Supplementary Table 1: Kegg_Maturity Onset Diabetes of the Young (MODY) and Reactome_Regulation of Beta Cell Development

SNP*	Gene	Chr	Position	Ref Allele	Risk Allele	OR	95% CI Lower	95% CI Upper	P-value†
rs1169296	*HNF1A*	12	121428407	A	G	1.12	1.07	1.17	2.63E-07
rs2244608	*HNF1A*	12	121416988	A	G	1.11	1.07	1.16	1.54E-06
rs12951345	*HNF1B*	17	36077863	A	C	0.88	0.84	0.93	1.38E-06
rs7223387	*HNF1B*	17	36082473	T	G	0.89	0.85	0.94	3.46E-06
rs1853150	*HNF4A*	20	43081164	G	T	1.10	1.05	1.15	1.64E-05
rs1913641	*HNF4G*	8	76483239	T	G	1.10	1.05	1.14	1.55E-05
rs2943547	*HNF4G*	8	76451098	A	G	1.09	1.05	1.14	2.31E-05
rs118117270	*PAX4*	7	127263589	T	C	0.67	0.54	0.84	4.23E-04
rs62483175	*PAX4*	7	127247114	C	T	0.78	0.67	0.91	0.002

*SNPs contributing to the association of the Kegg_MODY (n=23 genes in pathway) and Reactome_Regulation of beta cell development (n=28 genes in pathway) with PDAC risk. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. Major allele is Ref (reference) allele. PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval

†SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2, 3 and PanC4.

Supplementary Table 2: Biocarta_Cardia EGF pathway

SNP*	Gene	Chr	Position	Ref Allele	Risk Allele	OR	95% CI Lower	95% CI Upper	P-value†
rs1326889	*AGT*	1	230862998	C	T	0.90	0.86	0.94	4.21E-07
rs35232409	*EDNRA*	4	148396281	G	C	0.88	0.84	0.92	3.20E-07
rs6537481	*EDNRA*	4	148396094	A	G	0.88	0.83	0.92	1.15E-07

*SNPs contributing to the association of the BioCarta_Cardia EGF pathway (n=17 genes in pathway) with PDAC risk. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. Major allele is Ref (reference) allele. PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval

†SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2, 3 and PanC4.

Supplementary Table 3: Nikolsky_breast cancer chr17 amplicon

SNP*	Gene	Chr	Position	Ref Allele	Risk Allele	OR	95% CI Lower	95% CI Upper	P-value†
rs876493	*ERBB2*	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs876493	*PGAP3*	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs876493	*TCAP*	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs876493	*STARD3*	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs876493	*PNMT*	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs12951345	*HNF1B*	17	36077863	A	C	0.88	0.84	0.93	1.38E-06
rs7223387	*HNF1B*	17	36082473	T	G	0.89	0.85	0.94	3.46E-06
rs8078692	*THRA*	17	38215117	A	G	0.91	0.87	0.95	6.71E-06
rs8078692	*MED24*	17	38215117	A	G	0.91	0.87	0.95	6.71E-06
rs7225411	*IGFBP4*	17	38620130	T	C	1.16	1.09	1.23	7.39E-06
rs7225411	*TNS4*	17	38620130	T	C	1.16	1.09	1.23	7.39E-06
rs3764351	*ERBB2*	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs3764351	*PGAP3*	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs3764351	*TCAP*	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs3764351	*STARD3*	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs3764351	*PNMT*	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs113557550	*TNS4*	17	38639070	C	T	1.25	1.13	1.38	2.35E-05
rs76592685	*IGFBP4*	17	38630459	A	G	1.17	1.09	1.26	3.04E-05
rs12451586	*CDK12*	17	37633835	T	A	0.91	0.87	0.95	6.58E-05
rs62074998	*FBXL20*	17	37480822	C	A	0.84	0.77	0.92	1.31E-04
rs72823344	*CACNB1*	17	37351774	G	A	1.18	1.08	1.29	1.91E-04
rs72823344	*RPL19*	17	37351774	G	A	1.18	1.08	1.29	1.91E-04
rs72823344	*STAC2*	17	37351774	G	A	1.18	1.08	1.29	1.91E-04
rs113520394	*THRA*	17	38212046	C	T	0.89	0.84	0.95	2.13E-04
rs113520394	*MED24*	17	38212046	C	T	0.89	0.84	0.95	2.13E-04
rs117811627	*CCR7*	17	38691196	T	C	1.34	1.15	1.56	2.16E-04

rs12453796	*FBXL20*	17	37454997	A	T	0.91	0.86	0.96	3.11E-04
rs883544	*STAC2*	17	37387413	A	G	0.91	0.87	0.96	3.28E-04
rs11652129	*FOXN1*	17	26817115	A	C	1.26	1.10	1.43	5.05E-04
rs1877032	*NEUROD2*	17	37771064	T	C	1.13	1.05	1.20	6.60E-04
rs1877032	*PPP1R1B*	17	37771064	T	C	1.13	1.05	1.20	6.60E-04
rs16964766	*PIPOX*	17	27393310	G	A	1.10	1.04	1.17	6.84E-04
rs16964766	*TIAF1*	17	27393310	G	A	1.10	1.04	1.17	6.84E-04
rs17721128	*C17orf63*	17	27143892	A	G	0.87	0.80	0.94	8.07E-04
rs78126981	*PIPOX*	17	27320567	T	A	0.76	0.65	0.89	8.18E-04
rs78126981	*SEZ6*	17	27320567	T	A	0.76	0.65	0.89	8.18E-04
rs7222039	*CSF3*	17	38165541	T	C	1.07	1.03	1.12	8.19E-04
rs7222039	*PSMD3*	17	38165541	T	C	1.07	1.03	1.12	8.19E-04
rs111935829	*GSDMB*	17	38081394	C	G	0.84	0.76	0.94	1.19E-03
rs111935829	*ORMDL3*	17	38081394	C	G	0.84	0.76	0.94	1.19E-03
rs2227324	*CSF3*	17	38172192	G	A	1.14	1.05	1.23	1.21E-03
rs2227324	*PSMD3*	17	38172192	G	A	1.14	1.05	1.23	1.21E-03
rs2470201	*TMEM98*	17	31250916	G	A	1.10	1.04	1.16	1.28E-03
rs17676191	*IKZF3*	17	37949924	A	G	1.12	1.04	1.20	1.68E-03
rs750409	*CACNB1*	17	37317211	G	A	0.87	0.80	0.95	1.78E-03
rs147225757	*CRYBA1*	17	27566770	G	C	0.72	0.58	0.89	2.12E-03
rs75646943	*IKZF3*	17	37954143	C	T	0.78	0.66	0.91	2.12E-03
rs117237010	*SEZ6*	17	27311692	G	A	1.32	1.10	1.58	2.31E-03
rs12103674	*PPP1R1B*	17	37804352	T	C	1.13	1.04	1.21	2.38E-03
rs4795393	*GRB7*	17	37893484	C	T	0.94	0.90	0.98	2.43E-03
rs4795393	*MIEN1*	17	37893484	C	T	0.94	0.90	0.98	2.43E-03
rs147849562	*FOXN1*	17	26855748	G	A	1.21	1.07	1.38	2.78E-03
rs141786375	*ERAL1*	17	27200588	A	G	0.77	0.64	0.91	2.82E-03
rs28986	*TMEM98*	17	31279321	C	A	1.20	1.06	1.37	3.45E-03
rs12453507	*GSDMB*	17	38053207	C	G	0.94	0.90	0.98	4.17E-03
rs12453507	*ZPBP2*	17	38053207	C	G	0.94	0.90	0.98	4.17E-03
rs74811341	*CCR7*	17	38720826	C	T	0.85	0.76	0.95	4.59E-03

