	89		89	105
	OVER_80	8		8	5		5	13
NHS Total		29		29	437		437	466
PHS	61_70		2	2				2
	71_80		9	9				9
	OVER_80		4	4				4
PHS Total			15	15				15
PLCO	51_60		1	1	15	316	331	332
	61_70	15	11	26	67	1624	1691	1717
	71_80	17	25	42	44	944	988	1030
	OVER_80	12	10	22		32	32	54
PLCO Total		44	47	91	126	2916	3042	3133
PANCRASII/SBCS	LESS_51	2	5	7	3	40	43	50
	51_60	7	14	21	5	97	102	123
	61_70	8	15	23	23	137	160	183
	71_80	13	14	27	27	112	139	166
	OVER_80	9	2	11		1	1	12
PANCRASII/SBCS Total		39	50	89	58	387	445	534
SELECT	51_60		2	2				2
	61_70		32	32				32
	71_80		15	15				15
	OVER_80		5	5				5
SELECT Total			54	54				54
VITAL	51_60	2		2				2

	61_70	6	12	18				18
	71_80	14	11	25				25
	OVER_80	2	1	3				3
VITAL Total		24	24	48				48
WHI	51_60	4		4				4
	61_70	29		29	226		226	255
	71_80	95		95				95
	OVER_80	41		41				41
WHI Total		169		169	226		226	395
Grand Total	LESS_51	39	40	79	90	57	147	226
	51_60	102	118	220	298	507	805	1025
	61_70	220	254	474	667	2006	2673	3147
	71_80	319	283	602	263	1235	1498	2100
	OVER_80	119	88	207	19	61	80	287
Grand Total		799	783	1582	1337	3866	5203	6785

Supplementary Table 4. Association results for 13 SNPs in stages 1 and 2 with combined $P < 5 \times 10^{-5}$

Chr	SNP	Position ^a	Minor allele	Major allele	Stage	Category ^b	Info ^c	Subjects		Minor allele frequency		Allelic OR ^e (95% CI)	P^f	P_{Het}^g
								Controls	Cases	Controls	Cases			
5p15.33	rs2736098	1,294,086	T	C	Stage 1	g	1	4683	1484	0.268	0.216	0.76 (0.68-0.86)	8.22x10 ⁻⁶	0.373
					Stage 2	i	0.609	3641	3524	0.284	0.259	0.82 (0.74-0.90)	2.63x10 ⁻⁵	
					Combined ^d			8324	5008			0.80 (0.74-0.86)	1.42x10⁻⁹	
7q32.3	rs6971499	130,680,521	C	T	Stage 1	g	1	5200	1582	0.155	0.127	0.79 (0.68-0.90)	6.58x10 ⁻⁴	0.705
					Stage 2	i	0.914	3641	3524	0.147	0.124	0.81 (0.74-0.90)	4.69x10 ⁻⁵	
					Combined ^d			8841	5106			0.80 (0.74-0.87)	1.23x10⁻⁷	
16q23.1	rs7190458	75,263,661	A	G	Stage 1	g	1	5185	1581	0.042	0.065	1.61 (1.32-1.96)	4.14x10 ⁻⁶	0.569
					Stage 2	i	0.585	3641	3524	0.039	0.049	1.47 (1.20-1.82)	2.17x10 ⁻⁴	
					Combined ^d			8826	5105			1.55 (1.34-1.79)	4.73x10⁻⁹	
13q12.2	rs9581943	28,493,997	A	G	Stage 1	g	1	5193	1580	0.397	0.441	1.23 (1.12-1.35)	1.34x10 ⁻⁵	0.116
					Stage 2	i	0.987	3641	3524	0.406	0.434	1.12 (1.05-1.20)	5.51x10 ⁻⁴	
					Combined ^d			8834	5104			1.16 (1.10-1.23)	9.94x10⁻⁸	
22q12.1	rs16986825	29,300,306	T	C	Stage 1	g	1	5155	1579	0.150	0.184	1.25 (1.10-1.42)	4.96x10 ⁻⁴	0.303
					Stage 2	i	0.987	3642	3525	0.149	0.168	1.15 (1.05-1.26)	2.11x10 ⁻³	
					Combined ^d			8797	5104			1.18 (1.10-1.27)	6.11x10⁻⁶	
8q24.21	rs1561927	129,568,078	C	T	Stage 1	g	1	5085	1559	0.269	0.251	0.88 (0.78-0.97)	1.59 x 10 ⁻²	0.842
					Stage 2	g	1	3637	3519	0.279	0.250	0.86 (0.80-0.93)	1.11x10 ⁻⁴	
					Combined ^d			8722	5078			0.87 (0.81-0.92)	5.36x10⁻⁶	
12q24.31	rs1182933	121,454,622	T	C	Stage 1	g	1	5189	1582	0.296	0.315	1.09 (0.98-1.21)	0.108	0.374
					Stage 2	i	0.982	3641	3525	0.300	0.333	1.15 (1.07-1.24)	1.18x10 ⁻⁴	
					Combined ^d			8830	5107			1.13 (1.07-1.20)	4.58x10⁻⁵	
22q11.21	rs451740	18,316,620	T	C	Stage 1	g	1	5201	1581	0.298	0.333	1.28 (1.15-1.41)	2.33x10 ⁻⁶	0.016
					Stage 2	g	1	3639	3523	0.292	0.310	1.09 (1.02-1.18)	0.014	
					Combined ^d			8840	5104			1.15 (1.09-1.22)	2.30x10⁻⁶	
10q23.33	rs4918797	96,750,251	T	C	Stage 1	g	1	5090	1565	0.203	0.187	0.82 (0.73-0.92)	1.19x10 ⁻³	0.418
					Stage 2	i	0.986	3641	3525	0.209	0.187	0.87 (0.8-0.95)	9.66x10 ⁻⁴	
					Combined ^d			8731	5090			0.85 (0.8-0.91)	5.25x10⁻⁶	
6p25.1	rs10214456	6,592,095	C	T	Stage 1	g	1	5192	1579	0.365	0.396	1.12 (1.02-1.25)	1.65x10 ⁻²	0.913
					Stage 2	i	0.993	3641	3524	0.364	0.393	1.14 (1.06-1.22)	2.61x10 ⁻⁴	
					Combined ^d			8833	5103			1.13 (1.07-1.2)	1.27x10⁻⁵	
5p12	rs10054519	43,444,233	A	G	Stage 1	g	1	4729	1491	0.477	0.503	1.12 (1.01-1.23)	0.026	0.884
					Stage 2	i	0.993	3641	3525	0.470	0.503	1.14 (1.06-1.2)	2.18x10 ⁻⁴	
					Combined ^d			8370	5016			1.13 (1.07-1.19)	1.56x10⁻⁵	
9q34.2	rs4962153	136,323,754	A	G	Stage 1	g	1	5191	1577	0.155	0.177	1.20 (1.06-1.37)	3.38x10 ⁻³	0.841
					Stage 2	i	0.683	3641	3524	0.158	0.174	1.19 (1.06-1.32)	1.84x10 ⁻³	
					Combined ^d			8832	5101			1.20 (1.10-1.30)	1.97x10⁻⁵	
7q36.3	rs167020	155,619,733	A	G	Stage 1	g	1	5200	1582	0.289	0.298	1.05 (0.94-1.16)	0.353	0.055
					Stage 2	g	1	3642	3525	0.269	0.305	1.19 (1.11-1.28)	3.20x10 ⁻⁶	
					Combined ^d			8842	5107			1.14 (1.08-1.21)	1.38x10⁻⁵	

Results from unconditional logistic regression of genotypes in participants from Stage 1 and Stage 2. ^aPosition of SNP in NCBI genome build 37 (Hg19). ^bCategory: i=imputed, g=genotyped. ^cInfo: imputation information content. ^dCombined meta-analysis results for Stages 1 and 2. ^eFor Stage 1, per allele OR for the minor allele was adjusted for age, sex, geographic region, and significant principal components; for Stage 2, per allele OR for the minor allele was adjusted for age, sex, study, arm and significant principal components. ^f1 d.f. score test. ^gP value for heterogeneity.

