Germline Variants and Risk for Pancreatic Cancer
A Systematic Review and Emerging Concepts

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTARY TABLE 2. Likely Pathogenic Variants

Gene	cDNA Nucleotide Change	Hg19 Position	Transcript	Amino Acid Change	dbSNP rs. id	ClinVar	PubMed ID	Population, Region*	MAF (ExAC)	CADD Score	Family History*	Co-segregation†
APC	c.3920T>A	chr5:112175211	NM_000038.4	p.Ile1307Lys	rs1801155	Conflicting (pathogenic [2]; uncertain significance [2])	26421687; 9973276	Unknown, Israel; Ashkenazi Jewish, Canada	A:1.688e-03	5.302	False	False
ATM	c.170G>A	chr11:108098600	NM_000051.3	p.Trp57Ter	rs587779818	Pathogenic	22585167	Unknown, United States	—	37	True	True
ATM	c.1978delA	chr11:108124620	NM_000051.3	p.Met660Trpfs	.	.	26658419	Mixed, United States	T:6.590e-05	33	True	True
ATM	c.3801delG	chr11:108155008	NM_000051.3	p.Val1268Terfs	rs587779834	Pathogenic	22585167; 25479140	Unknown, United States; Unknown, Canada	.	35	True	False
ATM	c.6095G>A	chr11:108186638	NM_000051.3	p.Arg2032Lys	rs139770721	Pathogenic/ likely pathogenic	22585167	Unknown, United States	A:4.118e-05	26.2	True	False
ATM	c.7327C>T	chr11:108200960	NM_000051.3	p.Arg2443Ter	rs121434220	Pathogenic/ likely pathogenic	26483394	Mixed, United States	—	43	True	False
BRCA1	c.5266insC	chr17:41209079-41209080	NM_007294.3	p.Gln1756Profs	rs397507247	Pathogenic	25356972	Mixed, United States	G:1.565e-04	35	True	False
BRCA1	c.2199delG	chr17:41245349	NM_007294.3	p.Lys734Asnfs	rs80357944	Pathogenic	18762988; 25072261	Mixed, Canada; Mixed, Israel	—	23.6	True	False
BRCA2	c.262_263delCT	chr13:32893408-32893409	NM_000059.3	p.Leu88Alafs	rs276174825	Pathogenic	25940717; 25072261	Mixed, Canada; Mixed, Israel	—	21.8	False	False
BRCA2	c.771_775delTCAAA	chr13:32905145-32905149	NM_000059.3	p.Asn257Lysfs	rs80359675	Pathogenic	9150155; 8673089	Icelanders, Iceland; Icelanders, Iceland	—	25.4	True	False
BRCA2	c.1736T>G	chr13:32907351	NM_000059.3	p.Leu579Ter	rs1131692274	Pathogenic	25940717; 25072261	Mixed, Canada; Mixed, Israel	—	36	False	False
BRCA2	c.1813dupA	chr13:32907428-32907429	NM_000059.3	p.Ile605Asnfs	rs80359308	Pathogenic	25356972; 25072261	Mixed, United States; Mixed, Israel	—	23.3	True	False
BRCA2	c.2806_2809delAAAC	chr13:32911298-32911301	NM_000059.3	p.Ala938Profs	rs80359351	Pathogenic	25479140	Unknown, Canada	—	27.7	True	False
BRCA2	c.2808_2811delACAA	chr13:32911300-32911303	NM_000059.3	p.Ala938Profs	rs80359352	Pathogenic	21598239	Ashkenazi Jewish, United States	—	27.7	True	False
BRCA2	c.2957_2958insG	chr13:32911449-32911450	NM_000059.3	p.Asn986Lysfs	rs80359365	Pathogenic	25940717; 25072261	Mixed, Canada; Mixed, Israel	—	22.9	False	False
BRCA2	c.3847_3848delGT	chr13:32912339-32912340	NM_000059.3	p.Val1283Lysfs	rs80359405	Pathogenic	12569143; 25356972; 25072261	German and British, Germany; Mixed, United States; Mixed, Israel	—	23.9	True	False
BRCA2	c.5722_5723delCT	chr13:32914214-32914215	NM_000059.3	p.Leu1908Argfs	rs80359531	Pathogenic	25356972; 25940717; 25072261	Mixed, United States; Mixed, Canada; Mixed, Israel	—	23.7	True	False
BRCA2	c.5796_5797delTA	chr13:32914288-32914289	NM_000059.3	p.His1932Glnfs	rs80359537	Pathogenic	24737347; 21989927; 27449771	Mixed, United States; Italian, Italy; Mixed, United States & Europe	—	25.8	True	False
BRCA2	c.6373dupA	chr13:32914865	NM_000059.3	p.Thr2125Asnfs	rs80359577	Pathogenic	26483394; 25356972	Mixed, United States; Mixed, United States	—	24.1	True	False
BRCA2	c.6444dupT	chr13:32914936-32914937	NM_000059.3	p.Ile2149Tyrfs	rs80359590	Pathogenic	12569143; 20195775	German and British, Germany; White, Germany	—	24.7	True	False
BRCA2	c.8537_8538delAG	chr13:32945142-32945143	NM_000059.3	p.Glu2846Glyfs	rs80359716	Pathogenic	25356972; 25072261	Mixed, United States; Mixed, Israel	—	35	True	False