rs191981826	*SGK494*	17	26931189	G	A	1.10	1.03	1.17	6.83E-03
rs191981826	*SPAG5*	17	26931189	G	A	1.10	1.03	1.17	6.83E-03
rs2665647	*NEUROD2*	17	37778907	C	G	1.25	1.06	1.48	7.23E-03
rs10853129	*ERAL1*	17	27191960	G	A	0.94	0.90	0.98	7.93E-03
rs62068170	*ORMDL3*	17	38103210	G	A	1.06	1.01	1.10	8.42E-03
rs117006142	*SGK494*	17	26939612	T	A	0.83	0.72	0.96	1.05E-02
rs117006142	*SPAG5*	17	26939612	T	A	0.83	0.72	0.96	1.05E-02
rs8614	*CRYBA1*	17	27588806	C	A	1.07	1.01	1.13	1.38E-02
rs79062097	*ZPBP2*	17	38043467	C	T	0.89	0.79	1.00	4.74E-02

*SNPs contributing to the association of the Nikolsky_Breast cancer chr 17 amplicon (n=131 genes in gene set) with PDAC risk. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. Major allele is Ref (reference) allele. PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval

†SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2,3 and PanC4.

Supplementary Table 4: Pujana_ATM_PCC Network

SNP*	Gene	Chr	Position	Ref Allele	Risk Allele	OR	95% CI Lower	95% CI Upper	P-value†
rs7859034	SMC2	9	106865692	G	T	0.90	0.86	0.93	3.07E-07
rs876493	PNMT	17	37824545	G	A	0.90	0.86	0.94	1.27E-06
rs12951345	HNF1B	17	36077863	A	C	0.88	0.84	0.93	1.38E-06
rs57791062	GRP	18	56880211	C	T	0.88	0.83	0.93	1.79E-06
rs7223387	HNF1B	17	36082473	T	G	0.89	0.85	0.94	3.46E-06
rs8078692	THRA	17	38215117	A	G	0.91	0.87	0.95	6.71E-06
rs1169291	HNF1A	12	121426064	C	T	1.11	1.06	1.16	8.39E-06
rs34825318	TAB1	22	39798237	G	A	1.35	1.18	1.54	1.11E-05
rs4710491	KHDRBS2	6	62507189	A	C	0.46	0.32	0.65	1.17E-05
rs3764351	PNMT	17	37824339	G	A	0.91	0.87	0.95	1.27E-05
rs1169297	HNF1A	12	121428455	G	A	1.10	1.05	1.15	1.40E-05
rs2160263	ACTR2	2	65509238	C	T	1.14	1.07	1.21	1.53E-05
rs1913641	HNF4G	8	76483239	T	G	1.10	1.05	1.14	1.55E-05
rs641652	TPP2	13	103339194	G	A	0.91	0.87	0.95	1.95E-05
rs10071714	GRIA1	5	153124891	T	C	0.90	0.85	0.94	1.98E-05
rs2943547	HNF4G	8	76451098	A	G	1.09	1.05	1.14	2.31E-05
rs11636684	HEXA	15	72663946	A	G	0.89	0.85	0.94	2.35E-05
rs7579797	ACTR2	2	65511539	A	G	0.91	0.88	0.95	2.61E-05
rs3124737	CASP7	10	115497095	A	G	0.91	0.88	0.95	3.29E-05
rs62208272	GHRH	20	35876666	T	C	1.31	1.15	1.48	3.57E-05
rs114958362	MED6	14	71032061	G	A	0.66	0.54	0.80	4.48E-05
rs2615921	HIPK3	11	33395054	T	C	0.86	0.80	0.93	5.55E-05
rs118102857	ITGBL1	13	102258101	C	T	1.40	1.19	1.64	5.83E-05
rs113897737	MED1	17	37581353	C	T	1.15	1.07	1.23	6.28E-05
rs78106592	FCHSD2	11	72647161	G	A	0.86	0.80	0.93	7.10E-05

rs55717718	PHOX2B	4	41768765	T	C	0.79	0.71	0.89	8.58E-05
rs72919332	HIPK3	11	33392100	G	T	0.85	0.78	0.92	8.78E-05
rs12361597	TMEM123	11	102337777	G	A	0.83	0.76	0.91	9.61E-05
rs140127725	LDHB	12	21900930	A	G	1.49	1.22	1.83	0.0001
rs201611588	HEXA	15	72617472	T	C	0.91	0.86	0.95	0.0001
rs184199456	PFKFB4	3	48586891	G	A	1.39	1.17	1.64	0.0001
rs111345106	CD47	3	107775269	C	T	1.28	1.13	1.45	0.0002
rs138947508	MAPK8	10	49566274	A	G	0.72	0.60	0.85	0.0002
rs146071727	HNRNPL	19	39315847	C	G	1.26	1.12	1.43	0.0002
rs72823344	RPL19	17	37351774	G	A	1.18	1.08	1.29	0.0002
rs72779276	TELO2	16	1551826	C	G	0.90	0.85	0.95	0.0002
rs12522289	HNRNPAB	5	177640864	A	G	1.16	1.07	1.25	0.0002
rs7212868	MED1	17	37608052	C	A	0.92	0.88	0.96	0.0002
rs7585054	BCL2L11	2	111944927	A	G	0.92	0.89	0.96	0.0002
rs113520394	THRA	17	38212046	C	T	0.89	0.84	0.95	0.0002
rs7148005	BAZ1A	14	35319411	C	G	0.89	0.83	0.95	0.0002
rs11070327	OIP5	15	41602866	G	A	1.08	1.04	1.13	0.0002
rs140573271	CDC123	10	12305979	G	A	0.77	0.67	0.88	0.0002
rs17215231	PFDN6	6	33239869	C	T	0.86	0.79	0.93	0.0002
rs7321404	PIBF1	13	73351180	A	T	1.15	1.07	1.24	0.0003
rs77381836	NR2C1	12	95469581	A	G	0.74	0.63	0.87	0.0003
rs10064416	BTF3	5	72809050	A	G	1.17	1.07	1.27	0.0003
rs114629468	FBL	19	40320168	G	A	0.80	0.71	0.90	0.0003
rs116905840	ANGEL1	14	77271613	G	A	1.41	1.17	1.70	0.0003
rs112646694	PCF11	11	82893611	C	T	1.40	1.16	1.68	0.0003
rs58812167	GSR	8	30554938	C	A	0.93	0.89	0.97	0.0003
rs73802720	GRIA1	5	153067523	T	C	0.90	0.85	0.95	0.0003
rs74704910	FCHSD2	11	72799737	T	G	0.85	0.78	0.93	0.0003
rs3749812	HNRNPAB	5	177650210	T	C	1.16	1.07	1.26	0.0003
rs76504832	POP4	19	30109535	G	A	0.78	0.68	0.90	0.0004
rs6795254	TRA2B	3	185622421	C	T	0.85	0.78	0.93	0.0004

