In the following Supplementary Tables, variant classification provided by HGMD database is reported. Briefly, a score is computed by HGMD using a Random Forest supervised machine learning approach, based upon multiple lines of evidence:

1. HGMD literature support for pathogenicity (placed on a scale of 1–10, with 1 being the lowest score and 10 being the highest),
2. evolutionary conservation (100-way vertebrate alignment),
3. variant allele frequency and
4. *in silico* pathogenicity prediction (CADD, PolyPhen2 and MutPred).

HGMD data are used to train the model with disease-causing mutations forming the positive class and possible/probable disease-causing mutations making up the negative class. Individually, ranking scores may be interpreted as relative probabilities of pathogenicity (i.e. the higher the score, the more likely the variant is to be disease-causing).
For further details, see Stenson et al., 2020[14].

Supplementary Table 1. List of *KRIT1* gene variants

MISSENSE – NONSENSE VARIANTS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.46C>T	p.Arg16Cys	Probably disease-causing mutation	[41]
c.47G>C	p.Arg16Pro	Probably disease-causing mutation	[81]
c.167C>T	p.Thr56Met	Probably disease-causing mutation	[82]
c.196C>T	p.Gln66Ter	Disease-causing mutation	[57,83,84]
c.206T>A	p.Leu69Ter	Disease-causing mutation	[85,86]
c.268C>T	p.Arg90Ter	Disease-causing mutation	[83,87,88]
c.301G>A	p.Gly101Arg	Probably disease-causing mutation	[41]
c.406C>T	p.Gln136Ter	Disease-causing mutation	[78]
c.410A>G	p.Asp137Gly	Disease-causing mutation	affects splicing [34,72]
c.409G>C	p.Asp137His	Disease-causing mutation	[89]
c.418C>T	p.Arg140Ter	Disease-causing mutation	[90]
c.535C>T	p.Arg179Ter	Disease-causing mutation	[83,87,91]
c.596C>G	p.Ser199Ter	Disease-causing mutation	[92]
c.601C>G	p.Gln201Glu	Disease-causing mutation	affects splicing [72,93,94]
c.601C>T	p.Gln201Ter	Disease-causing mutation	[83,95]
c.690C>G	p.Tyr230Ter	Disease-causing mutation	[83,87]
c.691A>G	p.Asn231Asp	Probably disease-causing mutation	[69]
c.703G>A	p.Gly235Arg	Disease-causing mutation	affects splicing [73,85,86,96]
c.707C>T	p.Ser236Leu	Probably disease-causing mutation	[82]
c.715C>T	p.Gln239Ter	Disease-causing mutation	[97]
c.730G>T	p.Val244Leu	Disease-causing mutation	reduces CCM2 binding [41]
c.805G>T	p.Glu269Ter	Disease-causing mutation	[83,87]
c.813G>A	p.Trp271Ter	Disease-causing mutation	[83,93]
c.814C>T	p.Gln272Ter	Disease-causing mutation	[98]
c.817A>T	p.Arg273Ter	Disease-causing mutation	[83,87]
c.838G>T	p.Glu280Ter	Disease-causing mutation	[99]
c.858G>A	p.Trp286Ter	Disease-causing mutation	[9,83]
c.879C>G	p.His293Gln	Probably disease-causing mutation	[100]
c.880C>T	p.Arg294Ter	Disease-causing mutation	[86,98]
c.902C>G	p.Ser301Ter	Disease-causing mutation	[63,83]
c.923T>A	p.Leu308His	Disease-causing mutation	[68]
c.922C>T	p.Leu308Phe	Probably disease-causing mutation	[98]

c.966G>A	p.Trp322Ter	Disease-causing mutation	[85,86]
c.987C>A	p.Cys329Ter	Disease-causing mutation	[66,83]
c.990G>A	p.Trp330Ter	Disease-causing mutation	[98]
c.992A>G	p.Tyr331Cys	Disease-causing mutation	[101]
c.1048C>T	p.Leu350Phe	Disease-causing mutation	[85,86]
c.1060C>T	p.Gln354Ter	Disease-causing mutation	[83,93]
c.1093G>T	p.Gly365Ter	Disease-causing mutation	[78]
c.1114C>T	p.Gln372Ter	Disease-causing mutation	[69]
c.1160A>C	p.Gln387Pro	Disease-causing mutation	[102]
c.1162C>T	p.Gln388Ter	Disease-causing mutation	[98]
c.1172C>T	p.Ser391Phe	Disease-causing mutation	[102]
c.1201C>T	p.Gln401Ter	Disease-causing mutation	[103]
c.1211G>A	p.Trp404Ter	Disease-causing mutation	[9,83]
c.1258G>T	p.Glu420Ter	Disease-causing mutation	[64,83]
c.1267C>T	p.Arg423Ter	Disease-causing mutation	[83,86,87]
c.1289C>G	p.Ser430Ter	Disease-causing mutation	[83,104]
c.1303G>T	p.Glu435Ter	Disease-causing mutation	[105]
c.1363C>T	p.Gln455Ter	Disease-causing mutation	[63,83,106]
c.1380T>G	p.Tyr460Ter	Disease-causing mutation	[107]
c.1391G>A	p.Trp464Ter	Disease-causing mutation	[83,87]
c.1400C>T	p.Ser467Leu	Disease-causing mutation	[108]
c.1405A>C	p.Asn469His	Disease-causing mutation	[109]
c.1419A>C	p.Gln473His	Probably disease-causing mutation	[41]
c.1431T>A	p.Tyr477Ter	Disease-causing mutation	[78]
c.1436A>C	p.Lys479Thr	Disease-causing mutation	[5]
c.1444C>T	p.Gln482Ter	Disease-causing mutation	[60,83,86]
c.1460G>A	p.Trp487Ter	Disease-causing mutation	[98]
c.1498C>T	p.Gln500Ter	Disease-causing mutation	[98]
c.1513C>T	p.Gln505Ter	Disease-causing mutation	[83,93]
c.1517T>G	p.Leu506Arg	Disease-causing mutation	[85,86]
c.1611T>A	p.Tyr537Ter	Disease-causing mutation	[63,83]
c.1619T>A	p.Leu540Ter	Disease-causing mutation	[78]
c.1678C>T	p.Gln560Ter	Disease-causing mutation	[64,83]
c.1699G>T	p.Glu567Ter	Disease-causing mutation	[5,83]
c.1708A>T	p.Lys570Ter	Disease-causing mutation	[83,87,88]

