Variants in the Netrin-1 Receptor UNC5C Prevent Apoptosis and Increase Risk for Familial Colorectal Cancer

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Supplementary Data

Supplementary Table 1, Supplementary Figure 1, Supplementary Figure 2

Suppl. Table/Figure Legends

Supplementary Table 1: List of all coding variants found in *UNC5C*

Supplementary Figure 1: Pedigrees of the families in which the proband had a mutation D353N, R603C and Q630E in *UNC5C*.

The probands screened for *UNC5C* mutations are indicated by red arrows. Individuals with cancer are shown as filled circles/squares. Different cancers are indicated beneath the relevant individuals, with age at diagnosis next to the cancer type. WT, normal sequence observed; X000X, mutations in *UNC5C* gene are indicated beneath individuals. Absence of a genotype indicates that DNA samples could not be obtained. BC (Breast Cancer). CaSU (Cancer Site Unknown). Crohn's (Crohn's disease). CRC (Colorectal Cancer). H&N (Head&Neck cancer). Roman numerals refer to generations, and individuals within a generation are numbered from left to right. ? indicates lack of information. Lozenge with a number inside indicates the number of siblings (brothers and sisters) with only fragmentary information. Family origin USA, F:France, P:Portugal.

Supplementary Figure 2: Analysis of methylation profile of the *UNC5C* promoter region.

Change in MeCpG content in the region of the *UNC5C* promoter in tumors of the probands of families 4, 5, 11, 12 and 14. The position of each CpG is indicated from the *UNC5C* translation start site (ATG); the transcriptional start is indicated. At least 10 PCR clones were sequenced from each tumor (black) and from the corresponding normal blood tissues (red) to determine the percentage of methylation at the CpG sites in the analyzed region.