rs118117270	PAX4	7	127263589	T	C	0.67	0.54	0.84	0.0004
rs601269	TPP2	13	103321992	G	C	0.91	0.86	0.96	0.0004
rs111918710	SIKE1	1	115309588	C	A	0.60	0.46	0.80	0.0004
rs118025182	BRCA1	17	41181639	G	A	0.80	0.71	0.91	0.0005
rs10881645	KIF20B	10	91490087	A	G	1.08	1.03	1.12	0.0005
rs7188875	NAE1	16	66917267	A	C	1.12	1.05	1.20	0.0005
rs144972902	ATXN3	14	92563474	T	C	1.24	1.10	1.41	0.0005
rs34501420	FAM53B	10	126304770	G	C	1.09	1.04	1.14	0.0005
rs13260089	GSR	8	30531154	T	C	0.89	0.83	0.95	0.0005
rs182312279	TACR3	4	104551730	T	C	0.81	0.72	0.91	0.0006
rs2444857	RPL30	8	99062480	A	T	0.93	0.89	0.97	0.0006
rs140048312	PMS2P1	7	99915673	C	T	0.73	0.61	0.87	0.0006
rs1588327	NPHP1	2	110891433	A	C	1.08	1.03	1.12	0.0006
rs72847518	TAF5	10	105127191	A	C	0.84	0.75	0.93	0.0006
rs35223775	NSL1	1	212879952	C	T	0.91	0.86	0.96	0.0006
rs33948247	E2F4	16	67235672	C	T	0.85	0.78	0.93	0.0006
rs143786818	FAM53B	10	126303382	T	C	1.29	1.11	1.49	0.0007
rs142824527	TACR3	4	104623592	A	G	0.79	0.69	0.90	0.0007
rs11079803	SP2	17	46019901	G	A	0.93	0.89	0.97	0.0007
rs1062225	MAPK8	10	49643226	A	G	0.90	0.84	0.96	0.0008
rs7222039	CSF3	17	38165541	T	C	1.07	1.03	1.12	0.0008
rs7222039	PSMD3	17	38165541	T	C	1.07	1.03	1.12	0.0008
rs17037193	SNRNP27	2	70103504	T	C	0.91	0.87	0.96	0.0009
rs72856970	NMI	2	152135335	G	A	1.20	1.08	1.33	0.0009
rs2248014	RPL30	8	99030280	T	C	0.92	0.88	0.97	0.0009
rs72826897	NPHP1	2	110926458	A	G	0.84	0.76	0.93	0.0009
rs10416586	POP4	19	30112997	G	A	0.85	0.78	0.94	0.0009
rs8008960	ANGEL1	14	77289618	T	C	0.92	0.88	0.97	0.0009
rs76331936	USP19	3	49141714	G	A	0.73	0.61	0.88	0.001
rs192123848	SP2	17	46013386	G	A	0.74	0.62	0.89	0.001
rs676119	BCL2L11	2	111912718	A	G	0.93	0.90	0.97	0.001

rs11852609	OIP5	15	41582598	T	G	1.08	1.03	1.12	0.001
rs72678745	BAZ1A	14	35272925	C	T	0.82	0.73	0.92	0.001
rs2227324	CSF3	17	38172192	G	A	1.14	1.05	1.23	0.001
rs2227324	PSMD3	17	38172192	G	A	1.14	1.05	1.23	0.001
rs76790404	AOC2	17	41018481	G	C	0.82	0.73	0.93	0.001
rs141981996	PMS2P1	7	99929614	C	T	0.90	0.84	0.96	0.001
rs190904708	HNRNPL	19	39346267	G	A	0.73	0.60	0.88	0.001
rs4951457	NSL1	1	212879500	A	C	1.08	1.03	1.13	0.001
rs8014854	ATXN3	14	92550658	G	A	1.07	1.03	1.12	0.001
rs11687575	NMI	2	152156771	C	T	1.14	1.05	1.23	0.002
rs10794501	GPR3	1	27699449	A	T	1.09	1.03	1.16	0.002
rs62483175	PAX4	7	127247114	C	T	0.78	0.67	0.91	0.002
rs11707940	USP4	3	49363772	T	A	0.92	0.87	0.97	0.002
rs368987508	KIF20B	10	91548385	A	T	1.07	1.02	1.12	0.002
rs1050450	USP4	3	49394834	G	A	0.93	0.89	0.98	0.003
rs2504765	GPR3	1	27741131	C	T	0.90	0.84	0.96	0.003
rs146494007	PCF11	11	82867659	T	G	0.79	0.68	0.92	0.003
rs35996049	RPL19	17	37375354	G	A	1.13	1.04	1.22	0.003
rs145088470	AOC2	17	41020181	G	T	0.71	0.57	0.89	0.003
rs12923138	E2F4	16	67233266	A	C	0.94	0.91	0.99	0.008
rs185050272	USP19	3	49151003	G	A	0.83	0.70	0.97	0.02

*SNPs contributing to the association of the Pujana_ATM PCC network (n=1350 genes in pathway) with PDAC risk. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. Major allele is Ref (reference) allele. PCC, Pearson's correlation coefficient; PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval

†SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2,3 and PanC4.

Supplementary Table 5: Top SNPs in genes in the top ranked PDAC associated gene sets and pathways

Candidate SNP*	Gene	Chr	Position	Ref Allele	Risk Allele	OR	95% CI Lower	95% CI Upper	P-value†	Pathway/gene set
rs6537481	EDNRA	4	148396094	A	G	0.88	0.83	0.92	1.15E-07	Cardiac EGF Pathway
rs1169296	HNF1A	12	121428407	A	G	1.12	1.07	1.17	2.63E-07	MODY, Beta Cell Dev
rs7859034	SMC2	9	106865692	G	T	0.90	0.86	0.93	3.07E-07	Pujana
rs35232409	EDNRA	4	148396281	G	C	0.88	0.84	0.92	3.20E-07	Cardiac EGF Pathway
rs1326889	AGT	1	230862998	C	T	0.90	0.86	0.94	4.21E-07	Cardiac EGF Pathway
rs876493	ERBB2 PGAP3 TCAP STARD3 PNMT	17	37824545	G	A	0.90	0.86	0.94	1.27E-06	Nikolsky, Pujana
rs12951345	HNF1B	17	36077863	A	C	0.88	0.84	0.93	1.38E-06	MODY, Beta Cell Dev, Nikolsky, Pujana
rs2244608	HNF1A	12	121416988	A	G	1.11	1.07	1.16	1.54E-06	MODY, Beta Cell Dev
rs57791062	GRP	18	56880211	C	T	0.88	0.83	0.93	1.79E-06	Pujana
rs7223387	HNF1B	17	36082473	T	G	0.89	0.85	0.94	3.46E-06	MODY, Beta Cell Dev, Nikolsky, Pujana
rs8078692	THRA MED24	17	38215117	A	G	0.91	0.87	0.95	6.71E-06	Nikolsky, Pujana
rs7225411	IGFBP4 TNS4	17	38620130	T	C	1.16	1.09	1.23	7.39E-06	Nikolsky
rs1169291	HNF1A	12	121426064	C	T	1.11	1.06	1.16	8.39E-06	Pujana
rs34825318	TAB1	22	39798237	G	A	1.35	1.18	1.54	1.11E-05	Pujana
rs4710491	KHDRBS2	6	62507189	A	C	0.46	0.32	0.65	1.17E-05	Pujana
rs3764351	ERBB2 PGAP3 TCAP STARD3 PNMT	17	37824339	G	A	0.91	0.87	0.95	1.27E-05	Nikolsky, Pujana
rs1169297	HNF1A	12	121428455	G	A	1.10	1.05	1.15	1.40E-05	Pujana
rs2160263	ACTR2	2	65509238	C	T	1.14	1.07	1.21	1.53E-05	Pujana
rs1913641	HNF4G	8	76483239	T	G	1.10	1.05	1.14	1.55E-05	MODY, Beta Cell Dev, Pujana