Supplementary Table 5A. Characteristics of cases and controls from studies included in the replication stage

Group A (CGR)	Age category	Case		Case Total	Control		Control Total	Grand Total
		Female	Male		Female	Male		
AgHealth	61_70	3	2	5				5
	OVER_70		2	2				2
AgHealth Total		3	4	7				7
CARET	LESS_60	2	4	6				6
	61_70	3	19	22				22
	OVER_70	5	13	18				18
CARET Total		10	36	46				46
CPSII	OVER_70	1	2	3				3
CPSII Total		1	2	3				3
DFCI	LESS_60		3	3				3
	61_70	3	4	7				7
	OVER_70	1	1	2				2
DFCI Total		4	8	12				12
EPIC	LESS_60		1	1				1
	61_70		1	1				1
EPIC Total			2	2				2
Heidelberg	LESS_60	5	10	15				15
	61_70	5	11	16				16
	OVER_70	6	3	9				9
Heidelberg Total		16	24	40				40
HPFS	61_70		1	1				1
HPFS Total			1	1				1
MCCS	LESS_60	1	7	8				8
	61_70	15	9	24				24
	OVER_70	15	17	32				32
MCCS Total		31	33	64				64
MEC	LESS_60	1		1				1
	61_70	3	3	6				6
	OVER_70	3	4	7				7
MEC Total		7	7	14				14
PHS	61_70		1	1				1
	OVER_70		12	12				12

PHS Total			13	13			13
PLCO	LESS_60				31	45	76
	61_70	3	3	6	111	138	255
	OVER_70	9	19	28	14	39	81
PLCO Total		12	22	34	156	222	412
VITAL	LESS_60		2	2			2
	61_70	4	6	10			10
	OVER_70	4	3	7			7
VITAL Total		8	11	19			19
WHI	61_70	2		2			2
	OVER_70	12		12			12
WHI Total		14		14			14
Grand Total	LESS_60	9	27	36	31	45	76
	61_70	41	60	101	111	138	249
	OVER_70	56	76	132	14	39	53
Grand Total	Grand Total	106	163	269	156	222	378

Group B	Age category	Case		Case Total	Control		Control Total	Grand Total
		Female	Male		Female	Male		
PANDoRA	LESS_40	13	17	30	211	247	458	488
	40_50	51	95	146	329	460	789	935
	50_60	179	264	443	648	703	1351	1794
	60_70	322	418	740	570	863	1433	2173
	OVER_70	285	356	641	379	387	766	1407
PANDoRA Total		850	1150	2000	2137	2660	4797	6797

Group C	Age category	Case		Case Total	Control		Control Total	Grand Total
		Female	Male		Female	Male		
CALGB	LESS_60	39	49	88				88
	60_69	43	47	90				90
	OVER_70	57	72	129				129
CALGB Total		139	168	307				307
PLCO	LESS_60				38	43	81	81
	60_69				103	130	233	233
	OVER_70				27	36	63	63
PLCO Total					168	209	377	377

CALGB/PLCO							
Total	139	168	307	168	209	377	684

Supplementary Table 5B. Subjects genotyped for replication, quality control exclusions, and subjects included in the European ancestry analysis

Replication study	Samples genotyped		Control GWAS study	Exclusions*	Sample completion cutoff	Final subjects included in the analysis		Locus completion cutoff (n loci)
	Cases	Controls				Cases	Controls	
CGR	334	379	PLCO	66	80%	269	378	None (n=13)
CALGB 80303	351	378	PLCO	45	98%	307	377	90% (n=492,023)
PANDoRA	2196	4839	NA	238	80%	2000	4797	None (n=13)
Total						2576	5552	

*Exclusions were based on low completion, non-European ancestry or missing phenotypes. NA: not applicable as PANDoRA samples were used for both cases and controls.

Supplementary Table 6. Association results for the 13 SNPs in the replication studies

Chr	SNP	Position ^a	Minor allele	Major allele	Study	Category ^b	Info ^c	Subjects		Minor allele frequency		Allelic OR ^e (95% CI)	<i>P</i> ^f	<i>P</i> _{Het} ^g
								Controls	Cases	Controls	Cases			
5p15.33	rs2736098	1,294,086	T	C	CGR	g	0.703	377	267	0.287	0.213	0.66 (0.49-0.88)	4.98x10 ⁻³	0.045
					PANDoRA	g	1	4044	1613	0.266	0.243	0.86 (0.78-0.95)	3.15x10 ⁻³	
					CALGB	i	0.499	376	306	0.330	0.261	0.60 (0.42-0.84)	3.43x10 ⁻³	
					Combined^d			4797	2186			0.81 (0.74-0.89)	1.36x10⁻⁵	
7q32.3	rs6971499	130,680,521	C	T	CGR	g	0.937	377	268	0.162	0.104	0.58 (0.41-0.83)	2.44x10 ⁻³	0.257
					PANDoRA	g	1	3695	1750	0.145	0.117	0.79 (0.70-0.89)	2.49x10 ⁻⁴	
					CALGB	i	0.884	376	306	0.146	0.139	0.82 (0.58-1.16)	2.64x10 ⁻¹	
					Combined^d			4448	2324			0.77 (0.69-0.86)	4.37x10⁻⁶	
16q23.1	rs7190458	75,263,661	A	G	CGR	g	0.716	377	245	0.040	0.046	1.14 (0.56-2.27)	7.19x10 ⁻¹	0.744
					PANDoRA	g	1	3712	1751	0.037	0.047	1.33 (1.08-1.64)	7.28x10 ⁻³	
					CALGB	i	0.529	376	306	0.047	0.058	1.67 (0.83-3.33)	1.55x10 ⁻¹	
					Combined^d			4465	2302			1.33 (1.10-1.61)	3.14x10⁻³	
13q12.2	rs9581943	28,493,997	A	G	CGR	g	0.992	377	267	0.392	0.427	1.16 (0.91-1.49)	2.29x10 ⁻¹	0.933
					PANDoRA	g	1	3699	1733	0.410	0.438	1.11 (1.02-1.22)	1.36x10 ⁻²	
					CALGB	i	0.985	376	306	0.419	0.435	1.10 (0.86-1.39)	4.52x10 ⁻¹	
					Combined^d			4452	2306			1.11 (1.03-1.20)	4.80x10⁻³	
22q12.1	rs16986825	29,300,306	T	C	CGR	g	0.987	378	265	0.170	0.196	1.28 (0.95-1.73)	1.10x10 ⁻¹	0.351
					PANDoRA	g	1	3644	1732	0.179	0.198	1.15 (1.03-1.27)	1.27x10 ⁻²	
					CALGB	i	0.983	377	307	0.150	0.205	1.42 (1.06-1.91)	1.99x10 ⁻²	
					Combined^d			4399	2304			1.18 (1.08-1.30)	5.13x10⁻⁴	
8q24.21	rs1561927	129,568,078	C	T	CGR	g	1	378	263	0.245	0.261	0.99 (0.75-1.32)	9.48x10 ⁻¹	0.171
					PANDoRA	g	1	3798	1834	0.278	0.258	0.91 (0.83-0.99)	3.77x10 ⁻²	
					CALGB	i	0.943	376	306	0.283	0.233	0.71 (0.55-0.93)	1.00x10 ⁻²	
					Combined^d			4552	2403			0.89 (0.82-0.97)	6.44x10⁻³	
12q24.31	rs1182933	121,454,622	T	C	CGR	g	0.99	378	266	0.292	0.316	1.06 (0.82-1.37)	6.41x10 ⁻¹	0.902
					PANDoRA	g	1	3810	1821	0.327	0.346	1.11 (1.02-1.21)	1.57x10 ⁻²	
					CALGB	i	0.979	376	306	0.296	0.329	1.15 (0.90-1.49)	2.62x10 ⁻¹	
					Combined^d			4564	2393			1.11 (1.03-1.20)	7.74x10⁻³	
22q11.21	rs451740	18,316,620	T	C	CGR	g	1	378	269	0.306	0.314	1.05 (0.81-1.35)	7.10x10 ⁻¹	0.588
					PANDoRA	g	1	3797	1827	0.293	0.291	0.98 (0.89-1.07)	6.35x10 ⁻¹	
					CALGB	g	1	377	307	0.296	0.301	1.11 (0.87-1.41)	4.02x10 ⁻¹	
					Combined^d			4552	2403			1.00 (0.92-1.08)	9.81x10⁻¹	
10q23.33	rs4918797	96,750,251	T	C	CGR	g	0.986	377	269	0.192	0.175	0.80 (0.59-1.09)	1.62x10 ⁻¹	
					PANDoRA	g	1	3811	1814	0.202	0.201	0.96 (0.87-1.06)	4.41x10 ⁻¹	

6p25.1	rs10214456	6,592,095	C	T	CALGB	i	0.988	376	306	0.191	0.213	1.12 (0.84-1.50)	4.27x10 ⁻¹	0.295
					Combined^d			4564	2389			0.96 (0.88-1.05)	3.92x10⁻¹	
					CGR	g	0.993	377	267	0.359	0.351	0.93 (0.72-1.20)	5.95x10 ⁻¹	
					PANDoRA	g	1	3804	1818	0.364	0.371	1.02 (0.94-1.11)	6.02x10 ⁻¹	
					CALGB	i	0.992	376	306	0.372	0.396	1.15 (0.91-1.45)	2.55x10 ⁻¹	
5p12	rs10054519	43,444,233	A	G	Combined^d			4557	2391			1.03 (0.95-1.11)	4.94x10⁻¹	0.502
					CGR	g	0.995	377	265	0.474	0.467	0.96 (0.75-1.22)	7.23x10 ⁻¹	
					PANDoRA	g	1	3803	1802	0.480	0.492	1.05 (0.97-1.15)	1.74x10 ⁻¹	
					CALGB	i	0.99	376	306	0.491	0.533	1.22 (0.97-1.54)	8.30x10 ⁻²	
					Combined^d			4556	2373			1.06 (0.99-1.15)	9.64x10⁻²	
9q34.2	rs4962153	136,323,754	A	G	CGR	g	0.791	377	267	0.160	0.202	1.45 (1.03-2.04)	3.12x10 ⁻²	0.331
					PANDoRA	g	1	3671	1725	0.162	0.183	1.16 (1.04-1.30)	6.36x10 ⁻³	
					CALGB	i	0.633	376	306	0.168	0.196	1.28 (0.89-1.85)	1.73x10 ⁻¹	
					Combined^d			4424	2298			1.2 (1.09-1.33)	4.44x10⁻⁴	
					CGR	g	1	378	269	0.283	0.250	0.85 (0.64-1.11)	2.33x10 ⁻¹	
7q36.3	rs167020	155,619,733	A	G	PANDoRA	g	1	3975	1805	0.304	0.285	0.88 (0.81-0.97)	1.10x10 ⁻²	0.458
					CALGB	g	1	377	307	0.280	0.293	1.10 (0.85-1.41)	4.55x10 ⁻¹	
					Combined^d			4730	2381			0.91 (0.83-0.98)	1.69x10⁻²	

Results from unconditional logistic regression of genotypes in participants from the replication studies. ^aPosition of SNP in NCBI genome build 37 (Hg19). ^bCategory: i=imputed, g=genotyped. ^cInfo: imputation information content. ^dCombined meta-analysis results for the replication studies. ^ePer allele OR for the minor allele adjusted for age, sex, and study. ^f1 d.f. score test. ^gP value for heterogeneity.