c.1815C>G	p.Tyr605Ter	Disease-causing mutation	[64,83,110]
c.1849G>T	p.Glu617Ter	Disease-causing mutation	[83,111]
c.1864C>T	p.Gln622Ter	Disease-causing mutation	[112]
c.1877T>A	p.Leu626Ter	Disease-causing mutation	[64,83,86]
c.1879C>T	p.Gln627Ter	Disease-causing mutation	[9,83]
c.1890G>A	p.Trp630Ter	Disease-causing mutation	[34,83]
c.1905T>G	p.Tyr635Ter	Disease-causing mutation	[83,87]
c.1927C>T	p.Gln643Ter	Disease-causing mutation	[113]
c.1980A>G	p.Val660=	Disease-associated polymorphism	[100,114]
c.2000T>G	p.Leu667Arg	Probably disease-causing mutation	[41]
c.2064G>A	p.Trp688Ter	Disease-causing mutation	[83,115]
c.2092C>T	p.Gln698Ter	Disease-causing mutation	[83,116]
c.2140C>T	p.Gln714Ter	Disease-causing mutation	[83,117]

SPLICING VARIANTS				
Nucleotide change	**Old nomenclature**	**Effect**	**Splicing site**	**Additional information**
c.103-1G>T	IVS4-1G>T	Disease-causing mutation	Acceptor	[98]
c.263-10A>G	IVS5-10A>G	Disease-causing mutation	Upstream of acceptor site	[118]
c.413T>C	IVS6+58T>C	Disease-causing mutation	Upstream of acceptor site	[95,119]
c.486-2A>G	IVS7-2A>G	Disease-causing mutation	Acceptor	[87]
c.485+1G>C	IVS7+1G>C	Disease-causing mutation	Donor	[116]
c.730-2A>G	IVS8-2A>G	Disease-causing mutation	Acceptor	[5,83]
c.730-1G>A	IVS8-1G>A	Disease-causing mutation	Acceptor	[83,93]
c.1146-1G>C	IVS8-1G>C	Disease-causing mutation	Acceptor	[120]
c.730-1G>T	IVS8-1G>T	Disease-causing mutation	Acceptor	[83,111]
c.712C>T	IVS8-18C>T	Disease-causing mutation	Donor	[115]
c.729G>A	IVS8-1G>A	Disease-causing mutation	Acceptor	[52]
c.729+1G>A	IVS8+1G>A	Disease-causing mutation	Donor	[85,86]
c.729+2T>C	IVS8+2T>C	Disease-causing mutation	Donor	[79]
c.729+5G>A	IVS8+5G>A	Disease-causing mutation	Downstream of donor site	[78,119]
c.842A>G	IVS9-4A>G	Disease-causing mutation	Donor	p.Asp281GlyfsTer5 [69]
c.845+1G>C	IVS9+1G>C	Disease-causing mutation	Donor	[121]
c.845+1G>T	IVS9+1G>T	Disease-causing mutation	Donor	[78]
c.845+2T>C	IVS9+2T>C	Disease-causing mutation	Donor	[83,122]
c.845+2T>G	IVS9+2T>G	Disease-causing mutation	Donor	[83,95]

c.990-15T>A	IVS10-15T>A	Disease-causing mutation	Upstream of acceptor site (PP)	[87]
c.990-1G>C	IVS10-1G>C	Disease-causing mutation	Acceptor	[87]
c.1147-13C>G	IVS11-13C>G	Disease-causing mutation	Upstream of acceptor site (PP)	[123]
c.1146+1G>A	IVS11+1G>A	Disease-causing mutation	Donor	[59,63,83]
c.1146+2T>A	IVS11+2T>A	Disease-causing mutation	Donor	[98]
NA	IVS12-4C>T	Disease-causing mutation	Upstream of acceptor site	[102]
c.1255-1G>A	IVS12-1G>A	Disease-causing mutation	Acceptor	[87]
NA	IVS12-1G>T	Disease-causing mutation	Acceptor	[117]
c.1254+14T>A	IVS12+14T>A	Disease-causing mutation	Downstream of donor site	[124]
c.1412-1G>A	IVS13-1G>A	Disease-causing mutation	Acceptor	[125]
c.1412-1G>C	IVS13-1G>C	Disease-causing mutation	Acceptor	[78]
c.1412-1G>T	IVS13-1G>T	Disease-causing mutation	Acceptor	[111]
c.1564-14C>G	IVS14-14C>G	Disease-causing mutation	Upstream of acceptor site (PP)	[98]
NA	IVS14-2°>G	Disease-causing mutation	Acceptor	[126]
c.1564-1G>A	IVS14-1G>A	Disease-causing mutation	Acceptor	[78]
c.1579G>A	IVS14+16G>A	Disease-causing mutation	Acceptor	[87]
c.1563+1G>A	IVS14+1G>A	Disease-causing mutation	Donor	[59]
NA	IVS15-13T>A	Disease-causing mutation	Upstream of acceptor site (PP)	[117]
c.1731-2A>C	IVS15-2A>C	Disease-causing mutation	Acceptor	[98]
c.1731-2A>G	IVS15-2A>G	Disease-causing mutation	Acceptor	[63]
c.1731-1G>C	IVS15-1G>C	Disease-causing mutation	Acceptor	[53]
c.1730+3A>T	IVS15+3A>T	Disease-causing mutation	Downstream of donor site	[98]
c.1730+5G>A	IVS15+5G>A	Disease-causing mutation	Downstream of donor site	[98]
c.1819-1G>T	IVS16-1G>T	Disease-causing mutation	Acceptor	[107]
c.1818+2T>A	IVS16+2T>A	Disease-causing mutation	Donor	[5]
c.2026-66A>T	IVS17-66A>T	Probably disease-causing mutation	Upstream of acceptor site (PP)	[61]
c.2026-12A>G	IVS17-12A>G	Disease-causing mutation	Upstream of acceptor site (PP)	[9,86]
c.2026-11T>G	IVS17-11T>G	Disease-causing mutation	Upstream of acceptor site (PP)	[59]
c.2026-3C>A	IVS17-3C>A	Disease-causing mutation	Upstream of acceptor site (PP)	[86,119]
c.1943C>T	IVS17-83C>T	Disease-causing mutation	Donor	Described as "84-bp cDNA deletion (nt 1,348-1,431)" in [9,87]
c.2025G>C	IVS17-1G>C	Disease-causing mutation	Acceptor	[98,119]
c.2025+1G>A	IVS17+1G>A	Disease-causing mutation	Donor	[53,86]
c.2143-2A>G	IVS18-2A>G	Disease-causing mutation	Acceptor	p.A715VfsTer14 [64]
c.2142+1G>C	IVS18+1G>C	Disease-causing mutation	Donor	[98]
c.2142+2T>G	IVS18+2T>G	Disease-causing mutation	Donor	[53,98]