rs1853150	HNF4A	20	43081164	G	T	1.10	1.05	1.15	1.64E-05	MODY, Beta Cell Dev
rs641652	TPP2	13	103339194	G	A	0.91	0.87	0.95	1.95E-05	Pujana
rs10071714	GRIA1	5	153124891	T	C	0.90	0.85	0.94	1.98E-05	Pujana
rs2943547	HNF4G	8	76451098	A	G	1.09	1.05	1.14	2.31E-05	MODY, Beta Cell Dev, Pujana
rs11636684	HEXA	15	72663946	A	G	0.89	0.85	0.94	2.35E-05	Pujana
rs113557550	TNS4	17	38639070	C	T	1.25	1.13	1.38	2.35E-05	Nikolsky
rs7579797	ACTR2	2	65511539	A	G	0.91	0.88	0.95	2.61E-05	Pujana
rs76592685	IGFBP4	17	38630459	A	G	1.17	1.09	1.26	3.04E-05	Nikolsky
rs3124737	CASP7	10	115497095	A	G	0.91	0.88	0.95	3.29E-05	Pujana
rs62208272	GHRH	20	35876666	T	C	1.31	1.15	1.48	3.57E-05	Pujana
rs114958362	MED6	14	71032061	G	A	0.66	0.54	0.80	4.48E-05	Pujana
rs2615921	HIPK3	11	33395054	T	C	0.86	0.80	0.93	5.55E-05	Pujana
rs118102857	ITGBL1	13	102258101	C	T	1.40	1.19	1.64	5.83E-05	Pujana
rs113897737	MED1	17	37581353	C	T	1.15	1.07	1.23	6.28E-05	Pujana
rs12451586	CDK12	17	37633835	T	A	0.91	0.87	0.95	6.58E-05	Nikolsky
rs78106592	FCHSD2	11	72647161	G	A	0.86	0.80	0.93	7.10E-05	Pujana
rs55717718	PHOX2B	4	41768765	T	C	0.79	0.71	0.89	8.58E-05	Pujana
rs72919332	HIPK3	11	33392100	G	T	0.85	0.78	0.92	8.78E-05	Pujana
rs12361597	TMEM123	11	102337777	G	A	0.83	0.76	0.91	9.61E-05	Pujana
rs140127725	LDHB	12	21900930	A	G	1.49	1.22	1.83	0.0001	Pujana
rs201611588	HEXA	15	72617472	T	C	0.91	0.86	0.95	0.0001	Pujana
rs62074998	FBXL20	17	37480822	C	A	0.84	0.77	0.92	0.0001	Nikolsky
rs184199456	PFKFB4	3	48586891	G	A	1.39	1.17	1.64	0.0001	Pujana
rs111345106	CD47	3	107775269	C	T	1.28	1.13	1.45	0.0002	Pujana
rs138947508	MAPK8	10	49566274	A	G	0.72	0.60	0.85	0.0002	Pujana
rs146071727	HNRNPL	19	39315847	C	G	1.26	1.12	1.43	0.0002	Pujana
rs72823344	CACNB1 RPL19 STAC2	17	37351774	G	A	1.18	1.08	1.29	0.0002	Nikolsky, Pujana
rs72779276	TELO2	16	1551826	C	G	0.90	0.85	0.95	0.0002	Pujana
rs12522289	HNRNPAB	5	177640864	A	G	1.16	1.07	1.25	0.0002	Pujana
rs7212868	MED1	17	37608052	C	A	0.92	0.88	0.96	0.0002	Pujana
rs7585054	BCL2L11	2	111944927	A	G	0.92	0.89	0.96	0.0002	Pujana
rs113520394	THRA	17	38212046	C	T	0.89	0.84	0.95	0.0002	Nikolsky, Pujana

	MED24									
rs117811627	CCR7	17	38691196	T	C	1.34	1.15	1.56	0.0002	Nikolsky
rs7148005	BAZ1A	14	35319411	C	G	0.89	0.83	0.95	0.0002	Pujana
rs11070327	OIP5	15	41602866	G	A	1.08	1.04	1.13	0.0002	Pujana
rs140573271	CDC123	10	12305979	G	A	0.77	0.67	0.88	0.0002	Pujana
rs17215231	PFDN6	6	33239869	C	T	0.86	0.79	0.93	0.0002	Pujana
rs7321404	PIBF1	13	73351180	A	T	1.15	1.07	1.24	0.0003	Pujana
rs77381836	NR2C1	12	95469581	A	G	0.74	0.63	0.87	0.0003	Pujana
rs10064416	BTF3	5	72809050	A	G	1.17	1.07	1.27	0.0003	Pujana
rs114629468	FBL	19	40320168	G	A	0.80	0.71	0.90	0.0003	Pujana
rs116905840	ANGEL1	14	77271613	G	A	1.41	1.17	1.70	0.0003	Pujana
rs12453796	FBXL20	17	37454997	A	T	0.91	0.86	0.96	0.0003	Nikolsky
rs112646694	PCF11	11	82893611	C	T	1.40	1.16	1.68	0.0003	Pujana
rs58812167	GSR	8	30554938	C	A	0.93	0.89	0.97	0.0003	Pujana
rs73802720	GRIA1	5	153067523	T	C	0.90	0.85	0.95	0.0003	Pujana
rs883544	STAC2	17	37387413	A	G	0.91	0.87	0.96	0.0003	Nikolsky
rs74704910	FCHSD2	11	72799737	T	G	0.85	0.78	0.93	0.0003	Pujana
rs3749812	HNRNPAB	5	177650210	T	C	1.16	1.07	1.26	0.0003	Pujana
rs76504832	POP4	19	30109535	G	A	0.78	0.68	0.90	0.0004	Pujana
rs6795254	TRA2B	3	185622421	C	T	0.85	0.78	0.93	0.0004	Pujana
rs118117270	PAX4	7	127263589	T	C	0.67	0.54	0.84	0.0004	MODY, Pujana
rs601269	TPP2	13	103321992	G	C	0.91	0.86	0.96	0.0004	Pujana
rs111918710	SIKE1	1	115309588	C	A	0.60	0.46	0.80	0.0004	Pujana
rs118025182	BRCA1	17	41181639	G	A	0.80	0.71	0.91	0.0005	Pujana
rs10881645	KIF20B	10	91490087	A	G	1.08	1.03	1.12	0.0005	Pujana
rs7188875	NAE1	16	66917267	A	C	1.12	1.05	1.20	0.0005	Pujana
rs11652129	FOXN1	17	26817115	A	C	1.26	1.10	1.43	0.0005	Nikolsky
rs144972902	ATXN3	14	92563474	T	C	1.24	1.10	1.41	0.0005	Pujana
rs34501420	FAM53B	10	126304770	G	C	1.09	1.04	1.14	0.0005	Pujana
rs13260089	GSR	8	30531154	T	C	0.89	0.83	0.95	0.0005	Pujana
rs182312279	TACR3	4	104551730	T	C	0.81	0.72	0.91	0.0006	Pujana
rs2444857	RPL30	8	99062480	A	T	0.93	0.89	0.97	0.0006	Pujana
rs140048312	PMS2P1	7	99915673	C	T	0.73	0.61	0.87	0.0006	Pujana
rs1588327	NPHP1	2	110891433	A	C	1.08	1.03	1.12	0.0006	Pujana