Supplemental Table 7. Chromosomal regions of newly implicated pancreatic cancer susceptibility loci

Chr	Index SNP	Position ^a	Nearest gene ^b	Genes located within chromosomal region ^c	Genes implicated in glucose homeostasis	Previously identified GWAS SNPs within chromosomal region and $r^2 > 0.2$ with index SNP ^d	r^2 with index SNP ^e	Associated disease or trait ^d
5p15.33	rs2736098	1,294,086	<i>TERT</i> (synonymous)	<i>ZDHHC11</i> , <i>BRD9</i> , <i>TRIP13</i> , <i>LOC100506688</i> , <i>NKD2</i> , <i>SLC12A7</i> , <i>MIR4635</i> , <i>SLC6A19</i> , <i>SLC6A18</i> , <i>TERT</i> , <i>MIR4457</i> , <i>CLPTM1L</i> , <i>SLC6A3</i> , <i>LPCAT1</i> , <i>SDHAP3</i> , <i>LOC728613</i> , <i>MIR4277</i>		rs2853677 rs4975616 rs401681	0.229 0.236 0.216	Lung adenocarcinoma Lung cancer Melanoma, PSA level, Bladder cancer, Pancreatic cancer, Lung cancer
7q32.3	rs6971499	130,680,521	<i>LINC-PINT</i> (intronic)	<i>COPG2</i> , <i>TSGA13</i> , <i>KLF14</i> , <i>MIR29A</i> , <i>MIR29B1</i> , <i>LOC646329</i> , <i>LINC-PINT</i> , <i>MKLN1</i>	<i>KLF14</i> ¹⁹			
16q23.1	rs7190458	75,263,661	<i>BCAR1</i> (synonymous)	<i>FA2H</i> , <i>WDR59</i> , <i>ZNFR1</i> , <i>LDHD</i> , <i>ZFP1</i> , <i>CTRB2</i> , <i>CTRB1</i> , <i>BCAR1</i> , <i>CFDP1</i> , <i>TMEM170A</i> , <i>CHST6</i> , <i>CHST5</i> , <i>TMEM231</i> , <i>GABARAPL2</i> , <i>ADAT1</i> , <i>KARS</i> , <i>TERF21P</i>		rs7202877	0.322	Type 1 diabetes
13q12.2	rs9581943	28,493,997	<i>PDX1</i> (171 bp)	<i>GSX1</i> , <i>PDX1-AS1</i> , <i>PDX1</i> , <i>ATP5EP2</i> , <i>CDX2</i> , <i>URAD</i> , <i>FLT3</i> , <i>PAN3-AS1</i> , <i>PAN3</i>	<i>PDX-I</i> ³¹⁻³³	rs2293941	0.201	Fasting glucose related traits
22q12.1	rs16986825	29,300,306	<i>ZNRF3</i> (intronic)	<i>TTC28</i> , <i>CHEK2</i> , <i>HSCB</i> , <i>CCDC117</i> , <i>XBPI</i> , <i>ZNRF3</i> , <i>ZNRF3-AS1</i> , <i>C22orf31</i> , <i>KREMEN1</i> , <i>EMID1</i> , <i>RHBDD3</i> , <i>EWSR1</i> , <i>GAS2L1</i> , <i>RASL10A</i> , <i>AP1B1</i> , <i>MIR3653</i> , <i>SNORD125</i>	<i>XBPI</i> ⁷⁹	rs2239815 rs4823006	0.486 0.221	Esophageal SCC Waist-hip ratio
8q24.21	rs1561927	129,568,078	<i>MIR1208</i> (406 kb)	<i>PVT1</i> , <i>MIR1208</i>		rs10088218 rs6651252	0.373 0.373	Ovarian cancer Crohn's disease

^aPosition of SNP in NCBI Genome Build 37 (Hg19). ^bThe RefSeq gene within which the index SNP is located. For SNPs not located within a gene, the nearest gene is provided with distance to index SNP in parentheses. ^cGenes within the chromosomal region of 1 MB flanking the index SNP. ^dData from the NHGRI GWAS catalogue and UCSC Genome Browser. ^e r^2 LD values from 1000 Genomes Project CEU data. Chr: chromosome and band.

Supplementary Table 8. Association results for five new pancreatic cancer susceptibility loci and one suggestive locus stratified by geographic region

SNP	Chr	Subgroup ^a	Cases	Controls	OR (95% CI)	<i>P</i> ^c	<i>P</i> _{Het}	<i>I</i> ²
rs2736098	5p15.33	Region US	3907	7146	0.79 (0.73-0.86)	4.50 x 10 ⁻⁸		
		Region CNE	1100	1177	0.84 (0.71-1.00)	0.051		
		Region SE ^b						
		Combined	5007	8323	0.80 (0.74-0.86)	8.06 x 10⁻⁹	0.499	0
rs6971499	7q32.3	Region US	3916	7203	0.79 (0.71-0.86)	2.88 x 10 ⁻⁷		
		Region CNE	1100	1192	0.78 (0.64-0.96)	0.020		
		Region SE	89	445	0.99 (0.56-1.75)	0.982		
		Combined	5105	8840	0.79 (0.72-0.85)	2.43 x 10⁻⁸	0.731	0
rs7190458	16q23.1	Region US	3915	7191	1.52 (1.27-1.82)	4.56 x 10 ⁻⁶		
		Region CNE	1100	1190	1.49 (1.08-2.08)	0.016		
		Region SE	89	445	1.72 (0.85-3.57)	0.130		
		Combined	5104	8826	1.52 (1.30-1.75)	7.25 x 10⁻⁸	0.928	0
rs9581943	13q12.2	Region US	3914	7197	1.18 (1.11-1.27)	2.10 x 10 ⁻⁷		
		Region CNE	1100	1191	1.05 (0.93-1.19)	0.434		
		Region SE	89	445	1.10 (0.76-1.59)	0.611		
		Combined	5103	8833	1.15 (1.09-1.22)	5.22 x 10⁻⁷	0.265	24.63
rs16986825	22q12.1	Region US	3914	7161	1.17 (1.08-1.28)	2.00 x 10 ⁻⁴		
		Region CNE	1101	1191	1.18 (0.99-1.39)	0.059		
		Region SE	89	445	1.67 (1.07-2.60)	0.025		
		Combined	5104	8797	1.19 (1.10-1.28)	7.20 x 10⁻⁶	0.320	12.28
rs1561927	8q24.21	Region US	3896	7121	0.85 (0.79-0.91)	7.86 x 10 ⁻⁶		
		Region CNE	1094	1158	0.93 (0.80-1.08)	0.317		
		Region SE	88	443	1.06 (0.71-1.59)	0.757		
		Combined	5078	8722	0.87 (0.81-0.93)	1.37 x 10⁻⁵	0.340	7.28

Results from unconditional logistic regression of genotypes in participants from Stage 1 and Stage 2 stratified by geographic region. ^aRegions include, US: The United States, CNE: Central and Northern Europe and SE: Southern Europe. Participants from Region SE were only available from stage 1. ^brs2736098 was not polymorphic in subjects from Region SE. ^c1 d.f. score test. Chr: chromosome and band; OR, per-allele OR for the minor allele adjusted for age, sex and significant principal components for Stage 1; per-allele OR adjusted for age, sex and significant principal components for Stage 2. The analysis was performed separately in subjects from each geographic region followed by meta-analysis (results shown in bold). *P*_{Het}: heterogeneity *P*-value; *I*²: heterogeneity statistic.

Supplementary Table 9: Association results for five new pancreatic cancer susceptibility loci and one suggestive locus stratified by smoking status.