SMALL DELETIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.262+132_262+133delAA	NA	Disease-causing mutation	[75]
c.*137delC	NA	Disease-causing mutation	[124]
c.112delC	p.(His38MetfsTer27)	Disease-causing mutation	[8]
c.146_147delGA	p.(Arg49LysfsTer14)	Probably disease-causing mutation	[127]
c.151_154delAAAG	p.(Lys51PhefsTer13)	Disease-causing mutation	[86,87]
c.152_155delAAGT	p.(Lys51IlefsTer13)	Disease-causing mutation	[128]
c.196_197delCA	p.(Gln66ArgfsTer54)	Disease-causing mutation	[85,86]
c.539delC	p.(Pro180LeufsTer7)	Disease-causing mutation	[59]
c.646_647delAA	p.(Lys216GlufsTer2)	Disease-causing mutation	[85,86]
c.681delC	p.(Cys228ValfsTer17)	Disease-causing mutation	[53]
c.699delG	p.(Leu233PhefsTer12)	Disease-causing mutation	[122,129]
c.700_703delTTTG	p.(Phe234AspfsTer10)	Disease-causing mutation	[111]
c.746delT	p.(Ile249LysfsTer7)	Disease-causing mutation	[85,86]
c.763delC	p.(Leu255Ter)	Disease-causing mutation	[85,86]
c.801delA	p.(Lys267AsnfsTer9)	Disease-causing mutation	[69]
c.800_803delAACA	p.(Lys267ArgfsTer8)	Disease-causing mutation	[66]
c.816delG	p.(Arg273GlufsTer3)	Disease-causing mutation	[130]
c.825delG	p.(Met275IlefsTer13)	Disease-causing mutation	[85,86]
c.842delA	p.(Asp281AlafsTer7)	Disease-causing mutation	[78]
c.845+1_845+4delGTAC	NA	Disease-causing mutation	[131]
c.877delC	p.(His293ThrfsTer12)	Disease-causing mutation	[78]
c.940_943delGTCA	p.(Val314ThrfsTer3)	Disease-causing mutation	[132]
c.1002delT	p.(Glu335ArgfsTer7)	Disease-causing mutation	[88]
c.1024_1028delGAGAA	p.(Glu342ArgfsTer13)	Disease-causing mutation	[111]
c.1034delA	p.(Lys345SerfsTer7)	Disease-causing mutation	[9]
c.1060delC	p.(Gln354AsnfsTer17)	Disease-causing mutation	[87]
c.1088delC	p.(Ala363ValfsTer8)	Disease-causing mutation	[133]
c.1097delG	p.(Gly366AspfsTer5)	Disease-causing mutation	[88]
c.1114_1115delCA	p.(Gln372AspfsTer10)	Disease-causing mutation	[68]
c.1133delC	p.(Pro378GlnfsTer7)	Disease-causing mutation	[134]
c.1153delA	p.(Thr385GlnfsTer9)	Disease-causing mutation	[135]

c.1166delG	p.(Gly389GlufsTer5)	Disease-causing mutation	[78]
c.1179_1185delAAATATT	p.(Leu393PhefsTer17)	Disease-causing mutation	[93]
c.1197_1199delCAA	p.(Asn399del)	Probably disease-causing mutation	[78]
c.1201_1204delCAAA	p.(Gln401ThrfsTer10)	Disease-causing mutation	[117,136,137]
c.1202_1205delAAAA	p.(Gln401ProfsTer10)	Disease-causing mutation	[87]
c.1204_1208delAACAA	p.(Asn402LeufsTer13)	Disease-causing mutation	[128]
c.1229delT	p.(Leu410CysfsTer2)	Disease-causing mutation	[9]
c.1237_1240delGAAG	p.(Glu413GlnfsTer23)	Disease-causing mutation	[87]
c.1249_1252delAAAC	p.(Lys417HisfsTer19)	Disease-causing mutation	[64,86,138]
c.1253delC	p.(Pro418HisfsTer19)	Disease-causing mutation	[64]
c.1254delA	p.(Tyr419MetfsTer18)	Disease-causing mutation	[111]
c.1255-1_1256delGTA	NA	Disease-causing mutation	[34,86,116]
c.1257delT	p.(Tyr419Ter)	Disease-causing mutation	[139]
c.1278_1281delAATG	p.(Asp428GlyfsTer8)	Disease-causing mutation	[9]
c.1258_1273del16	p.(Glu420ThrfsTer12)	Disease-causing mutation	[78]
c.1292_1293delAT	p.(Tyr431SerfsTer4)	Disease-causing mutation	[86,140]
c.1306_1310delTTGAA	p.(Leu436AlafsTer4)	Disease-causing mutation	[60]
c.1314_1324del11	p.(Gly439HisfsTer37)	Disease-causing mutation	[69]
c.1360_1363delTCTC	p.(Ser454LysfsTer40)	Disease-causing mutation	[87]
c.1396delT	p.(Cys466ValfsTer29)	Disease-causing mutation	[141]
c.1411+2_1411+5delTAAG	NA	Disease-causing mutation	[52]
c.1501delA	p.(Arg501GlyfsTer8)	Disease-causing mutation	[117]
c.1505_1511delAAACACC	p.(Glu502ValfsTer5)	Disease-causing mutation	[85,86]
c.1524_1528delAAGAA	p.(Arg510CysfsTer8)	Disease-causing mutation	[85,86]
c.1527_1528delAA	p.(Asp511CysfsTer8)	Disease-causing mutation	[87]
c.1531delG	p.(Asp511MetfsTer2)	Disease-causing mutation	[78]
c.1535_1536delTG	p.(Val512GlufsTer7)	Disease-causing mutation	[142]
c.1542delT	p.(Leu516TrpfsTer11)	Disease-causing mutation	[143]
c.1579_1588del10	p.(Ala527PhefsTer11)	Disease-causing mutation	[85,86]
c.1585delC	p.(Ile530PhefsTer11)	Disease-causing mutation	[144]
c.1595_1596delTT	p.(Phe532Ter)	Disease-causing mutation	[93]
c.1599_1601delTGA	p.(Asp533del)	Disease-causing mutation	[145]
c.1632_1634delTAC	p.(Tyr544Ter)	Disease-causing mutation	[114]
c.1651delC	p.(Leu551Ter)	Disease-causing mutation	[146]
c.1660_1678del19	p.(Leu554LysfsTer2)	Disease-causing mutation	[78]