rs72847518	TAF5	10	105127191	A	C	0.84	0.75	0.93	0.0006	Pujana
rs35223775	NSL1	1	212879952	C	T	0.91	0.86	0.96	0.0006	Pujana
rs33948247	E2F4	16	67235672	C	T	0.85	0.78	0.93	0.0006	Pujana
rs143786818	FAM53B	10	126303382	T	C	1.29	1.11	1.49	0.0007	Pujana
rs142824527	TACR3	4	104623592	A	G	0.79	0.69	0.90	0.0007	Pujana
rs1877032	NEUROD2 PPP1R1B	17	37771064	T	C	1.13	1.05	1.20	0.0007	Nikolsky
rs16964766	PIPOX TIAF1	17	27393310	G	A	1.10	1.04	1.17	0.0007	Nikolsky
rs11079803	SP2	17	46019901	G	A	0.93	0.89	0.97	0.0007	Pujana
rs1062225	MAPK8	10	49643226	A	G	0.90	0.84	0.96	0.0008	Pujana
rs17721128	C17orf63	17	27143892	A	G	0.87	0.80	0.94	0.0008	Nikolsky
rs78126981	PIPOX SEZ6	17	27320567	T	A	0.76	0.65	0.89	0.0008	Nikolsky
rs7222039	CSF3 PSMD3	17	38165541	T	C	1.07	1.03	1.12	0.0008	Nikolsky, Pujana
rs17037193	SNRNP27	2	70103504	T	C	0.91	0.87	0.96	0.0009	Pujana
rs72856970	NMI	2	152135335	G	A	1.20	1.08	1.33	0.0009	Pujana
rs2248014	RPL30	8	99030280	T	C	0.92	0.88	0.97	0.0009	Pujana
rs72826897	NPHP1	2	110926458	A	G	0.84	0.76	0.93	0.0009	Pujana
rs10416586	POP4	19	30112997	G	A	0.85	0.78	0.94	0.0009	Pujana
rs8008960	ANGEL1	14	77289618	T	C	0.92	0.88	0.97	0.0009	Pujana
rs76331936	USP19	3	49141714	G	A	0.73	0.61	0.88	0.001	Pujana
rs192123848	SP2	17	46013386	G	A	0.74	0.62	0.89	0.001	Pujana
rs676119	BCL2L11	2	111912718	A	G	0.93	0.90	0.97	0.001	Pujana
rs11852609	OIP5	15	41582598	T	G	1.08	1.03	1.12	0.001	Pujana
rs111935829	GSDMB ORMDL3	17	38081394	C	G	0.84	0.76	0.94	0.001	Nikolsky
rs72678745	BAZ1A	14	35272925	C	T	0.82	0.73	0.92	0.001	Pujana
rs2227324	CSF3 PSMD3	17	38172192	G	A	1.14	1.05	1.23	0.001	Nikolsky, Pujana
rs76790404	AOC2	17	41018481	G	C	0.82	0.73	0.93	0.001	Pujana
rs2470201	TMEM98	17	31250916	G	A	1.10	1.04	1.16	0.001	Nikolsky
rs141981996	PMS2P1	7	99929614	C	T	0.90	0.84	0.96	0.001	Pujana

rs190904708	HNRNPL	19	39346267	G	A	0.73	0.60	0.88	0.001	Pujana
rs4951457	NSL1	1	212879500	A	C	1.08	1.03	1.13	0.001	Pujana
rs8014854	ATXN3	14	92550658	G	A	1.07	1.03	1.12	0.001	Pujana
rs11687575	NMI	2	152156771	C	T	1.14	1.05	1.23	0.002	Pujana
rs17676191	IKZF3	17	37949924	A	G	1.12	1.04	1.20	0.002	Nikolsky
rs10794501	GPR3	1	27699449	A	T	1.09	1.03	1.16	0.002	Pujana
rs750409	CACNB1	17	37317211	G	A	0.87	0.80	0.95	0.002	Nikolsky
rs147225757	CRYBA1	17	27566770	G	C	0.72	0.58	0.89	0.002	Nikolsky
rs75646943	IKZF3	17	37954143	C	T	0.78	0.66	0.91	0.002	Nikolsky
rs62483175	PAX4	7	127247114	C	T	0.78	0.67	0.91	0.002	MODY, Pujana
rs117237010	SEZ6	17	27311692	G	A	1.32	1.10	1.58	0.002	Nikolsky
rs11707940	USP4	3	49363772	T	A	0.92	0.87	0.97	0.002	Pujana
rs12103674	PPP1R1B	17	37804352	T	C	1.13	1.04	1.21	0.002	Nikolsky
rs368987508	KIF20B	10	91548385	A	T	1.07	1.02	1.12	0.002	Pujana
rs4795393	GRB7 MIEN1	17	37893484	C	T	0.94	0.90	0.98	0.002	Nikolsky
rs1050450	USP4	3	49394834	G	A	0.93	0.89	0.98	0.003	Pujana
rs2504765	GPR3	1	27741131	C	T	0.90	0.84	0.96	0.003	Pujana
rs146494007	PCF11	11	82867659	T	G	0.79	0.68	0.92	0.003	Pujana
rs35996049	RPL19	17	37375354	G	A	1.13	1.04	1.22	0.003	Pujana
rs147849562	FOXN1	17	26855748	G	A	1.21	1.07	1.38	0.003	Nikolsky
rs141786375	ERAL1	17	27200588	A	G	0.77	0.64	0.91	0.003	Nikolsky
rs145088470	AOC2	17	41020181	G	T	0.71	0.57	0.89	0.003	Pujana
rs28986	TMEM98	17	31279321	C	A	1.20	1.06	1.37	0.003	Nikolsky
rs12453507	GSDMB ZPBP2	17	38053207	C	G	0.94	0.90	0.98	0.004	Nikolsky
rs74811341	CCR7	17	38720826	C	T	0.85	0.76	0.95	0.005	Nikolsky
rs191981826	SGK494 SPAG5	17	26931189	G	A	1.10	1.03	1.17	0.007	Nikolsky
rs2665647	NEUROD2	17	37778907	C	G	1.25	1.06	1.48	0.007	Nikolsky
rs10853129	ERAL1	17	27191960	G	A	0.94	0.90	0.98	0.008	Nikolsky
rs62068170	ORMDL3	17	38103210	G	A	1.06	1.01	1.10	0.008	Nikolsky
rs12923138	E2F4	16	67233266	A	C	0.94	0.91	0.99	0.008	Pujana

rs117006142	SGK494, SPAG5	17	26939612	T	A	0.83	0.72	0.96	0.01	Nikolsky
rs8614	CRYBA1	17	27588806	C	A	1.07	1.01	1.13	0.01	Nikolsky
rs185050272	USP19	3	49151003	G	A	0.83	0.70	0.97	0.02	Pujana
rs79062097	ZPBP2	17	38043467	C	T	0.89	0.79	1.00	0.05	Nikolsky

*SNPs in the top ranked PDAC associated gene sets and pathways. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. Major allele is Ref (reference) allele. PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval

†SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2, 3 and PanC4.