SNP	Chr	Subgroup ^a	Cases	Controls	OR (95% CI)	<i>P</i> ^b	<i>P</i> _{Het}	I ²	<i>P</i> _{Int}
rs2736098	5p15.33	Smoker	2580	4177	0.86 (0.78-0.96)	6.56 x 10 ⁻³	0.305	5.00	0.355
		Nonsmoker	1601	3035	0.79 (0.70-0.90)	3.16 x 10 ⁻⁴			
		Combined	4181	7212	0.83 (0.77-0.90)	1.11 x 10⁻⁵			
rs6971499	7q32.3	Smoker	2633	4539	0.83 (0.74-0.93)	1.94 x 10 ⁻³	0.663	0	0.469
		Nonsmoker	1642	3185	0.79 (0.69-0.91)	1.05 x 10 ⁻³			
		Combined	4275	7724	0.81 (0.75-0.89)	7.18 x 10⁻⁶			
rs7190458	16q23.1	Smoker	2633	4534	1.49 (1.20-1.82)	1.88 x 10 ⁻⁴	0.247	25.37	0.262
		Nonsmoker	1641	3179	1.79 (1.41-2.33)	4.17 x 10 ⁻⁶			
		Combined	4274	7713	1.61 (1.37-1.89)	6.13 x 10⁻⁹			
rs9581943	13q12.2	Smoker	2632	4537	1.15 (1.06-1.23)	5.94 x 10 ⁻⁴	0.924	0	0.894
		Nonsmoker	1641	3180	1.14 (1.04-1.25)	6.74 x 10 ⁻³			
		Combined	4273	7717	1.15 (1.08-1.22)	1.23 x 10⁻⁵			
rs16986825	22q12.1	Smoker	2632	4516	1.19 (1.08-1.32)	8.46 x 10 ⁻⁴	0.878	0	0.941
		Nonsmoker	1641	3164	1.21 (1.06-1.37)	3.75 x 10 ⁻³			
		Combined	4273	7680	1.20 (1.11-1.30)	1.00 x 10⁻⁵			
rs1561927	8q24.21	Smoker	2620	4479	0.89 (0.81-0.97)	0.011	0.604	0	0.499
		Nonsmoker	1633	3131	0.86 (0.77-0.95)	5.54 x 10 ⁻³			
		Combined	4253	7610	0.88 (0.82-0.94)	2.00 x 10⁻⁴			

Results from unconditional logistic regression of genotypes in participants from Stage 1 and Stage 2 stratified by smoking status. ^aSmoker: current and past smokers; Nonsmoker: never smokers. ^b1 d.f. score test. Chr: chromosome and band; OR, per-allele OR for the minor allele adjusted for age, sex, geographic region and significant principal components for Stage 1; per-allele OR adjusted for age, sex, study, arm and significant principal components for Stage 2. The analysis was performed separately in smokers and nonsmokers followed by meta-analysis (results shown in bold). *P*_{Het}: heterogeneity *P*-value; I²: heterogeneity statistic; *P*_{Int}: interaction *P*-value.

Supplementary Table 10: Association results for PanScan susceptibility loci among Asian subjects from SMWHS

SNP	Chr	Minor allele	Major allele	No. of Subjects		Minor allele frequency		Allelic OR ^a (95% CI)	<i>P</i> ^b	Effect Direction ^c
				Controls	Cases	Controls	Cases			
rs10919791	1q32.1	G	A	425	169	0.321	0.287	0.84 (0.63-1.12)	0.237	Different*
rs31490	5p15.33	A	G	429	171	0.159	0.149	0.97 (0.68-1.38)	0.855	Different
rs687289	9q34.2	A	G	430	173	0.428	0.462	1.11 (0.86-1.44)	0.421	Same
rs9543325	13q22.1	C	T	430	173	0.442	0.5	1.28 (0.99-1.64)	0.059	Same
rs2736098 ^d	5p15.33	T	C							
rs6971499	7q32.3	C	T	409	173	0.032	0.035	1.17 (0.58-2.35)	0.669	Different
rs7190458	16q23.1	A	G	415	171	0	0.018			Same
rs9581943	13q12.2	A	G	402	171	0.346	0.386	1.16 (0.89-1.52)	0.272	Same
rs16986825	22q12.1	T	C	424	173	0.395	0.425	1.13 (0.87-1.46)	0.362	Same
rs1561927	8q24.21	C	T	430	172	0.051	0.038	0.75 (0.39-1.43)	0.380	Same

Results from unconditional logistic regression of genotypes in participants from Shanghai Men's and Women's Health Study. ^aPer allele OR for the minor allele adjusted for age, sex, and significant principal components. ^b1 d.f. score test; ^cDirection of effect of the OR per minor allele for subjects of European and Asian descent. ^drs2736098 could not be accurately imputed in the majority of Asian subjects. Chr: chromosome and band. *Note that while the effect for the minor allele is the same, the minor allele in Europeans is the major allele in Asians.

Supplementary Table 11. Association results for Chinese and Japanese pancreatic cancer risk loci in participants of European descent in Stages 1 and 2

Chr	GWAS	SNP	SNP surrogate	r ²	r ² 1000G Population	Surrogate type	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	rs3849766	0.895	Asians	Indirect	g	1	C	T	4746	1492	Stage 1	0.960	0.961	1.03 (0.80-1.33)	0.819	0.160
							i	0.97	C	T	3642	3524	Stage 2	0.966	0.960	0.82 (0.69-0.98)	0.033	
											8388	5016	Combined			0.89 (0.76-1.03)	0.105	
10q26.11	Chinese	rs12413624	rs4523612	1	Asians	Indirect	g	1	C	T	5187	1579	Stage 1	0.436	0.428	0.95 (0.86-1.04)	0.249	0.507
							g	1	C	T	3637	3522	Stage 2	0.439	0.433	0.98 (0.92-1.05)	0.624	
											8824	5101	Combined			0.97 (0.92-1.03)	0.288	
21q22.3	Chinese	rs1547374	rs1547374	1	Asians	Direct	g	1	A	G	5198	1582	Stage 1	0.313	0.340	1.14 (1.03-1.26)	0.013	0.037
							g	1	A	G	3641	3524	Stage 2	0.312	0.313	1.00 (0.93-1.07)	0.929	
											8839	5106	Combined			1.04 (0.98-1.10)	0.173	
21q21.3	Chinese	rs372883	rs388707	1	Asians	Indirect	g	1	C	T	5201	1581	Stage 1	0.574	0.570	0.99 (0.90-1.09)	0.823	0.815
							i	1.00	C	T	3641	3524	Stage 2	0.589	0.583	0.98 (0.91-1.04)	0.463	
											8842	5105	Combined			0.98 (0.93-1.03)	0.465	
22q13.32	Chinese	rs5768709	rs916283	0.899	Asians	Indirect	g	1	T	C	4751	1493	Stage 1	0.400	0.405	1.00 (0.91-1.11)	0.930	0.954
							i	0.91	T	C	3641	3524	Stage 2	0.393	0.397	1.01 (0.94-1.08)	0.821	
											8392	5017	Combined			1.01 (0.95-1.07)	0.814	
6p25.3	Japanese	rs9502893	rs9502893	1	Asians	Direct	g	1	C	T	5197	1582	Stage 1	0.564	0.538	0.86 (0.78-0.95)	0.002	0.043
							g	1	C	T	3641	3525	Stage 2	0.550	0.543	0.97 (0.91-1.04)	0.391	
											8838	5107	Combined			0.93 (0.89-0.99)	0.015	
7q36.2	Japanese	rs6464375	rs7779540	1	Asians	Indirect	g	1	A	G	5188	1578	Stage 1	0.942	0.939	0.98 (0.80-1.20)	0.849	0.783
							g	1	A	G	3637	3523	Stage 2	0.945	0.943	0.95 (0.82-1.09)	0.460	
											8825	5101	Combined			0.96 (0.85-1.08)	0.477	
12p11.21	Japanese	rs708224	rs813784	0.989	Asians	Indirect	g	1	C	T	4668	1489	Stage 1	0.647	0.642	0.98 (0.89-1.09)	0.762	0.355
							i	0.99	C	T	3641	3524	Stage 2	0.667	0.651	0.93 (0.87-1.00)	0.037	
											8309	5013	Combined			0.95 (0.89-1.00)	0.058	
5p13.1	Chinese	rs2255280 ^f																
10q26.11	Chinese	rs12413624	rs4523612	1	CEU	Indirect	g	1	C	T	5187	1579	Stage 1	0.436	0.428	0.95 (0.86-1.04)	0.249	0.507
							g	1	C	T	3637	3522	Stage 2	0.439	0.433	0.98 (0.92-1.05)	0.624	
											8824	5101	Combined			0.97 (0.92-1.03)	0.288	
21q22.3	Chinese	rs1547374	rs1547374	1	CEU	Direct	g	1	A	G	5198	1582	Stage 1	0.313	0.340	1.14 (1.03-1.26)	0.013	0.037
							g	1	A	G	3641	3524	Stage 2	0.312	0.313	1.00 (0.93-1.07)	0.929	
											8839	5106	Combined			1.04 (0.98-1.10)	0.173	
21q21.3	Chinese	rs372883	rs733610	0.884	CEU	Indirect	g	1	A	G	5199	1581	Stage 1	0.508	0.501	0.96 (0.87-1.05)	0.382	0.568
							g	1	A	G	3637	3521	Stage 2	0.519	0.517	0.99 (0.93-1.06)	0.797	
											8836	5102	Combined			0.98 (0.93-1.04)	0.477	
22q13.32	Chinese	rs5768709	rs916283	1	CEU	Indirect	g	1	T	C	4751	1493	Stage 1	0.400	0.405	1.01 (0.91-1.11)	0.930	0.954
							i	0.91	T	C	3641	3524	Stage 2	0.393	0.397	1.01 (0.94-1.08)	0.821	
											8392	5017	Combined			1.01 (0.95-1.07)	0.814	
6p25.3	Japanese	rs9502893	rs9502893	1	CEU	Direct	g	1	C	T	5197	1582	Stage 1	0.564	0.538	0.86 (0.78-0.95)	0.002	0.043
							g	1	C	T	3641	3525	Stage 2	0.550	0.543	0.97 (0.91-1.04)	0.391	
											8838	5107	Combined			0.93 (0.89-0.99)	0.015	
7q36.2	Japanese	rs6464375	rs7779540	1	CEU	Indirect	g	1	A	G	5188	1578	Stage 1	0.942	0.939	0.98 (0.80-1.20)	0.849	0.783
							g	1	A	G	3637	3523	Stage 2	0.945	0.943	0.95 (0.82-1.09)	0.460	
											8825	5101	Combined			0.96 (0.85-1.08)	0.477	
12p11.21	Japanese	rs708224	rs813784	0.719	CEU	Indirect	g	1	C	T	4668	1489	Stage 1	0.647	0.642	0.98 (0.89-1.09)	0.762	0.355
							i	0.99	C	T	3641	3524	Stage 2	0.667	0.651	0.93 (0.87-1.00)	0.037	
											8309	5013	Combined			0.95 (0.89-1.00)	0.058	

Results from unconditional logistic regression of Chinese and Japanese pancreatic cancer susceptibility loci in participants of European descent from Stage 1 and Stage 2. ^aGenotype category: g=genotyped, i=imputed. ^bInfo: imputation information content/accuracy score. ^cFor stage 1, per allele OR for the effect allele adjusted for age, sex, geographic region, and significant principal components; For stage 2, per allele OR for the effect allele adjusted for age, sex, study, arm and significant principal components. ^d1 d.f. score test. ^eP value for heterogeneity. ^frs2255280 is monomorphic in the 1000G CEU population. Chr: chromosome and band.