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SUPPLEMENTARY TABLE 2. *(Continued)*

Gene	cDNA Nucleotide Change	Hg19 Position	Transcript	Amino Acid Change	dbSNP rs. id	ClinVar	PubMed ID	Population, Region*	MAF (ExAC)	CADD Score	Family History*	Co-segregation†
BRCA2	c.9076C>T	chr13:32954009	NM_000059.3	p.Gln3026Ter	rs80359159	Pathogenic	27732944	Unknown, Japan	G:1.648e-05	52	True	False
BRCA2	c.9976A>T	chr13:32972626	NM_000059.3	p.Lys3326Ter	rs11571833	Benign	12097290; 15806175; 26041759	White, United States; Unselected, US; Mixed, Europe	T:7.010e-03	38	True	False
CDKN2A	c.301G>A	chr9:21971057	NM_000077.4	p.Gly101Arg	rs104894094	Uncertain significance	25356972	Mixed, United States	G:1.671e-05	34	True	False
CDKN2A	c.284_285insG	chr9:21971074-21971075	NM_000077.4	p.Val95Glyfs	.	.	12454511	German, Germany	—	24.7	True	True
CDKN2A	c.260G>C	chr9:21971098	NM_000077.4	p.Arg87Pro	rs878853647	Pathogenic	15173226; 15146471	White, United States; Mixed	—	35	True	False
CDKN2A	c.240_253del14	chr9:21971105-21971118	NM_000077.4	p.Pro81Cysfs	rs730881675	Pathogenic	15146471	Mixed	—	35	True	False
CDKN2A	c.238_251del14	chr9:21971107-21971120	NM_000077.4	p.Arg80fs	—	—	21150883	White, United States	—	35	False	False
CDKN2A	c.199G>C	chr9:21971159	NM_000077.4	p.Gly67Arg	rs758389471	Uncertain significance	22368299	Italian, Italy	T:8.402e-06	32	True	False
CDKN2A	c.159G>C	chr9:21971199	NM_000077.4	p.Met53Ile	rs104894095	Pathogenic, risk factor	25356972; 10719365	Mixed, United States; Unknown, Canada	G:1.671e-05	28.3	True	False
CDKN2A	c.146T>G	chr9:21974681	NM_000077.4	p.Ile49Ser	—	—	10667595; 15146471; 10719365	Mixed, Canada; Mixed; Unknown, Canada	G:4.365e-04	28.2	True	False
CDKN2A	c.71G>C	chr9:21974756	NM_000077.4	p.Arg24Pro	rs104894097	Pathogenic/ Likely pathogenic, risk factor	25356972; 16905682; 15146471; 21150883	Mixed, United States; Mixed; Mixed; White, US	—	24.7	True	False
CDKN2A	c.47T>G	chr9:21974780	NM_000077.4	p.Leu16Arg	rs864622263	Conflicting (likely pathogenic [1]; uncertain significance [1])	25356972; 21150883	Mixed, United States; White, United States	—	23.7	True	False
CFTR	c.350G>A	chr7:117171029	NM_000492.3	p.Arg117His	rs78655421	Pathogenic	25675422; 19885835; 16227367	Unknown, United Kingdom; Mixed, United States; Unknown, US	A:1.524e-03,T:8.237e-06	24.9	False	False
CFTR	c.1521_1523delCTT	chr7:117199646-117199648	NM_000492.3	p.Phe508del	rs113993960	Pathogenic	19885835; 7522998; 25003218; 11115825; 14688470; 17072959; 16227367	Mixed, United States; White, United States; Mixed, Germany; Unknown, Spain; Unknown, United States; Italian, Italy; Unknown, United States	.	21.3	False	False
CFTR	c.1652G>A	chr7:117227860	NM_000492.3	p.Gly551Asp	rs75527207	Pathogenic	19885835	Mixed, United States	A:1.400e-04	33	False	False
CHEK2	c.470T>C	chr22:29121087	NM_007194.3	p.Ile157Thr	rs17879961	Conflicting (likely pathogenic [3]; pathogenic [4]; uncertain significance [1]), risk factor	27488870; 20643596; 27038244	Polish, Poland; White, Czech Republic; Polish, Poland	—	21.1	True	False
CHEK2	c.319+1G>A	chr22:29130390	NM_007194.3	—	rs765080766	—	20643596; 27488870; 27038244	White, Czech Republic; Polish, Poland; Polish, Poland	—	26.9	False	False
MLH1	c.2252_2253delAA	chr3:37092125-37092126	NM_000249.3	p.Lys751Serfs	rs267607907	Uncertain significance	24802709	Italian, Italy	—	35	True	True
MSH2	c.942+3A>T	chr2:47641560	NM_000251.2	—	rs193922376	Pathogenic	25479140	Unknown, Canada	—	14.19	True	False
MSH2	c.1046C>T	chr2:47643538	NM_000251.2	p.Pro349Leu	rs587779067	Pathogenic	21926548	Northern European, United States	—	33	True	True