c.1667delG	p.(Ser556IlefsTer6)	Disease-causing mutation	[98]
c.1682_1683delTA	p.(Ile561SerfsTer6)	Disease-causing mutation	[95]
c.1688_1689delAT	p.(Tyr563TrpfsTer4)	Disease-causing mutation	[53,86]
c.1702_1703delAG	p.(Ser568Ter)	Disease-causing mutation	[111]
c.1702delA	p.(Ser568ValfsTer9)	Disease-causing mutation	[87]
c.1710delA	p.(Lys570AsnfsTer7)	Disease-causing mutation	[63]
c.1715delA	p.(Lys572SerfsTer5)	Disease-causing mutation	[87]
c.1717_1720delCAAG	p.(Gln573ValfsTer3)	Disease-causing mutation	[117]
c.1719delA	p.(Gly574ValfsTer3)	Disease-causing mutation	[87]
c.1730+5delG	NA	Disease-causing mutation	[147]
c.1730+4_1730+7delAGTA	NA	Disease-causing mutation	[87]
c.1757_1758delCT	p.(Pro586ArgfsTer7)	Disease-causing mutation	[111]
c.1773_1774delAA	p.(Ser592Ter)	Disease-causing mutation	[88]
c.1780delG	p.(Ala594HisfsTer67)	Disease-causing mutation	[125]
c.1807delC	p.(His603MetfsTer58)	Disease-causing mutation	[111]
c.1813delT	p.(Tyr605ThrfsTer56)	Disease-causing mutation	[34]
c.1818+2delT	NA	Disease-causing mutation	[52]
c.1848delA	p.(Glu617LysfsTer44)	Disease-causing mutation	[116]
c.1885delT	p.(Cys629AlafsTer32)	Disease-causing mutation	[87]
c.1919delT	p.(Phe640SerfsTer21)	Disease-causing mutation	[148]
c.1935delT	p.(Phe645LeufsTer16)	Disease-causing mutation	[63]
c.1940delA	p.(Lys647ArgfsTer14)	Disease-causing mutation	[9]
c.1961_1962delAA	p.(Lys654SerfsTer21)	Disease-causing mutation	[78]
c.2012delA	p.(Asn671ThrfsTer36)	Disease-causing mutation	[149]
c.2042_2043delTT	p.(Leu681GlnfsTer13)	Disease-causing mutation	[93]
c.2054_2058delGTTTT	p.(Cys685TyrfsTer8)	Disease-causing mutation	[98]

Small insertions			
Nucleotide change	**Protein change**	**class**	**additional information**
c.143dupA	p.(Arg49GlufsTer15)	Disease-causing mutation	[87]
c.457dupA	p.(Thr153AsnfsTer10)	Disease-causing mutation	[98]
c.557dupT	p.(Thr188AsnfsTer2)	Disease-causing mutation	[78]
c.658_659dupTT	p.(Leu220PhefsTer2)	Disease-causing mutation	[60]
c.679dupA	p.(Thr227AsnfsTer20)	Disease-causing mutation	[53]