SNP/Chr	pos (hg19)	LD		variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNase	Proteins bound	Motifs changed	REFSEQ or GENCODE genes	dbSNP func annot	MuTHER eQTL			Blood eQTL			
		(r ²)	(D')																Gene	neg log 10 P	Tissue	Cis Gene	Cis P value	Cis Gene	Cis P value
rs2736098																									
5	1294086	1	1	rs2736098	C	T	0.06	0.2	0.33	0.23			H1	H1-hESC Myomere		9	TERT	synonymous							
	1295349	0.74	0.98	rs2853669	A	G	0.08	0.23	0.31	0.29		HepG2, H1	GM12878	GM12892, H1-hESC Myomere	POL2	7	16bp 5' of TERT								
	1297075	0.65	0.81	rs201878070	CCA	C	0.07	0.2	0.25	0.24						21	1.9kb 5' of TERT								
5	1297077	0.73	0.94	rs145844133	AAC	A	0.07	0.21	0.24	0.27						19	1.9kb 5' of TERT								
5	1297081	0.73	0.93	rs201278885	CCA	C	0.06	0.19	0.24	0.27						22	1.9kb 5' of TERT								
	1297488	0.75	0.97	rs27286108	C	T	0.07	0.23	0.26	0.28			10 cell types		EBF1	HEN1Zfp161	2.3kb 5' of TERT								
5	1297854	0.65	0.86	rs27286107	C	T	0.07	0.22	0.22	0.26						ERalpha-a, GATA3, RXRA	2.7kb 5' of TERT								
rs6971499																									
7	130676942	0.84	0.96	rs28651880	C	T	0.15	0.11	0.04	0.13			NHLF	IPS, Adul, CD4, Th0		ATF3, ERalpha-a	LINC-PINT	intronic							
	130677808	0.76	0.91	rs111819262	G	A	0.15	0.1	0.04	0.11						7	LINC-PINT	intronic							
7	130680521	1	1	rs6971499	T	C	0.15	0.11	0.04	0.12						4	LINC-PINT	intronic							
	130681773	1	1	rs6970779	G	A	0.15	0.11	0.04	0.12		H1vec, GM12878	5 cell types	8 cell types	TCF4	5	LINC-PINT	intronic							
	130689908	0.99	1	rs10248190	T	A	0.14	0.11	0.04	0.12			5 cell types	34 cell types		5	LINC-PINT	intronic							
	130690134	0.98	1	rs28460527	C	T	0.14	0.11	0.04	0.13							LINC-PINT	intronic							
	130690299	0.98	1	rs28413549	C	T	0.14	0.11	0.04	0.13							LINC-PINT	intronic							
	130690862	0.86	0.94	rs10282782	T	C	0.14	0.11	0.04	0.12							Pax-4	LINC-PINT	intronic						
	130691182	0.91	0.96	rs10270308	C	T	0.15	0.11	0.06	0.13							7	LINC-PINT	intronic						
rs7190458																									
16	75263661	1	1	rs7190458	G	A	0.26	0.08	0.03	0.04				Caco-2	TAF1	p300	BCAR1	synonymous							
rs9581943																									
13	28461726	0.93	0.98	rs61652270	C	T	0.13	0.29	0.39	0.43						3	PDX1-AS1								
13	28461789	0.93	0.98	rs60004782	G	A	0.13	0.28	0.39	0.43						4	PDX1-AS1								
13	28462132	0.93	0.97	rs9554188	G	A	0.13	0.28	0.39	0.42						ATF3, Pax-5	PDX1-AS1								
13	28462645	0.93	0.98	rs9581927	G	T	0.13	0.28	0.39	0.43						Ik-1, VDR	PDX1-AS1								
13	28464201	0.94	0.97	rs20176782	TAC	T	0.1	0.28	0.38	0.42					</										

SNP/Chr	pos (hg19)	LD		variant	Ref	Alt	AFR freq	AMR freq	ASN freq	EUR freq	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNase	Proteins bound	Motifs changed	REFSEQ or GENCODE genes	dbSNP func annot	MuTHER eQTL			Blood eQTL			
		(r ²)	(D')																Gene	neg log 10 P	Tissue	Cis Gene	Cis P value	Cis Gene	Cis P value
rs2736098																									
5	1294086	1	1	rs2736098	C	T	0.06	0.2	0.33	0.23			H1	H1-hESC Myomere			9	TERT	synonymous						
	1295349	0.74	0.98	rs2853669	A	G	0.08	0.23	0.31	0.29		HepG2, H1	GM12878	GM12892, H1-hESC Myomere	POL2		7	16bp 5' of TERT							
	1297075	0.65	0.81	rs201878070	CCA	C	0.07	0.2	0.25	0.24							21	1.9kb 5' of TERT							
5	1297077	0.73	0.94	rs145844133	AAC	A	0.07	0.21	0.24	0.27							19	1.9kb 5' of TERT							
5	1297081	0.73	0.93	rs201278885	CCA	C	0.06	0.19	0.24	0.27							22	1.9kb 5' of TERT							
	1297488	0.75	0.97	rs27286108	C	T	0.07	0.23	0.26	0.28			10 cell types		EBF1		HEN1Zfp161	2.3kb 5' of TERT							
5	1297854	0.65	0.86	rs27286107	C	T	0.07	0.22	0.22	0.26							ERalpha-a, GATA3, RXRA	2.7kb 5' of TERT							
rs6971499																									
7	130676942	0.84	0.96	rs28651880	C	T	0.15	0.11	0.04	0.13			NHLF	IPS, Adip, CD4, Th0			ATF3, ERalpha-a	LINC-PINT	intronic						
7	130677808	0.76	0.91	rs111819262	G	A	0.15	0.1	0.04	0.11							7	LINC-PINT	intronic						
7	130680521	1	1	rs6971499	T	C	0.15	0.11	0.04	0.12							4	LINC-PINT	intronic						
7	130681773	1	1	rs6970779	G	A	0.15	0.11	0.04	0.12		H1ac, GM12878	5 cell types	8 cell types	TCF4		5	LINC-PINT	intronic						
7	130689908	0.99	1	rs10248190	T	A	0.14	0.11	0.04	0.12			5 cell types	34 cell types			5	LINC-PINT	intronic						
7	130690134	0.98	1	rs28405227	C	T	0.14	0.11	0.04	0.13								LINC-PINT	intronic						
7	130690299	0.98	1	rs28413549	C	T	0.14	0.11	0.04	0.13								LINC-PINT	intronic						
7	130690862	0.86	0.94	rs10282782	T	C	0.14	0.11	0.04	0.12								Pax-4	LINC-PINT	intronic					
7	130691182	0.91	0.96	rs10270308	C	T	0.15	0.11	0.06	0.13								7	LINC-PINT	intronic					
rs7190458																									
16	75263661	1	1	rs7190458	G	A	0.26	0.08	0.03	0.04				Caco-2	TAF1		p300	BCAR1	synonymous						
rs9581943																									
13	28461726	0.93	0.98	rs61652270	C	T	0.13	0.29	0.39	0.43							3	PDX1-AS1							
13	28461789	0.93	0.98	rs60004782	G	A	0.13	0.28	0.39	0.43							4	PDX1-AS1							
13	28462132	0.93	0.97	rs9554188	G	A	0.13	0.28	0.39	0.42							ATF3, Pax-5	PDX1-AS1							
13	28462645	0.93	0.98	rs9581927	G	T	0.13	0.28	0.39	0.43							Ik-1, VDR	PDX1-AS1							
13	28464201	0.94	0.97	rs201726782	TAC	T	0.1	0.28	0.38	0.42							8	PDX1-AS1							
13	28464203	0.93	0.98	rs9581929	C	T	0.09	0.28	0.39	0.42							6	PDX1-AS1							
13	28464690	0.95	0.98	rs2285481	A	C	0.17	0.29	0.39	0.42							5	PDX1-AS1							
13	28468222	0.95	0.98	rs9581931	A	G	0.14	0.29	0.39	0.42							Ets-1	PDX1-AS1							
13	28470544	0.95	0.98	rs4424773	C	G	0.14	0.29	0.39	0.42							8	PDX1-AS1							
13	28471366	0.95	0.98	rs9554193	G	A	0.14	0.29	0.39	0.42							5	PDX1-AS1							
13	28472724	0.95	0.98	rs7995917	T	C	0.15	0.29	0.39	0.42							Hox9, Hoxb8, Hoxb9	PDX1-AS1							
13	28474236	0.89	0.97	rs19990582	TC	T	0.15	0.28	0.38	0.41							7	PDX1-AS1							
13	28476277	0.96	0.99	rs7993114	A	G	0.16	0.29	0.38	0.42							TCF12	PDX1-AS1		POMP	1.6/1.2	Skin/Liver			
13	28476911	0.96	0.99	rs11618591	G	A	0.16	0.29	0.38	0.42							ATF3, ZEB1	PDX1-AS1		POMP	1.7/1.2	Skin/Liver			
13	28476978	0.95	0.99	rs9554197	C	T	0.16	0.28	0.38	0.43							6	PDX1-AS1		POMP	1.7/1.2	Skin/Liver			
13	28477058	0.96	0.99	rs11618036	T	C	0.16	0.29	0.38	0.42							ERalpha-a, RXRA	PDX1-AS1							
13	28477111	0.92	0.97	rs11618832	G	A	0.16	0.29	0.38	0.41							GATA1, UN-1, STAT	PDX1-AS1							
13	28477117	0.92	0.97	rs11616678	C	T	0.16	0.29	0.38	0.42								PDX1-AS1							
13	28477149	0.96	0.99	rs11618052	T	C	0.16	0.29	0.38	0.42							MeCP2, Pucp32	PDX1-AS1							
13	28477268	0.96	0.99	rs9579127	A	G	0.16	0.29	0.38	0.42							Zeb3	PDX1-AS1							
13	28477401	0.96	0.99	rs7999100	C	A	0.16	0.29	0.38	0.42							HDAC2, p300	PDX1-AS1		POMP	1.7/1.2	Skin/Liver			
13	28477590	0.96	0.99	rs8000004	A	G	0.16	0.29	0.38	0.42							5	PDX1-AS1		POMP	1.7/1.2	Skin/Liver			
13	28481938	0.96	0.99	rs9579128	T	C	0.13	0.28	0.38	0.42		H1ac	HepG2	5 cell types			4	PDX1-AS1		POMP	1.7/1.3	Skin/Liver			
13	28490211	0.97	0.99	rs2297316	G	A	0.09	0.28	0.36	0.42			HMEC				4	PDX1-AS1							
13	28493997	1	1	rs9581943	G	A	0.09	0.28	0.38	0.42		5 cell types		24 cell types		7	5	PDX1-AS1, PDX1							