Supplementary Table 6: Pathways and gene sets associated with PDAC after exclusion of 4 new GWAS SNPs[*] (plus 1 MB exclusion region)

Gene set and Pathway Description	Pathway source	Gene, n	SNP, n	P-value†	Genes contributing to the association of pathway and PDAC development
Breast cancer chr17q11q21 amplicon	Nikolsky	109	4052	5.71E-06	*C17orf63,CACNB1,CASC3,CCL3,CCL4,CCR7,CDK12,CRYBA1,CSF3,DHRS13,ERAL1,ERBB2,FBXL20,FLOT2, FOXN1,GRB7,GSDMA,GSDMB,IGFBP4,IKZF3,KIAA0100,KRT24,KRTAP9-4, LSP1,MED24,MSL1,MYO18A,NEUROD2,NR1D1,NUFIP2,ORMDL3,PGAP3,PHF12,PIPOX,PPP1R1B,PSMD3,RAPGEFL1,RPL19,SLC13A2,SPAG5,STAC2,STARD3,TCAP,THRA,TMEM98,TNS4,TRAF4,UNC119,WIPF2, ZPBP2*
ATM Pearson Correlation Coefficient network	Pujana	1343	78689	3.59E-04	*ACTR2,ANGEL1,AOC2,ATXN3,BAZ1A,BCL2L11,BRCA1,BTF3,CASP7,CD47,CDC123,CR1,CSF3,E2F4,FAM53B,FBL,FCHSD2,GHRH,GPR3,GRIA1,GSR,HEXA,HIPK3,HNF1A,HNRNPAB,HNRNPL,ITGBL1,KHDRBS2,KIF20B,LDHB,MAPK8,MED1,MED6,NAE1,NMI,NPHP1,NR2C1,NSL1,OIP5,PAX4,PCF11,PDAP1,PFDN6,PFKFB4,PHOX2B,PIBF1,PMS2P1,PNMT,POP4,PSMD3,RPL19,RPL30,SIKE1,SMC2,SNRNP27,SP2,TAB1,TACR3,TAF5,TELO2,THRA,TMEM123,TNFAIP8,TPP2,TRA2B,USP19,USP4*
Breast cancer basal (down)	SMID	666	60866	4.29E-04	*BAI2,BBS4,C5orf30,C9orf116,CAMP,CANT1,CAPN9,CDK12,CSF3R,CXXC4,ERBB2,EVL,HPGD,IFT140,IGFBP4,ITGA7,ITGBL1,KRT8,MED13L,MED24,PGAP3,PNMT,RAB27B,RAPGEF3,RARA,RHOH,SCGB2A2,SLC19A2,SLC48A1,STARD3,TMEM143,UBA7,VAV3*
Developmental biology	Reactome	363	37609	4.36E-04	*AP2S1,CACNA1I,CACNB1,DPYSL4,ERBB2,EVL,EZR,FES,FURIN,HFE2,HNF1A,HNF4A,HSP90AB1,ITGA2,ITGAV,KIAA1598,MED1,MED13L,MED21,MED24,MED6,MET,MYH10,MYL8P,NCOR1,NR2F2,PLXND1,RHOC,ROBO1,ROCK1P1,SDCBP,SEMA3E,SRGAP1,TCF4,UNC5A,WASL*
Maturity onset diabetes of the young	KEGG	21	1177	5.49E-04	*HNF1A,HNF4A,PAX4*
Regulation of gene expression in beta cells	Reactome	18	1135	5.63E-04	*HNF1A,HNF4A*
Regulation of beta cell development	Reactome	26	1786	0.001	*HNF1A,HNF4A*
Prostate cancer HCP with H3K27ME3	Kondo	90	10568	0.01	*KIAA1109,LIMCH1,LINC00273,NKX2-3*

[*] Four newly confirmed GWAS hits (rs13303010 at 1p36.33 (NOC2L); rs2941471 at 8q21.11 (HNF4G); rs4795218 at 17q12 (HNF1B) and rs1517037 at 18q21.32 (GRP) (Klein et al. 2018)) were removed from the analysis.

† The pathway-level association *P*-values were estimated from the resampled null distribution through up to one hundred million resampling steps as described in methods section. All statistical tests were two-sided.

Supplementary Table 7: eQTL prediction of top signals in normal tissues using GTEx data and replication in independent normal pancreas dataset*.

Gene in pathway /gene set analysis	Chr	SNP	Ref Allele	Risk Allele	GTEx Pancreas (n=220) Gene† P-value‡	NCI LTG Normal pancreas tissue (n=95) Gene† P-value‡	GTEx Nerve Tibial (n=361) Gene† P-value‡	GTEx Thyroid (n=399) Gene† P-value‡	GTEx Artery Tibial (n=388) Gene† P-value‡	GTEx Lung (n=383) Gene† P-value‡	GTEx Sun Exposed Skin (LL) (n=414) Gene† P-value‡	GTEx Adipose Sub-cutaneous (n=385) Gene† P-value‡	GETx Whole blood (n=369) Gene† P-value‡	GETx Liver (n=153) Gene† P-value‡	GTEX Artery Aorta (n=267) Gene† P-value‡	GTEx Testis (n=225) Gene† P-value‡	GTEx Colon-Transverse (n=246) Gene† P-value‡	GTEx Brain-Cerebellum (n=154) Gene† P-value‡
Kegg_Maturity Onset Diabetes of the Young (MODY) and Reactome_Regulation of Beta Cell Development																		
HNF1A	12	rs2244608	A	G	—	—	SPPL3 ↓ 1.1E-07	ACADS ↑ 3.8E-07	C12orf43 ↓ 2.3E-08	C12orf43 ↓ 1.6E-06	MLEC ↓ 1.5E-08	C12orf43 ↓ 1.8E-07	—	—	—	HNF1A ↑ 3.0E-05	C12orf43 ↓ 5.1E-07	—
HNF4G	8	rs2943547	A	G	—	HNF4G ↑ 0.05	No significant eQTLs were found for rs2943547 all eQTL tissues											
Biocarta_Cardiac EGF pathway																		
EDNRA	4	rs35232409	G	C	—	NA	No significant eQTLs were found for rs35232409 all eQTL tissues											
		rs6537481	A	G	—	EDNRA ↑ 0.2	No significant eQTLs were found for rs35232409 all eQTL tissues											
AGT	1	rs1326889	C	T	—	AGT ↑ 0.13	—	—	—	—	—	AGT ↑ 5.4E-10	—	—	—	—	AGT ↑ 3.2E-08	AGT ↓ 1.4E-11
Nikolsky_breast cancer chr17 amplicon																		
ERBB2 PGAP3 TCAP STARD3 PNMT	17	rs876493	G	A	PGAP3 ↓ 3.9E-07	PGAP3 ↓ 1.16E-05	PGAP3 ↓ 3.2E-08	PGAP3 ↓ 1.3E-12	—	PGAP3 ↓ 3.0E-09	PGAP3 ↓ 1.1E-08	GSDMA ↑ 3.3E-05	GSDMB ↓ 7.9E-10	PGAP3 ↓ 2.1E-07	PGAP3 ↓ 2.4E-06	—	PGAP3 ↓ 6.5E-13	—
		rs3764351	G	A	PGAP3 ↓ 6.6E-09	PGAP3 ↓ 9.7E-05	PGAP3 ↓ 3.1E-11	PGAP3 ↓ 2.0E-18	—	PGAP3 ↓ 3.3E-11	PGAP3 ↓ 1.3E-12	—	—	PGAP3 ↓ 3.3E-07	PGAP3 ↓ 1.3E-05	—	PGAP3 ↓ 9.6E-14	—
GRB7 MIEN1	17	rs4795393	C	T	PGAP3 ↓ 4.0E-10	PGAP3 ↓ 3.8E-05	PGAP3 ↓ 6.4E-08	PGAP3 ↓ 3.0E-15	—	PGAP3 ↓ 4.8E-08	PGAP3 ↓ 2.5E-10	GSDMA ↑ 8.6E-07	GSDMB ↓ 6.8E-10	PGAP3 ↓ 5.2E-08	—	ZPBP2 ↓ 3.3E-06	PGAP3 ↓ 2.9E-10	—
GSDMB ZPBP2	17	rs12453507	C	G	PGAP3 ↓ 2.7E-07	PGAP3 ↓ 2.8E-05	PGAP3 ↓ 7.8E-07	PGAP3 ↓ 7.4E-12	—	PGAP3 ↓ 1.1E-06	GSDMB ↓ 8.5E-06	GSDMA ↑ 4.8E-11	—	—	—	—	PGAP3 ↓ 3.5E-06	—
STAC2	17	rs72823344	G	A	—	STAC2 ↑ 0.297	—	—	STAC2 ↑ 4.8E-06	—	STAC2 ↑ 7.1E-07	—	—	—	—	—	—	—
THRA MED24	17	rs113520394	C	T	MED24 ↑ 2.2E-06	MED24 ↓ 0.110	MED24 ↑ 1.9E-08	MED24 ↑ 1.4E-10	MED24 ↑ 6.9E-09	—	—	MED24 ↑ 1.0E-05	—	—	—	—	—	MED24 ↑ 3.1E-05