c.700_703dupTTTG	p.(Gly235ValfsTer13)	Disease-causing mutation	[52]
c.702dupT	p.(Gly235TrpfsTer12)	Disease-causing mutation	[98]
c.704_705insT	p.(Ser236IlefsTer11)	Disease-causing mutation	[109]
c.795dupA	p.(Pro266ThrfsTer2)	Disease-causing mutation	[150]
c.843dupC	p.(Lys282GlnfsTer8)	Disease-causing mutation	[9]
c.937dupT	p.(Ser313PhefsTer7)	Disease-causing mutation	[117]
c.947_948insAC	p.(Leu317ArgfsTer2)	Disease-causing mutation	[151]
c.968dupC	p.(Pro324ThrfsTer12)	Disease-causing mutation	[117]
c.970_973dupCCCA	p.(Ile325ThrfsTer12)	Disease-causing mutation	[68]
c.1018_1019dupTT	p.(Leu340PhefsTer3)	Disease-causing mutation	[98]
c.1066_1070dupAGTTC	p.(Pro358ValfsTer15)	Disease-causing mutation	[64]
c.1144dupA	p.(Arg382LysfsTer16)	Disease-causing mutation	[79]
c.1175dupC	p.(Leu393IlefsTer5)	Disease-causing mutation	[98]
c.1345dupG	p.(Glu449GlyfsTer31)	Disease-causing mutation	[111]
c.1487_1497dup11	p.(Gln500IlefsTer13)	Disease-causing mutation	[152]
c.1522dupC	p.(Leu508ProfsTer12)	Disease-causing mutation	[117]
c.1657dupA	p.(Thr553AsnfsTer15)	Disease-causing mutation	[93]
c.1683dupA	p.(Val562SerfsTer6)	Disease-causing mutation	[153]
c.1687dupT	p.(Tyr563LeufsTer5)	Disease-causing mutation	[115]
c.1710dupA	p.(His571ThrfsTer8)	Disease-causing mutation	[117]
c.1782_1785dupACCT	p.(His596ThrfsTer10)	Disease-causing mutation	[117]
c.1806_1807insAT	p.(His603IlefsTer59)	Disease-causing mutation	[78]
c.1825dupA	p.(Ser609LysfsTer4)	Disease-causing mutation	[98]
c.1867dupC	p.(Arg623ProfsTer32)	Disease-causing mutation	[9]
c.1896dupT	p.(Pro633SerfsTer22)	Disease-causing mutation	[154]
c.1904dupA	p.(Tyr635Ter)	Disease-causing mutation	[68]
c.1950dupC	p.(Ser651GlnfsTer4)	Disease-causing mutation	[78]
c.1961_1964dupAAGT	p.(Ile656SerfsTer21)	Disease-causing mutation	[34]
c.1970dupC	p.(Val658CysfsTer18)	Disease-causing mutation	[155]
c.1979_1980dupTA	p.(Gly661Ter)	Disease-causing mutation	[85,86]
c.2002dupC	p.(His668ProfsTer8)	Disease-causing mutation	[87]
c.2019_2020dupAA	p.(Thr674LysfsTer34)	Disease-causing mutation	[53]
c.2020dupA	p.(Thr674AsnfsTer2)	Disease-causing mutation	[85,86]
c.2029_2030insA	p.(Leu677TyrfsTer6)	Disease-causing mutation	[85,86]
c.2058dupT	p.(Met687TyrfsTer8)	Disease-causing mutation	[98]

c.2101dupA	p.(Ser701LysfsTer5)	Disease-causing mutation	[88]
c.2138_2139insG	p.(Gln714ThrfsTer20)	Disease-causing mutation	[109]

Small deletions/insertions			
Nucleotide change	**Protein change**	**Effect**	**additional information**
c.619_620delCAinsG	p.(His207ValfsTer7)	Disease-causing mutation	[69]
c.730-1_730delGGinsTT	NA	Disease-causing mutation	[93]
c.999_1000delAGinsT	p.(Lys333AsnfsTer9)	Disease-causing mutation	[98]
c.1197_1199delCAAinsAG	p.(Asn399LysfsTer13)	Disease-causing mutation	[87]
c.1780_1783delGCACins14	p.(Ala594TyrfsTer14)	Disease-causing mutation	[156]
c.1844_1846delGTAinsCT	p.(Ser615ThrfsTer46)	Disease-causing mutation	[88]

	Regulatory region variants		
Nucleotide change	**Regulatory sequence**	**Effect**	**additional information**
c.*132T>G	CACCCCTGTAATTCCAGCACTTTGGGAGGC(**T>G**)GGGGCAGGCGGATCACCTGAAGTCAGAGTT +132 relative to Termination codon	Disease-causing mutation	[124]

Large deletions				
Deletion	**Nucleotide change**	**Protein change**	**Effect**	**additional information**
~700 kb including entire gene	NA	NA	Disease-causing mutation	[157]
26 bp form c.1608, codon 536	c.1608_1633del26	p.(Arg536SerfsTer4)	Disease-causing mutation	[9,98,158]
31 bp c.1414_1444	c.1414_1444del31	p.(Leu472AsnfsTer13)	Disease-causing mutation	[98]
c.990_1146del, p.(Trp330CysfsTer3)	NA	NA	Disease-causing mutation	[85,86]
entire gene	NA	NA	Disease-causing mutation	[86,158,159]
exon 10	NA	NA	Disease-causing mutation	[85,86]
exon 11	NA	NA	Disease-causing mutation	[65]
exon 12	NA	NA	Disease-causing mutation	[85,86]
exons 15-19	NA	NA	Disease-causing mutation	[69]
exon 16	NA	NA	Disease-causing mutation	[85,86]
exons 17-18	NA	NA	Disease-causing mutation	[85,86]
exons 2-11	NA	NA	Disease-causing mutation	[88]
exon 5	NA	NA	Disease-causing mutation	[65]
exons 5-19	NA	NA	Disease-causing mutation	[42]
exons 9-10	NA	NA	Disease-causing mutation	[65]

including exons 1-17	NA	NA	Disease-causing mutation	[98]
including exons 1-19	NA	NA	Disease-causing mutation	[98]
including exons 1-3	NA	NA	Disease-causing mutation	[98]
including exons 1-5	NA	NA	Disease-causing mutation	[98]
including exons 11	NA	NA	Disease-causing mutation	[98]
including exons 11-14	NA	NA	Disease-causing mutation	[98]
including exons 11-17	NA	NA	Disease-causing mutation	[98]
including exons 15	NA	NA	Disease-causing mutation	[98]
including exons 15-17	NA	NA	Disease-causing mutation	[98]
including exons 18-19	NA	NA	Disease-causing mutation	[98]
including exon 19	c.-329392_-326582del2811	NA	Disease-causing mutation	[88]

Large insertions			
Type	**Nucleotide change**	**Effect**	**additional information**
Duplication	exons 7-17	Disease-causing mutation	[158]

Note: Acceptor site: AG sequence at the 3’ splice site of an intron; Donor site: GT sequence at the 5’ splice site of an intron; PP: polypyrimidine tract (C or T) of 20-50 nucleotides between the branch site and the acceptor splice site; NA=not available.