[illegible]

HaploReg, MuTHER and the Blood eQTL databases were used for this analysis. Note that no Trans-eQTLs were noted in the Blood eQTL database.

2. SUPPLEMENTARY FIGURES

Supplementary Figure 1. Flow diagram of PanScan III GWAS study design

Supplementary Figure 2. Risk allele counts (a) and odds ratios (95% confidence intervals) (b) for pancreatic cancer for a genetic risk score of the ten susceptibility loci identified in PanScan I, II, and III.

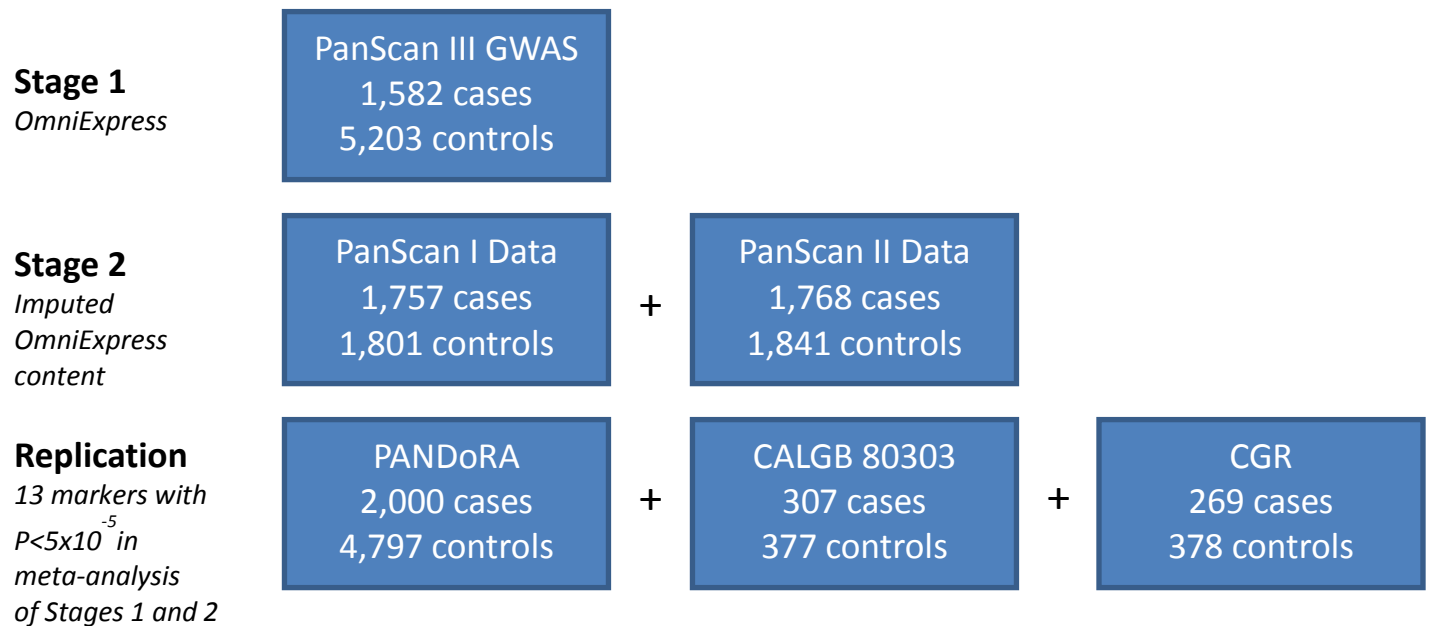
Supplementary Figure 3. Plot of estimated admixture for individuals in stage 1 of PanScan III GWAS

Supplementary Figure 4. Plot of top eigenvectors from stage 1 of PanScan III GWAS based on principal components analysis

Supplementary Figure 5. Quantile-quantile (Q-Q) plot of the association results in stages 1 and 2 of the PanScan III GWAS

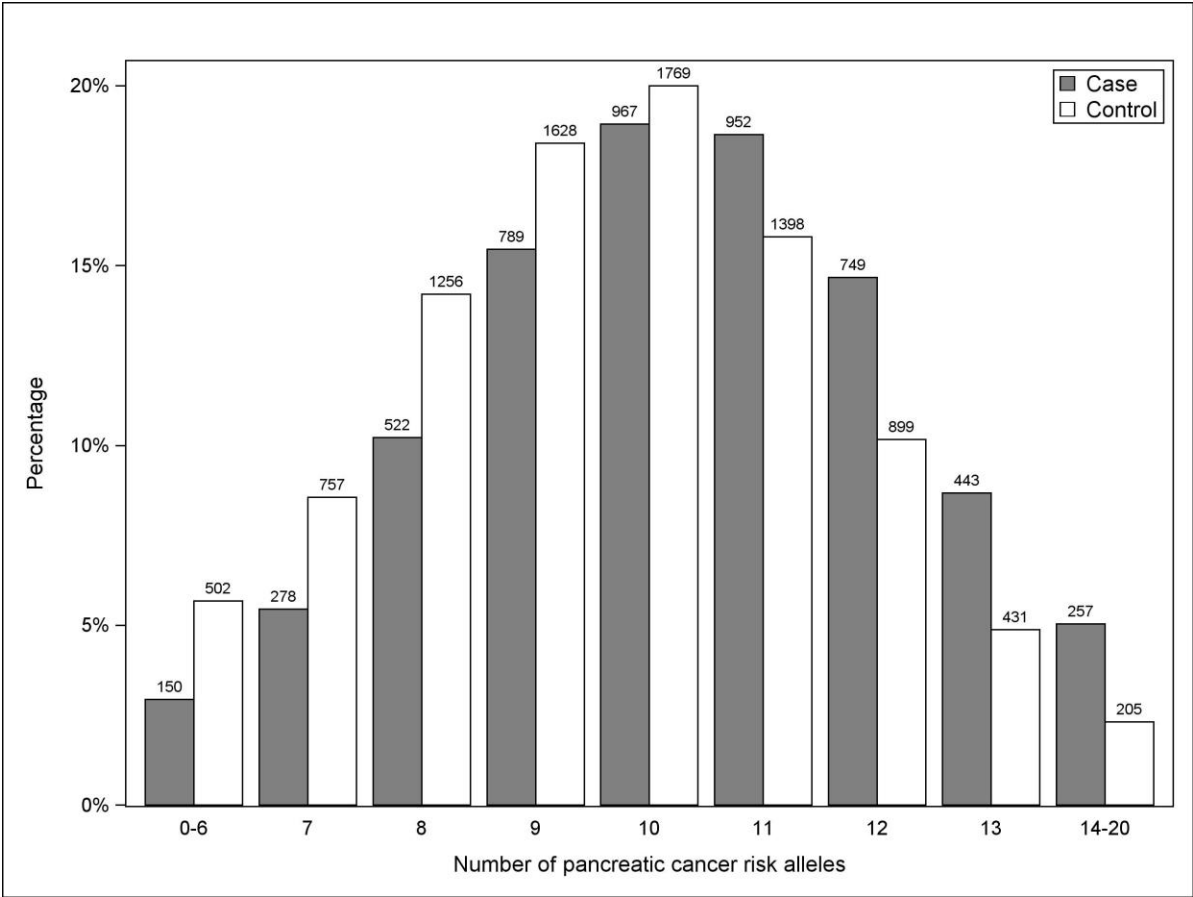
Supplementary Figure 6. Manhattan plot showing statistical significance of the association for all genotyped SNPs in stages 1 and 2 of PanScan III GWAS