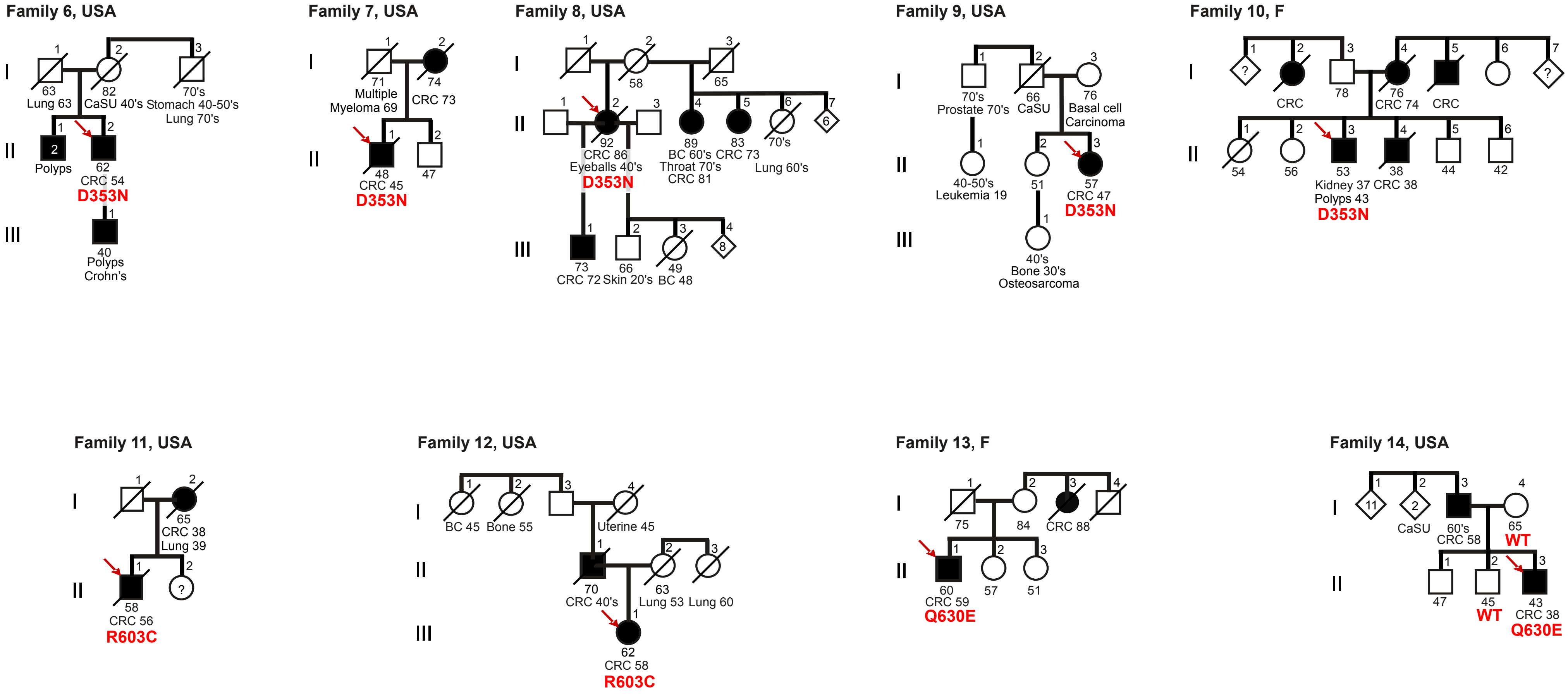
Supplementary Table 1

UNC5C Accession numbers NM_003728, ENST00000331502

SNP ID	AA Variation	Exon	Nucleotide position	Domain	No of Patients	No of controls
rs1843018	Synonymous	02	c.234C>T		56/191 (US), 7/105 (F)	
rs4699423	Synonymous	02	c.291T>C		53/191 (US), 6/105 (F)	
	Synonymous	03	c.447C>A		1/193 (US), 0/84 (F)	
	Synonymous	05	c.630C>T		1/190(US), 0/78 (F)	
	Synonymous	05	c.639T>C		1/190 (US), 0/78 (F)	
rs34875919	Synonymous	05	c.732T>C		13/190 (US), 0/78 (F)	
-	D353N	07	c.1057G>A	Thrombospondin	4/476 (US), 1/279 (F)	4/1416(US), 12/1648 (F)
-	I414V	08	c.1240A>G	Intracellullar domain	1/459 (US), 0/299 (F)	0/500 (US)
	Synonymous	09	c.1524G>A		0/489 (US), 1/262(F)	
	Synonymous	09	c.1614G>A		14/489 (US), 0/262(F)	
-	**R603C**	11	c.1807C>T	ZU5	2/489 (US), 0/328 (F)	8/1408 (US), 1/1811 (F)
rs2276322	Synonymous	11	c.1812A>C		416/489 (US), 279/328 (F)	
-	**A628K**	11	c.1882_1883GC>AA	ZU5	2/489 (US), 3/328 (F)	3/1408(US), 2/1811(F), 0/100(P)
-	**Q630E**	11	c.1888C>G	ZU5	1/489 (US), 1/328 (F)	1/1406(US), 3/1811(F)
	Synonymous	12	c.2025C>A		1/181 (US), 0/79(F)	
rs3733212	Synonymous	12	c.2037G>A		162/181 (US), 1/79(F)	
rs2289043	M721T	13	c.2162T>C	Intracellullar domain	164/193 (US), 50/67(F)	85/94(F)
	Synonymous	15	c.2514G>A		2/479 (US), 0/265 (F)	
rs34585936	A841T	15	c.2521G>A	Death Domain	23/498 (US), 4/265 (F)	24/499 (US), 38/983 (F)
	Synonymous	16	c.2670C>T		3/489 (US), 0/251 (F)	

SNP ID	AA Variation	Exon	Nucleotide position	Genotype details (US)	Genotype details (F)
rs1843018	Synonymous	02	c.234C>T	CC:0.707 CT:0.293 TT: 0	CC:0.933 CT:0.066 TT: 0
rs4699423	Synonymous	02	c.291T>C	TT: 0.722 CT:0.278 CC: 0	TT: 0.943 CT:0.057 CC: 0
	Synonymous	03	c.447C>A	CC:0.995 CA:0.005 AA:0	
	Synonymous	05	c.630C>T	CC:0.995 CT: 0.005 TT:0	
	Synonymous	05	c.639T>C	TT:0.995 TC:0.005 CC:0	
rs34875919	Synonymous	05	c.732T>C	TT:0.932 TC:0.068 CC:0	
-	D353N	07	c.1057G>A	GG:0.991 GA:0.009 AA:0	GG:0.996 GA:0.004 AA:0
-	I414V	08	c.1240A>G	AA:0.998 AG:0.002 GG:0	
	Synonymous	09	c.1524G>A		GG:0.996 GA:0.004 AA:0
	Synonymous	09	c.1614G>A	CC:0.971 CT:0.029 TT:0	
-	**R603C**	11	c.1807C>T	CC:0.996 CT:0.004 TT:0	
rs2276322	Synonymous	11	c.1812A>C	AA:0.150 AC:0.425 CC:0.425	AA:0.149 AC:0.427 CC:0.424
-	**A628K**	11	c.1882_1883GC>AA	GC/GC:0.996 GC/AA:0.004 AA/AA:0	GC/GC:0.991 GC/AA:0.009 AA/AA:0
-	**Q630E**	11	c.1888C>G	CC:0.998 CG:0.002 GG:0	CC:0.997 CG:0.003 GG:0
	Synonymous	12	c.2025C>A	CC:0.995 CA:0.005 AA:0	
rs3733212	Synonymous	12	c.2037G>A	GG:0.105 GA:0.486 AA:0.409	GG:0.987 GA:0.126 AA:0
rs2289043	M721T	13	c.2162T>C	TT:0.150 TC:0.451 CC:0.399	TT:0.254 TC:0.463 CC:0.283
	Synonymous	15	c.2514G>A	GG:0.996 GA:0.004 AA:0	
rs34585936	A841T	15	c.2521G>A	GG:0.954 GA:0.014 TT:0.032	GG:0.985 GA:0.015 TT:0
	Synonymous	16	c.2670C>T	CC:0.994 CT:0.006 TT:0	

Supplementary Figure 1



Supplementary Figure 2