Supplementary Table 2. List of *CCM2* gene variants

MISSENSE – NONSENSE VARIANTS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.1A>G	p.Met1Val	Disease-causing mutation	[10]
c.14G>A	p.Gly5Asp	Disease-causing mutation	[114]
c.48A>G	p.Pro16=	Probably disease-causing mutation	[95]
c.55C>T	p.Arg19Ter	Disease-causing mutation	[86,160,161]
c.319C>T	p.Gln107Ter	Disease-causing mutation	[36,83]
c.338T>C	p.Leu113Pro	Disease-causing mutation	Reduced solubility [39,41,98]
c.344T>G	p.Leu115Arg	Disease-causing mutation	[41]
c.346T>C	p.Ser116Pro	Disease-causing mutation	[39]
c.359T>A	p.Val120Asp	Disease-causing mutation	[162]
c.358G>A	p.Val120Ile	Disease-associated polymorphism	[92,100,114]
c.365T>G	p.Leu122Arg	Disease-causing mutation	[39]
c.364C>A	p.Leu122Met	Probably disease-causing mutation	[163]
c.367G>C	p.Ala123Pro	Disease-causing mutation	[39]
c.464T>C	p.Leu155Pro	Disease-causing mutation	Reduced solubility [41]
c.475C>T	p.Gln159Ter	Disease-causing mutation	[83]
c.579C>A	p.Cys193Ter	Disease-causing mutation	[59]
c.580T>G	p.Cys194Gly	Probably disease-causing mutation	[92]
c.593T>G	p.Leu198Arg	Disease-causing mutation	Reduced solubility [10,39,41]
c.593T>C	p.Leu198Pro	Disease-causing mutation	[39]
c.622G>T	p.Glu208Ter	Disease-causing mutation	[64,83]
c.635T>C	p.Leu212Pro	Disease-causing mutation	[59]
c.638T>C	p.Leu213Pro	Disease-causing mutation	Reduced solubility [41]
c.652C>T	p.Gln218Ter	Disease-causing mutation	[10,83]
c.713C>A	p.Ser238Tyr	Probably disease-causing mutation	[69]
c.810C>G	p.Phe270Leu	Probably disease-causing mutation	[41]
c.866G>A	p.Ser289Asn	Probably disease-causing mutation	[82]
c.926A>G	p.Lys309Arg	Probably disease-causing mutation	[82]
c.970G>A	p.Glu324Lys	Probably disease-causing mutation	[116]
c.1280A>C	p.Asp427Ala	Disease-causing mutation	[124]
c.1316T>C	p.Met439Thr	Probably disease-causing mutation	[98]

SPLICING VARIANTS				
Nucleotide change	**Old nomenclature**	**Effect**	**Splicing site**	**Additional information**
c.30G>A	IVS1-1G>A	Disease-causing mutation	Upstream of acceptor site	[36,119]
c.30+1G>A	IVS1+1G>A	Disease-causing mutation	Donor	[160]
c.30+5G>A	IVS1+5G>A	Disease-causing mutation	Downstream of donor site	[98,119]
c.205-2A>C	IVS2-2A>C	Disease-causing mutation	Acceptor	[98]
c.205-1G>A	IVS2-1G>A	Disease-causing mutation	Acceptor	[83,86,160]
c.204+1G>A	IVS2+1G>A	Disease-causing mutation	Donor	[164]
c.204+2T>C	IVS2+2T>C	Disease-causing mutation	Donor	[107,165]
c.289-1G>T	IVS3-1G>T	Disease-causing mutation	Acceptor	[52]
c.288G>A	IVS3-1G>A	Disease-causing mutation	Upstream of acceptor site	[119,166]
c.288+1G>A	IVS3+1G>A	Disease-causing mutation	Donor	[10]
c.610-1G>A	IVS5-1G>A	Disease-causing mutation	Acceptor	[36]
c.609G>A	IVS5-1G>A	Disease-causing mutation	Upstream 3’ acceptor site	[10,119]
c.1055-1G>A	IVS9-1G>A	Disease-causing mutation	Acceptor	[61]

SMALL DELETIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.23delG	p.(Gly8AlafsTer15)	Disease-causing mutation	[36]
c.54_55delAC	p.(Arg19SerfsTer6)	Disease-causing mutation	[57]
c.56delG	p.(Arg19GlnfsTer4)	Disease-causing mutation	[36]
c.97delC	p.(His33MetfsTer4)	Disease-causing mutation	[167]
c.113_116delAGAG	p.(Glu38GlyfsTer21)	Disease-causing mutation	[88]
c.134_135delTG	p.(Val45GlyfsTer6)	Disease-causing mutation	[85,86,164]
c.169_172delAGAC	p.(Arg57CysfsTer2)	Disease-causing mutation	[36]
c.193_204del12	p.(Lys65_Lys68del)	Disease-causing mutation	[114]
c.273delC	p.(Phe91LeufsTer2)	Disease-causing mutation	[98]
c.314delT	p.(Leu105Ter)	Disease-causing mutation	[36]
c.325_334del10	p.(His109CysfsTer44)	Disease-causing mutation	[168]
c.502_503delAG	p.(Leu169ValfsTer66)	Disease-causing mutation	[86,169]
c.557_570del14	p.(Ala186GlyfsTer45)	Disease-causing mutation	[68]
c.610-11_612del14	NA	Disease-causing mutation	[170]
c.642_655del14	p.(Gln215CysfsTer16)	Disease-causing mutation	[98]
c.652delC	p.(Gln218ArgfsTer74)	Disease-causing mutation	[52]
c.755delC	p.(Ser252LeufsTer40)	Disease-causing mutation	[171]

c.773delA	p.(Lys258ArgfsTer34)	Disease-causing mutation	[145]
c.775delG	p.(Glu259ArgfsTer33)	Disease-causing mutation	[98]
c.780delC	p.(Tyr261ThrfsTer31)	Disease-causing mutation	[86,98]
c.1054+1delG	NA	Disease-causing mutation	[172]
c.1250_1251delAG	p.(Glu417GlyfsTer3)	Disease-causing mutation	[10]

SMALL INSERTIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.85_86dupGA	p.(Asp29GlufsTer9)	Disease-causing mutation	[95]
c.169dupA	p.(Arg57LysfsTer8)	Disease-causing mutation	[164]
c.353dupA	p.(Tyr118Ter)	Disease-causing mutation	[64]
c.402_405dupGCCC	p.(Ile136AlafsTer4)	Disease-causing mutation	[116]
c.495dupC	p.(Ser166GlnfsTer70)	Disease-causing mutation	[10]
c.540_541insGG	p.(Ser181GlyfsTer34)	Disease-causing mutation	[98]
c.563_564dupGG	p.(Pro189GlyfsTer26)	Disease-causing mutation	[173]
c.1071_1074dupCCCT	p.(Glu359ProfsTer2)	Disease-causing mutation	[78]
c.1255dupG	p.(Asp419GlyfsTer2)	Disease-causing mutation	[78]