Supplementary Figure 1. Flow diagram of PanScan III study design. A schematic figure showing stage 1, stage 2 and replication stage with a total of 7,683 case and 14,397 control subjects included in the final analysis. Numbers of cases and controls in each stage are indicated as well as the array type, imputation and *P*-value threshold for SNPs moved forward to replication

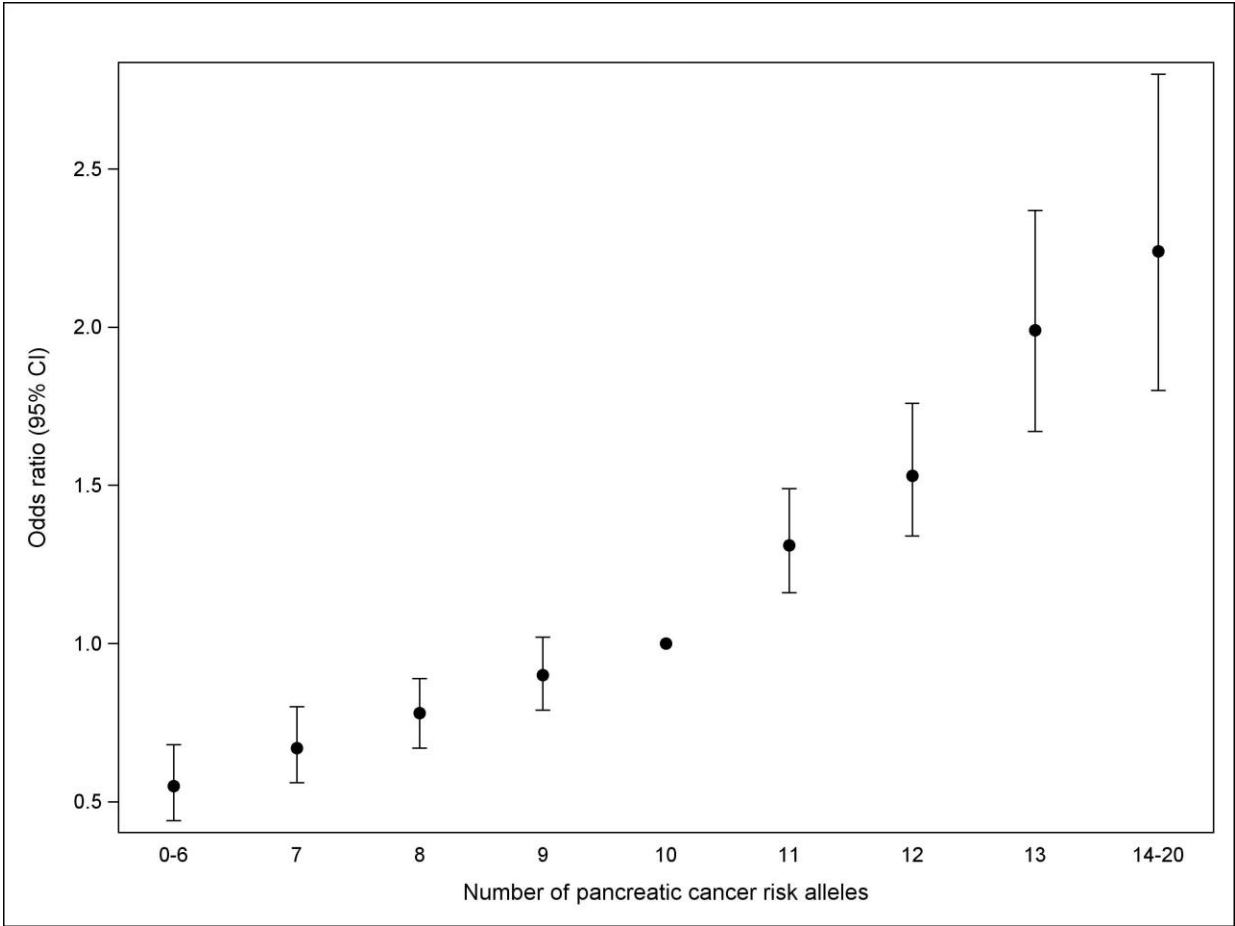


Supplementary Figure 2. Risk allele counts (a) and odds ratios (95% confidence intervals) (b) for pancreatic cancer for a genetic risk score of the ten susceptibility loci identified in PanScan I, II, and III. (a) Percentage of cases and controls with each total number of risk alleles. Absolute number of participants provided above each vertical bar. (b) Results from unconditional logistic regression of the pancreatic cancer genotype score in participants from Stage 1 and Stage 2 of the PanScan III GWAS. For stage 1, model adjusted for age, sex, geographic region, and significant principal components. For stage 2, model adjusted for age, sex, study, and significant principal components. Referent is the most prevalent risk allele count in controls (n=10 risk alleles).

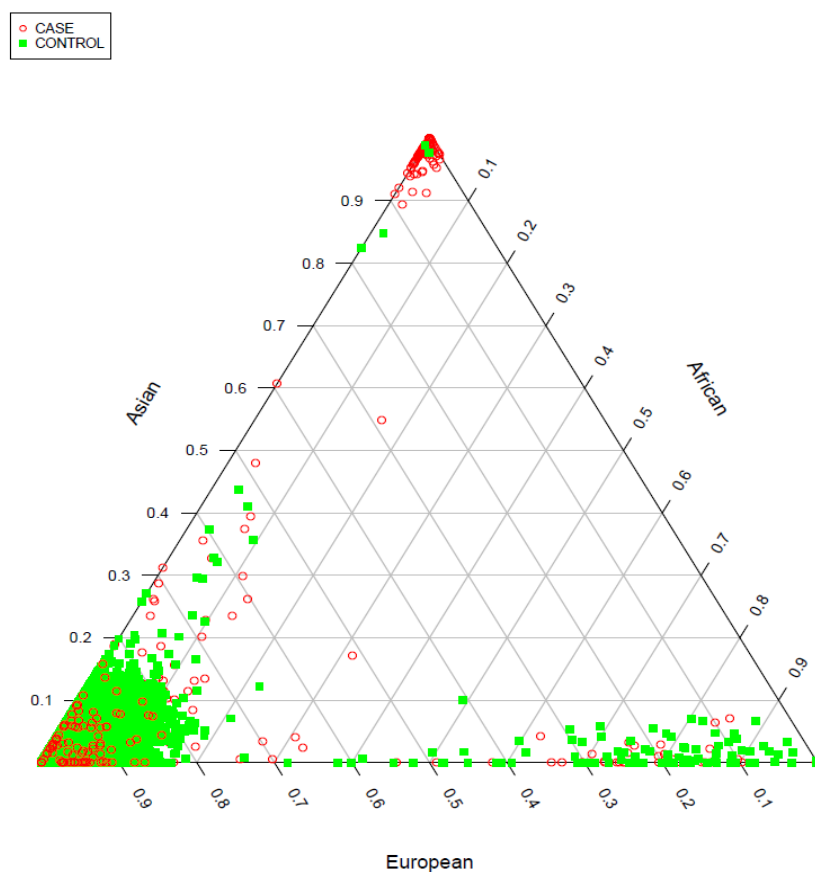
Panel (a)



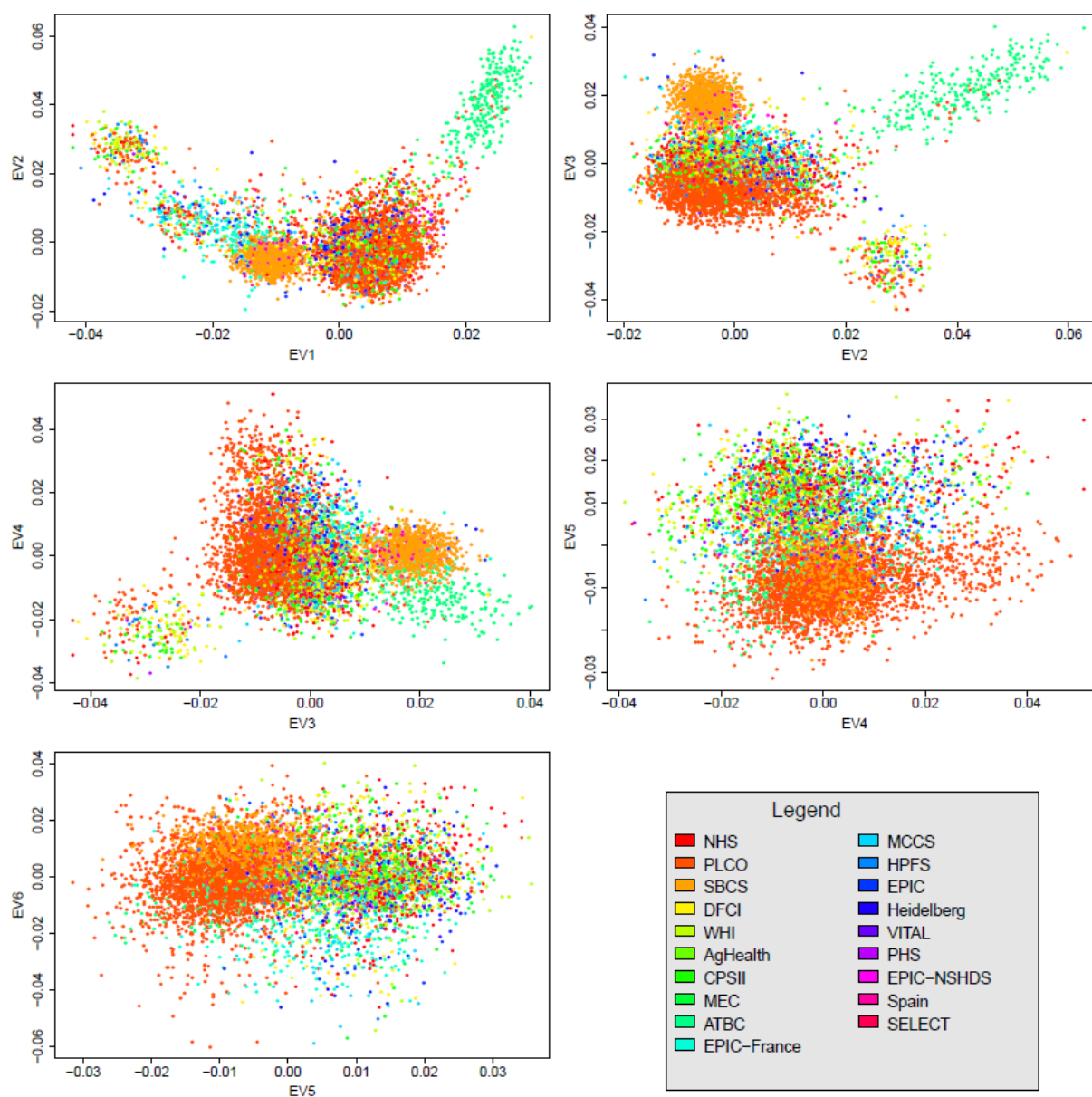
Panel (b)