TMEM98	17	rs2470201	G	A	—	TMEM98 ↓ 0.612	TMEM98 ↓ 3.8E-05	TMEM98 ↓ 2.4E-05	TMEM 98 ↓ 2.7E-13	—	TMEM98 ↓ 1.9E-08	—	—	—	—	TMEM98 ↓ 8.5E-07	—	TMEM98 ↓ 3.9E-06
Pujana ATM PCC Network																		
SMC2	9	rs7859034	G	T	—	SMC2 ↑ 0.097	SMC2 ↓ 6.9E-06	SMC2 ↓ 4.7E-52	SMC2 ↓ 5.0E-14	SMC2 ↓ 7.6E-06	SMC2 ↓ 3.2E-10	—	—	—	SMC2 ↓ 9.2E-07	—	—	SMC2 ↓ 4.2E-37
HNF1A	12	rs1169297	G	A	—	HNF1A ↑ 0.462	No significant eQTLs for rs1169297											
		rs1169291	C	T	—	HNF1A ↑ 0.470	No significant eQTLs for rs1169291											
CASP7	10	rs3124737	A	G	CASP7 ↑ 2.5E-08	CASP7 ↑ 0.02	CASP7 ↑ 4.5E-08	CASP7 ↑ 9.4E-10	CASP7 ↑ 5.4E-12	CASP7 ↑ 1.4E-06	CASP7 ↑ 1.1E-07	CASP7 ↑ 1.5E-07	CASP7 ↑ 1.0E-10	—	CASP7 ↑ 4.2E-05	RP11-211N11.5 ↑ 1.2E-09	—	—
FAM53B	10	rs34501420	G	C	—	FAM53B ↓ 0.230	METTL10 ↓ 5.6E-06	METTL10 ↓ 9.5E-11	METTL10 ↓ 1.3E-09	METTL10 ↓ 5.7E-11	METTL10 ↓ 8.9E-11	METTL10 ↓ 8.6E-16		METTL 10 ↓ 3.5E-07	METTL10 ↓ 3.8E-06	METTL10 ↓ 2.3E-05	METTL10 ↓ 4.1E-09	—
OIP5	15	rs11852609	T	G	OIP5-AS1 ↑ 1.8E-16	OIP5 ↑ 0.233	OIP5-AS1 ↑ 3.9E-05	OIP5-AS1 ↑ 1.2E-34	OIP5-AS1 ↑ 6.1E-42	OIP5-AS1 ↑ 2.8E-23	OIP5-AS1 ↑ 1.1E-31	OIP5-AS1 ↑ 6.4E-32	NDUFAF1 ↑ 1.7E-05	OIP5-AS1 ↑ 5.5E-06	OIP5-AS1 ↑ 2.3E-17	OIP5-AS1 ↑ 2.2E-14	OIP5-AS1 ↑ 7.4E-17	—
HNRNPAB	5	rs12522289	A	G	—	HNRNPAB ↓ 0.053	—	—	—	—	HNRNPAB ↓ 1.1E-07	—	—	—	—	—	HNRNPAB ↓ 1.1E-17	—
		rs3749812	T	C	—	HNRNPAB ↓ 0.069	—	—	—	—	—	—	—	—	—	RP11-281O15.2 ↓ 5.8E-06	HNRNPAB ↓ 4.4E-11	—
ANGEL1	5	rs8008960	G	A	—	ANGEL1 ↑ 0.016	—	—	—	—	—	—	—	—	ANGEL1 ↓ 9.2E-06	C14orf166B ↓ 1.3E-11	—	—

*Independent replication and tissue specificity for eQTL analysis was carried out using the Genotype-Tissue Expression project (GTEx) and normal pancreas from the LTG. Major allele is Ref (reference) allele. eQTL, Expression Qualitative Trait Loci; SNP, single nucleotide polymorphism; PCC, Pearson correlation coefficient; LTG, Laboratory of Translational Genomics; TSS, transcription start site.

† The direction of influence of the risk SNP on gene mRNA levels is depicted as: ↑ = increased mRNA level or positive influence; ↓ = decreased mRNA levels or negative influence; em-dash (—) = no data available.

‡ eQTL at FDR (≤ 0.05) using +/- 1 Mb *cis*-window around TSS. Statistical test was two-sided.