SMALL DELETIONS/INSERTIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.30+5_30+6delGCinsTT	NA	Disease-causing mutation	[67]
c.205-2_205-1delAGinsT	NA	Disease-causing mutation	[64]
c.471_472+6delAGGTACAGins13	NA	Disease-causing mutation	[10]
c.546delGinsTA	p.(Ser183IlefsTer53)	Disease-causing mutation	[98]

REGULATORY REGION VARIANTS			
Nucleotide change	**Regulatory sequence**	**Effect**	**Additional information**
c.*18G>A	GGACTCAGCATGATGGACAGTGGATGGGGG**(G>A)**GCACCCACACCTTCCGCGCAGTCGTCATAG +75875 relative to transcription initiation site	Disease-causing mutation	[161]

LARGE DELETIONS				
Deletion	**Nucleotide change**	**Protein change**	**Effect**	**Additional information**
~25.5-81 kb including exon 1	NA	NA	Disease-causing mutation	[10]

40bp c.1-36_4	c.-36_4del40	NA	Disease-causing mutation	[78]
5'UTR and exons 1-10	NA	NA	Disease-causing mutation	[158]
5'UTR and exon 1	NA	NA	Disease-causing mutation	[85,86]
77.6 kb including exons 2-10	NA	NA	Disease-causing mutation	[42]
81-120 kb including exon 1	NA	NA	Disease-causing mutation	[10]
exon 1	NA	NA	Disease-causing mutation	[42]
exons 1-2	NA	NA	Disease-causing mutation	[8]
exons 1-2	NA	NA	Disease-causing mutation	[42]
exon 2	NA	NA	Disease-causing mutation	[42]
exon 5	NA	NA	Disease-causing mutation	[114]
exons 5-6	NA	NA	Disease-causing mutation	[42]
exon 5-9	NA	NA	Disease-causing mutation	[65]
exon 8-9	NA	NA	Disease-causing mutation	[65]
exon 9	NA	NA	Disease-causing mutation	[65]
including exon 5	NA	NA	Disease-causing mutation	[66]
including exon 5	NA	NA	Disease-causing mutation	[98]
including exon 2	NA	NA	Disease-causing mutation	[86,98]
including exons 3-4	NA	NA	Disease-causing mutation	[98]
including exon 5	NA	NA	Disease-causing mutation	[98]
including exon 6	NA	NA	Disease-causing mutation	[98]
including exons 6-9	NA	NA	Disease-causing mutation	[98]
including exon 9	NA	NA	Disease-causing mutation	[85,86]

Complex variants		
Description	**Effect**	**Additional information**
24 kb inversion including promoter and exon 1	Disease-causing mutation	[76]
c.645G>T and c.686T>A, p.Gln215His and p.Leu229Gln	Disease-causing mutation	[174]

Note: Acceptor site: AG sequence at the 3' splice site of an intron; Donor site: GT sequence at the 5' splice site of an intron; NA=not available.

Supplementary Table 3. List of *PDCD10* gene variants

MISSENSE – NONSENSE VARIANTS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.34G>C	p.Ala12Pro	Probably disease-causing mutation	[175]
c.58A>G	p.Met20Val	Probably disease-causing mutation	[98]
c.103C>T	p.Arg35Ter	Disease-causing mutation	predicted to induce a large splicing change [11,83,114]
c.124C>T	p.Gln42Ter	Disease-causing mutation	[56]
c.131T>C	p.Leu44Pro	Disease-causing mutation	[56]
c.160G>T	p.Glu54Ter	Disease-causing mutation	[176]
c.272A>G	p.Tyr91Cys	Probably disease-causing mutation	[177]
c.283C>T	pArg95Ter	Disease-causing mutation	[49,50]
c.322C>T	p.Arg108Ter	Disease-causing mutation	[55,178]
c.371G>A	p.Arg124Lys	Probably disease-causing mutation	[82]
c.385C>T	p.Gln129Ter	Disease-causing mutation	[11,83]
c.396G>A	p.Lys132=	Probably disease-causing mutation	probably affecting splicing [83,95]
c.422T>G	p.Leu141Arg	Disease-causing mutation	[179]
c.456T>G	p.Tyr152Ter	Disease-causing mutation	[55]
c.496G>T	p.Glu166Ter	Disease-causing mutation	[98]
c.514A>T	p.Lys172Ter	Disease-causing mutation	[55]
c.586C>T	p.Arg196Ter	Disease-causing mutation	[11,86]
c.598C>T	p.Gln200Ter	Disease-causing mutation	[180]
c.608T>G	p.Leu203Ter	Disease-causing mutation	[181]

SPLICING SITE VARIANTS				
Nucleotide change	**Old nomenclature**	**Effect**	**Splicing site**	**Additional information**
c.97-2A>G	IVS4-2A>G	Disease-causing mutation	Acceptor	[98]
c.151-1G>C	IVS5-1G>C	Disease-causing mutation	Acceptor	[98]
c.269-1G>A	IVS6-1G>A	Probably disease-causing mutation	Acceptor	predicted to induce a large splicing change [83,100]
c.269-1G>T	IVS6-1G>T	Disease-causing mutation	Acceptor	[78]
c.396-3C>G	IVS7-3C>G	Disease-causing mutation	Acceptor	[55]
c.396-2A>G	IVS7-2A>G	Disease-causing mutation	Acceptor	[55,182]
c.418G>T	IVS7+23G>T	Disease-causing mutation	Downstream of donor site	[98]
c.395+1G>A	IVS7+1G>A	Disease-causing mutation	Donor	predicted to induce a large splicing change [83,95]
c.395+1G>C	IVS7+1G>C	Disease-causing mutation	Donor	[69]
c.475-2A>G	IVS8-2A>G	Disease-causing mutation	Donor	[78]