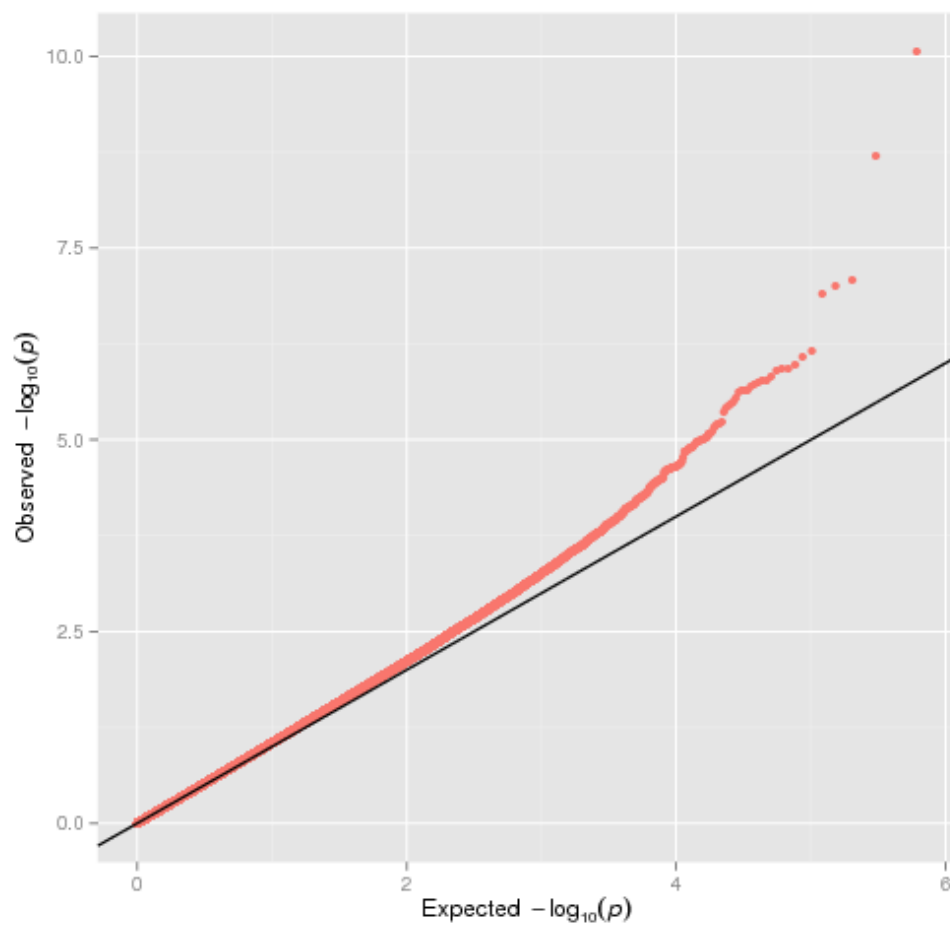
Supplementary Figure 3. Plot of estimated admixture for individuals in stage 1 of PanScan III GWAS. For details, see Online Methods. Individuals with <80% European ancestry were excluded from the main association analysis. Individuals with Asian ancestry from SMWHS were analyzed separately and included case and control subjects from SMWHS in stages 1 and 2 of PanScan III and control subjects from SMWHS that were previously genotyped.



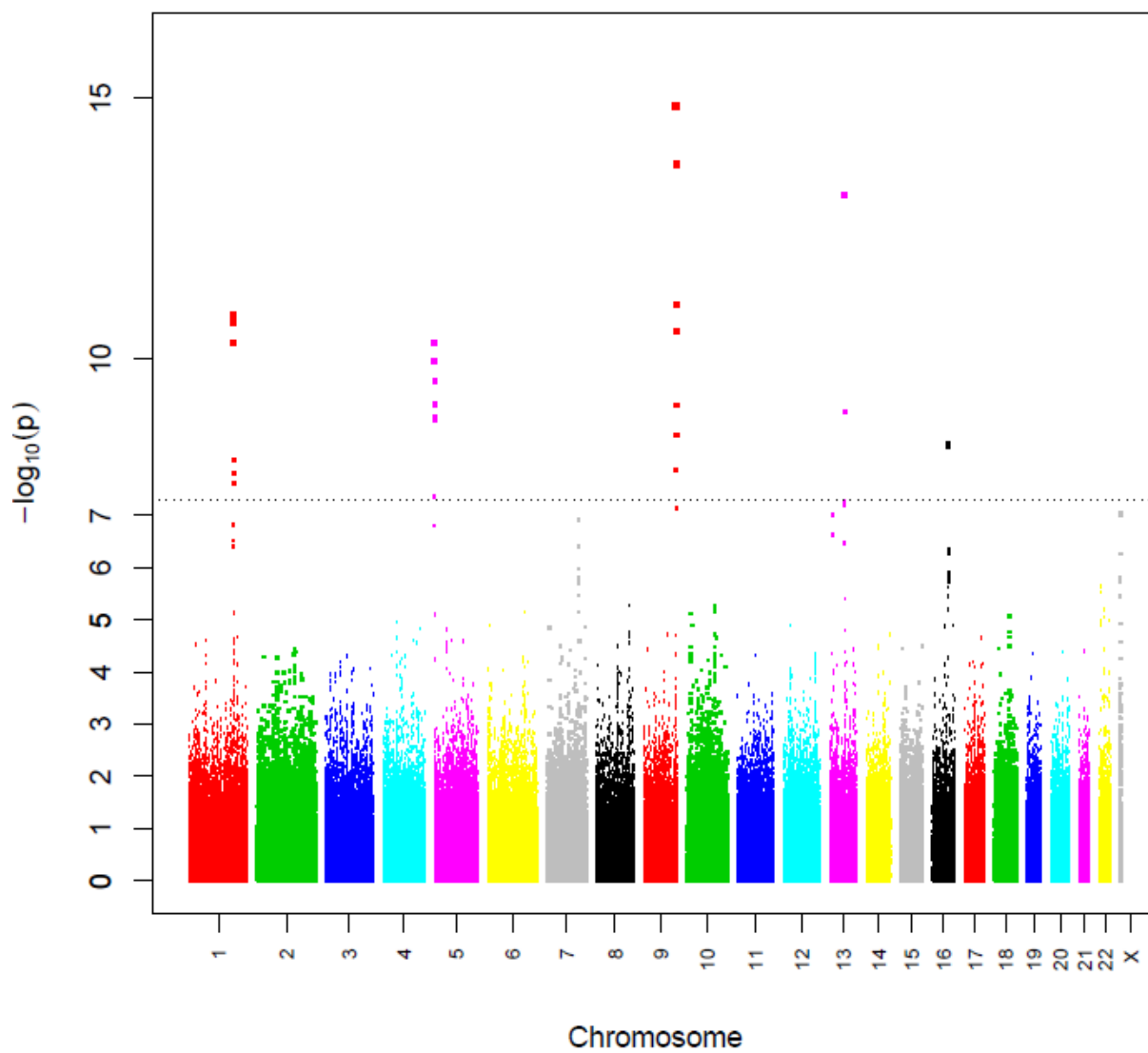
Supplementary Figure 4. Plot of top eigenvectors from stage 1 of PanScan III GWAS based on principal components analysis. For details, see Online Methods.



Supplementary Figure 5. Quantile-quantile (Q-Q) plot of the association results in stages 1 and 2 of the PanScan III GWAS



Supplementary Figure 6. Manhattan plot showing statistical significance of the association for all genotyped SNPs in stages 1 and 2 of PanScan III GWAS



3. SUPPLEMENTARY NOTE

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