Supplementary Table 8. Potential regulatory function of the top PDAC-associated and eQTLs SNP identified through gene set and pathway analysis

Gene	Chr	Top SNP*	Risk Allele	OR†	95% CI Lower	95% CI Upper	SNP P-value‡	Other coding annotation	RegulomeDB score	Regulatory function§	SNPs in LD
Kegg Maturity Onset Diabetes of the Young (MODY) and Reactome_Regulation of Beta Cell Development											
HNF1A	12	rs2244608	G	1.11	1.07	1.16	1.54E-06	HNF1A-AS1	2b	Potential eQTL SNP in multiple tissues. Located in active TSS in pancreas and pancreatic islet cells. Changes binding motif for ERalpha, ESR2, HNF4, RAR. Locates to a strong H3K27 acetylation enhancer mark and H3K4m3 promoter marks in pancreas islets and normal tissue	rs1169288 (r2=0.96)which results in a missense in HNF1A.
HNF4G	8	rs2943547	G	1.09	1.05	1.14	2.31E-05	Intronic variant HNF4G	6	No significant eQTLs were found for SNP rs2943547 in all GTEx eQTL Tissues, but weak positive eQTL for HNF4G (P=0.052) in LTG normal pancreas dataset. Chromatin enhancer state in fetal intestine.	__
Biocarta_Cardiac EGF Pathway											
EDNRA	4	rs35232409	C	0.88	0.84	0.93	3.19E-07	5.8kb 5' of EDNRA	6	No data as eQTL. Quiescent/Low chromatin state in pancreas.	rs4835083 ($r^2 > 0.7$) within intron 1 EDNRA. Flanking active TSS in normal pancreas with H3K4me1 and H3K27ac enhancer and H3K4me3 promotor marks in normal pancreas
		rs6537481	G	0.88	0.83	0.92	1.14E-07	5.8kb 5' of EDNRA	6	No data as eQTL. Quiescent/Low chromatin state in pancreas.	__
AGT	1	rs1326889	T	0.90	0.86	0.94	4.21E-07	RP11-99J16__A.2	5	Potential eQTL SNP in multiple tissues. Weak transcription and enhancer chromatin state in pancreas islets and liver cells, respectively. In LD with SNP rs699 resulting in missense mutation in AGT;	Rs699 r^2=0.7 which is a missense variant (M268T) in AGT

										strong enhancer in liver and brain and within a Dnase I site in liver	
Nikolsky_breast cancer chr17 amplicon											
ERBB2 PGAP3 TCAP STARD3 PNMT	17	rs876493	A	0.90	0.86	0.94	1.27E-06	5'UTR PNMT	4	Potential multi-tissue eQTL (34 hits) SNP reduced PGAP3 mRNA in pancreas tissue. Located in active TSS promoter in pancreas islets and enhancer region in pancreas. Promoter histone marks in 18 tissues, chromatin enhancer state in normal pancreas (and 9 tissues).	All SNPs rs876493, rs3764351, rs4795393 and rs12453507 in LD.
		rs3764351	A	0.91	0.87	0.95	1.27E-05	PNMT	2b	Potential Eqtl (GTEx) PGAP3 in multiple tissues including pancreas and replicated as PGAP3 eQTL in normal pancreas in independent dataset. SNP likely to affect binding. Enhancer chromatin state in pancreas and located in active TSS in pancreatic islet cells. Locates to CpG island and strong DNAse I site in ENCODE cell lines	Rs1877031 (r2=0.9176) results in missense mutation
GRB7 MIEN1	17	rs4795393	T	0.94	0.90	0.98	0.002	695bp 5' of GRB7	5	Potential eQTL (GTEx) PGAP3 in multiple tissues including pancreas and replicated as PGAP3 eQTL in normal pancreas in independent dataset. Enhancer chromatin state in pancreas	__
GSDMB ZPBP2	17	rs12453507	G	0.94	0.90	0.98	0.004	7.6kb 3' of GSDMB	no data	Potential eQTL (GTEx) PGAP3 in multiple tissues including pancreas and replicated as PGAP3 eQTL in normal pancreas in independent dataset. No data available on chromatin state in any tissue	__
Pujana ATM PCC network											
STAC2	17	rs72823344	A	1.18	1.08	1.29	1.91E-04	Intronic CACNB1	5	Potential eQTL in artery tibial (GTEx). Located in a weak transcripton site	__

										(promotor) in pancreas	
CASP7	10	rs3124737	G	0.91	0.88	0.95	3.29E-05	6.4 kb of 3' CASP7	6	Potential eQTL SNP in pancreas (LTG dataset) and multiple tissues (GTEx). Enhancer histone markers in lung, GI cells. Changes BRCA1, Pbx-1, Sox motifs.	__
FAM53B	10	rs34501420	C	1.09	1.04	1.14	5.15E-04	LHPP	4	Potential eQTL SNP in multiple tissues. Enhancer histone markers and DNAse I in 6 tissues.	__
OIP5	15	rs11852609	G	1.08	1.03	1.12	0.001	OIP5-AS1	5	Potential eQTL SNP in multiple tissues. Weak transcription site in pancreas and islet cells. Strong transcription site in liver. Enhancer region in HSC B-cells.	__
SMC2	9	rs7859034	T	0.90	0.86	0.93	3.07E-07	Intronic SMC2	7	GTEx eQTL SNP in multiple tissues (n=34) (non-pancreas). Regulatory motifs altered CIX, ZBTB33_disc3.	SNP in LD (r2=0.90) with rs3818626 located in the 5'UTR of SMC2. Rs3818626 has potential to affect binding as is in CpG island and an active TSS in normal pancreas and islet cells.
HNF1A	12	rs1169291	T	1.11	1.06	1.16	8.39E-06	Intronic HNF1A	6	GTEx eQTL SNP in multiple tissues. Weak transcription in pancreas and islet cells. Strong transdcription site for Liver and digestive tissues (GI). Regulatory motifs altered EGR-1, PBX-1, RREB-1 VDR-2 ZFP281	__
		rs1169297	A	1.10	1.05	1.15	1.40E-05	Intronic HNF1A	5	GTEx eQTL in multiple tissues. Locates to weak transcription in pancreas and islet cells. Strong transcription and enhancer in HepG liver cells.	__
HNF1B	17	rs12951345	C	0.88	0.84	0.93	1.38E-06	Intronic HNF1B	4	No eQTL data. Primary H3K27ac possible Enhancer in pancreas and islet cells.	__

* SNPs in the top ranked PDAC associated gene sets and pathways. The association evidence from the strongest SNP(s) (up to the two) in a gene were accumulated. The sARTP method adjusts for the size of genes (i.e., number of SNPs in a gene) and the size of pathways (i.e., number of genes in a pathway) through a resampling procedure. PDAC, pancreatic ductal adenocarcinoma; SNP, single nucleotide polymorphism; Chr, chromosome; OR, Odds Ratio; CI, confidence interval; eQTL, expression quantitative trait loci; GTEx, the Genotype-Tissue Expression project.

†Major allele is Ref (reference) allele.

‡ SNP P-values were calculated using the two-sided Wald's test. P-values and OR are shown in order of lowest P-value for PDAC in the combined PanScan 1, 2, 3 and PanC4.

§The potential regulatory function of the SNP of interest were evaluated using experimental data in the UCSC Genome browser (http://genome.ucsc.edu) using Roadmap and ENCODE data for pancreas and islet tissues. Data included chromatin tracks (DNaseI sites, histone modification [or regulatory regions designated using a Hidden Markov Model (HMM)] (Core 15-state model (5 marks, 127 epigenomes), transcription factor binding to DNA, CpG island sites. Protein coding and non-coding annotation for the location (Hg19) of each SNP using the UCSC browser and Ensembl. DNA binding motifs and individual histone marks were also identified and validated using HaploregV4.1 (http://archive.broadinstitute.org/mammals/haploreg/haploreg.php and RegulomeDB (http://www.regulomedb.org/).

Supplementary Information:

Notes

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