

Supplementary Table S2. Loss-of-function variants segregated with the disease in 15 colorectal cancer families.

Family_ID	Gene	Gene name	Chrom_Pos_Ref_Alt	Loss-of-function variation	Effect*	CADD_PHRED_score	Function
Family_4	ARRDC4	arrestin domain containing 4	15_98512490_C_T	stopgain SNV	p.Arg255Ter	44	protein ubiquitination, glucose metabolism, innate immunity
Family_7	ZNF471	zinc finger protein 471	19_57036072_C_CAA	frameshift insertion	p.Thr214LysfsTer176	35	transcription regulation
Family_7	HEXB	hexosaminidase B (beta polypeptide)	5_73989526_C_T	stopgain SNV	p.Arg170Ter	37	degradation of GM2 gangliosides
Family_8	CYBA	cytochrome b-245, alpha polypeptide	16_88713203_AG_A	frameshift deletion	p.Phe83AsnfsTer41	25.3	superoxide generation
Family_9	ZNF408	zinc finger protein 408	11_46726628_C_T	stopgain SNV	p.Gln460Ter	36	transcription regulation in retina
Family_11	TRPM4	transient receptor potential cation channel subfamily M member 4	19_49661448_G_T	splicing	c.25-1 G>T p.Ser9LeufsTer17	26.1	calcium-activated nonselective ion channel, regulation of mucin secretion
Family_12	LGALS3BP	lectin, galactoside-binding, soluble, 3 binding protein	17_76969123_C_T	stopgain SNV	p.Trp186Ter	35	integrin-mediated cell adhesion, immune response
Family_12	SEC23IP	SEC23 Interacting Protein	10_121685740_G_T	splicing	c.2313+1G>T	24.7	endoplasmic reticulum to Golgi vesicle-mediated transport
Family_13	GALNT5	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 5 (GalNAc-T5)	2_158157422_C_T	stopgain SNV	p.Arg784Ter	44	mucin-type O-glycosylation of Golgi proteins
Family_13	ABCA8	ATP-binding cassette, sub-family A (ABC1), member 8	17_66887690_C_T	stopgain SNV	p.Trp988Ter	36	ATP-dependent lipophilic drug transporter
Family_14	SEPT12	septin 12	16_4833555_G_A	stopgain SNV	p.Gln212Ter	37	filament-forming cytoskeletal GTPase, involved in spermatogenesis
Family_14	POLN	polymerase (DNA directed) nu	4_2230895_G_A	stopgain SNV	p.Gln22Ter	36	DNA repair and homologous recombination
Family_15	C1orf177	LEXM, lymphocyte expansion molecule	1_55272689_AT_A	frameshift deletion	p.Asn44ThrfsTer24	24.8	
Family_15	ESD	esterase D	13_47365507_TC_T	frameshift deletion	p.Gly14AspfsTer13	35	serine hydrolase involved in the detoxification of formaldehyde

* nomenclature according to Human Genome Structural Variation Consortium in the Ensembl canonical transcript