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SUPPLEMENTARY TABLE 2. *(Continued)*

Gene	cDNA Nucleotide Change	Hg19 Position	Transcript	Amino Acid Change	dbSNP rs. id	ClinVar	PubMed ID	Population, Region*	MAF (ExAC)	CADD Score	Family History*	Co-segregation†
NBN	c.657_661delACAAA	chr8:90983442-90983446	NM_002485.4	p.Lys219Asnfs	rs587776650	Pathogenic, risk factor	27150568; 26483394	Slavian (White), Czech; Mixed, United States	—	35	True	False
PALB2	c.1240C>T	chr16:23646627	NM_024675.3	p.Arg414Ter	rs180177100	Pathogenic	20412113; 27449771	Mixed, Europe; Mixed, United States & Europe	—	38	True	False
PALLD	c.415C>T	chr4:169799457	NM_001166110.1	p.Pro139Ser	rs121908291	Conflicting (benign [1]; uncertain significance [1]), risk factor	17194196; 17415588	White, US; Unknown, Canada	T:6.069e-05	13.12	True	True
PRSS1	c.86A>T	chr7:142458451	NM_002769.4	p.Asn29Ile	rs111033566	Pathogenic	15017610; 18184119	Mixed, Europe; French, France	T:0.470	18.21	True	False
TP53	c.916C>T	chr17:7577022	NM_000546.5	p.Arg306Ter	rs121913344	Pathogenic/ likely pathogenic	25479140	Unknown, Canada	—	37	False	False

*"Family history" of True indicates if any patient that carries this variant is reported to be found in a pancreatic cancer/pancreatitis family by its study. If this variant is further confirmed to co-segregate with familial disease, "Co-segregation" will be True.
cDNA indicates complementary DNA; hg19, human genome 19; dbSNP rs. Id; The Single Nucleotide Polymorphism database (dbSNP) reference SNP ID number (rs. ID); MAF, minor allele frequency; ExAC, Exome Aggregation Consortium; Combined Annotation Dependent Depletion.