c.475-1G>A	IVS8-1G>A	Disease-causing mutation	Acceptor	predicted to induce a large splicing change [11,83]
c.474+1G>A	IVS8+1G>A	Disease-causing mutation	Donor	predicted to induce a large splicing change [83,181]
c.474+1G>C	IVS8+1G>C	Disease-causing mutation	Donor	[98]
c.474+2T>C	IVS8+2T>C	Disease-causing mutation	Donor	[55]
c.474+5G>A	IVS8+5G>A	Disease-causing mutation	Donor	predicted to induce a large splicing change [83,173,181]
c.558-2A>C	IVS9-2A>C	Disease-causing mutation	Acceptor	[78]
c.558-1G>C	IVS9-1G>C	Disease-causing mutation	Acceptor	[78]
c.557+1G>C	IVS9+1G>C	Disease-causing mutation	Donor	[55]

SMALL DELETIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.-126_-125delTC	NA	Probably disease-causing mutation	[82]
c.81delT	p.(Pro28LeufsTer6)	Disease-causing mutation	[98]
c.113delT	p.(Leu38ArgfsTer7)	Disease-causing mutation	[78]
c.114_115delGT	p.(Ser39CysfsTer13)	Disease-causing mutation	[55]
c.129_138del10	p.(Arg45SerfsTer17)	Disease-causing mutation	[98]
c.165delT	p.(Pro56GlnfsTer9)	Disease-causing mutation	[183]
c.180delA	p.(Asp61ThrfsTer4)	Disease-causing mutation	[56]
c.196delA	p.(Ile66PhefsTer2)	Disease-causing mutation	[49,50]
c.211delA	p.(Ser71AlafsTer18)	Disease-causing mutation	[69]
c.212delG	p.(Ser71ThrfsTer18)	Disease-causing mutation	[184]
c.224delA	p.(Asn75ThrfsTer14)	Disease-causing mutation	[49]
c.275delT	p.(Met92ArgfsTer12)	Disease-causing mutation	[55]
c.317delA	p.(Lys106ArgfsTer20)	Disease-causing mutation	[78,185]
c.334_337delCAAA	p.(Gln112PhefsTer13)	Disease-causing mutation	[78,186]
c.372_373delAG	p.(Arg124SerfsTer12)	Disease-causing mutation	[98]
c.391delA	p.(Ile131SerfsTer4)	Disease-causing mutation	[78]
c.501delT	p.(Phe167LeufsTer2)	Disease-causing mutation	[56]
c.538delA	p.(Thr180ArgfsTer9)	Disease-causing mutation	[49]
c.557+4_557+7delAGTA	NA	Disease-causing mutation	[11]

SMALL INSERTIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.63_64dupCC	p.(Leu22ProfsTer13)	Disease-causing mutation	[78]

c.159dupA	p.(Glu54ArgfsTer22)	Disease-causing mutation	[176]
c.175dupA	p.(Thr59AsnfsTer17)	Disease-causing mutation	[98]
c.268+1dupG	NA	Disease-causing mutation	[55]
c.350dupT	p.(Asp119ArgfsTer2)	Disease-causing mutation	[47,64]
c.401_402dupTA	p.(Ala135Ter)	Disease-causing mutation	[55]
c.538dupA	p.(Thr180AsnfsTer4)	Disease-causing mutation	[69]

SMALL DELETIONS/INSERTIONS			
Nucleotide change	**Protein change**	**Effect**	**Additional information**
c.396-31_396-13del19insA	NA	Disease-causing mutation	[98]
c.394_395delAAinsGATT	p.(Lys132AspfsTer4)	Disease-causing mutation	[98]

REGULATORY REGION VARIANTS			
Nucleotide change	**Regulatory sequence**	**Effect**	**Additional information**
c.-562A>G	TCAGCCCGACAGCCCCAGGATCCCCACCAC(**A>G**)GGCCCCTCACCCCCTTCCTTCCTCTGCTCT -15094 relative to initiation codon	Disease-associated polymorphism	[187]
c.-514A>G	CTTCCTCTGCTCTGTCAGCCCGCCCCCTCA(**A>G**)TGGGTGAGGCGCCTGCGGGGCCTACTCCGC -15046 relative to initiation codon	Disease-associated polymorphism	[187]

LARGE DELETIONS				
Deletion	**Nucleotide change**	**Protein change**	**Effect**	**Additional information**
1.1-1.9 Mb including entire gene	NA	NA	Disease-causing mutation	[11]
2383-5618kb including entire gene	NA	NA	Disease-causing mutation	[188]
entire gene	NA	NA	Disease-causing mutation	[65,86]
exons 1-2	NA	NA	Disease-causing mutation	[55]
exons 1-3	NA	NA	Disease-causing mutation	[55]
exons 3-4	NA	NA	Disease-causing mutation	[55]
exon 4	NA	NA	Disease-causing mutation	[85,86]
exons 4-10	c.-116-2911_*146075del184952	NA	Disease-causing mutation	[85,86]
exon 5	NA	NA	Disease-causing mutation	[11,189]
exon 5	NA	NA	Disease-causing mutation	[55]
exons 5-6	NA	NA	Disease-causing mutation	[85,86]
exon 6	NA	NA	Disease-causing mutation	[85,86]

exons 8-10	NA	NA	Disease-causing mutation	[55]
including exons 1-4	NA	NA	Disease-causing mutation	[98]
including exons 2-10	NA	NA	Disease-causing mutation	[98]
including exons 8-10	NA	NA	Disease-causing mutation	[98]

LARGE INSERTIONS			
Type	**Nucleotide change**	**Effect**	**Additional information**
Duplication	21bp c.367_387	Disease-causing mutation	[176]

COMPLEX VARIANTS		
Description	**Effect**	**Additional information**
c.376_380del, c.392_393ins37bp	Disease-causing mutation	[176]

Note: Acceptor site: AG sequence at the 3' splice site of an intron; Donor site: GT sequence at the 5' splice site of an intron; NA=not available.

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