

Supplementary Table 1 – Clinical characteristics of CA-CRC patients used for WES

	IBD	Age	Sex	Tumour site	Samples sequenced	Colitis duration (years)	Disease extent	PSC	Histology	Stage	MSI
UC01	UC	30	M	Hepatic flexure	- Tumour (x2) - Pseudopolyp (x2) - Normal mucosa - Muscle	9	PC	No	Moderate, mucinous	T3N0 M0	No
UC02	UC	72	M	Splenic flexure	- Tumour (x2) - Normal mucosa (x2) - Blood	23	PC	Yes	Poor	T3N0 M0	Yes
UC03	UC	43	M	Sigmoid	- Tumour (x2) - Normal mucosa - Blood	28	PC	No	Moderate	T1N1 M0	No
UC04	UC	53	F	Rectum	- Tumour - Blood	≥10	U	No	Moderate	T1N0 MX	No
UC05	UC	60	M	Sigmoid	- Tumour (x2) - Normal mucosa - Blood	14	PC	No	Poor	T3N2 M1	No
UC06	UC	71	M	Rectum	- Tumour (x4) - HGD - LGD - Normal mucosa - Blood	21	PC	No	Well	T2N0 M0	No
UC07	UC	36	M	Caecum	- Tumour (x5) - LGD - Normal mucosa (x3) - Blood	14	PC	Yes	Poor, mucinous	T3N2 M0	No
UC08	UC	45	M	Sigmoid	- Tumour - Blood	≥10	U	No	Moderate	T3N0 M0	No
UC09	UC	78	U	Rectum	- Tumour - Blood	≥10	PC	No	Well	T3N1 M1	Yes
UC10	UC	36	M	Sigmoid	- Tumour (x2) - HGD (x2) - LGD (x3) - Normal mucosa (x2) - Blood	11	PC	No	Moderate, mucinous, signet ring	T2N0 M2	No
CD01	CD	31	F	Rectum	- Tumour (x2) - Normal mucosa - Blood	≥10	U	Yes	Moderate	T2N0 M0	No
CD02	CD	66	F	Caecum	- Tumour (x2) - Normal mucosa - Blood	10	PC	No	Moderate	T2N0 M0	No
CD03	CD	51	F	Sigmoid	- Tumour (x2) - Normal mucosa - Lymphocytes	≥10	Left-sided	No	Moderate	T2N0 M0	No

UC = ulcerative colitis, CD = Crohn's disease, PSC = primary sclerosing cholangitis, MSI = microsatellite instability, U = unknown, PC = pancolitis

Supplementary Table 2 – Clinical characteristics of CA-CRC patients used for SNP array analysis

	IBD	Disease Extent	Age	Sex	Tumour Site	Stage	Samples arrayed	Colitis duration (years)	PSC	MSI
UC11	UC	PC	64	M	Sigmoid	T2N0M0	- Tumour	20	No	No
UC12	UC	PC	87	M	Caecum	T1N0M0	- Tumour - Normal mucosa	8	Yes	No
UC13	UC	PC	35	M	Rectum	T2N0M0	- Tumour - Normal mucosa	11	No	Yes
UC14	UC	PC	29	F	Rectosigmoid	T2N1M0	- Tumour	12	No	No
UC15	UC	PC	74	F	Caecum	T2N0M0	- Tumour - Normal mucosa	17	No	Yes
UC16	UC	PC	86	F	Ascending	T1N0M0	- Tumour	23	No	Yes
UC17	UC	PC	72	M	Caecum	T2N1M0	- Tumour - Normal mucosa	17	No	No
UC18	UC	PC	49	F	Caecum	T1N0M0	- Tumour	≥ 10	No	No
UC19	UC	PC	60	F	Sigmoid	T3N0M0	- Tumour - Normal mucosa	29	No	No
UC20	UC	PC	47	M	Sigmoid	T3N0M0	- Tumour - Normal mucosa	20	No	No
UC21	UC	PC	62	M	Sigmoid	T1N0M0	- Tumour	≥ 10	No	No
UC22	UC	PC	67	M	Descending	T1N0M0	- Tumour - Normal mucosa	≥ 10	No	No

UC = ulcerative colitis, PSC = primary sclerosing cholangitis, MSI = microsatellite instability, U = unknown, PC = pan-colitis

Supplementary Table 3 – Clinical characteristics of CA-CRC patients used for LP-WGS

	IBD	Disease Extent	Age	Sex	Neoplastic lesion location	Samples sequenced	IBD duration (years)	PSC	MSI
UC23	UC	PC	73	F	Rectum (x3)	- HGD (x2) - LGD (x3)	53	No	No
UC24	UC	PC	42	M	Ascending	- Cancer (T2N0M0)	12	No	No
UC25	UC	PC	71	F	Rectum	- HGD (x3) - LGD	45	Yes	No
UC26	UC	PC	62	M	Rectum (x3)	- LGD (x6)	14	No	No
UC27	UC	PC	62	M	Rectum (x3) Sigmoid Descending	- HGD (x3) - Mixed LGD/HGD - LGD (x6)	16	No	No
UC28	UC	PC	65	M	Ascending (x2) Descending Rectum	- Cancer (T2N0M0) - HGD (x6) - Mixed LGD/HGD (x3) - Pseudopolyp	23	No	No
UC29	UC	PC	49	F	Ascending (x2)	- Cancer (T1N0M0) - LGD (x3)	38	Yes	Yes
UC30	UC	PC	54	M	Rectum	- Cancer (T1N0M0) - LGD (x2)	31	No	No
UC31	UC	PC	78	F	Rectum	- Mixed LGD/HGD	12	No	No
UC32	UC	PC	47	M	Sigmoid Rectum (x2)	- Mixed LGD/HGD (x4) - LGD	20	No	No
UC33	UC	PC	60	F	Rectum	- Mixed LGD/HGD - LGD	29	No	No
UC34	UC	PC	64	M	Sigmoid	- HGD (x2)	20	No	No
UC35	UC	PC	87	M	Caecum Ascending (x3)	- Cancer (T1N0M0) - HGD - LGD (x3)	8	No	No
UC36	UC	PC	63	M	Sigmoid	- HGD (x4)	17	No	No
UC37	UC	PC	26	M	Rectum	- LGD (x3)	9	Yes	No
UC38	UC	PC	50	M	Rectum	- Cancer (x2)	25	No	No
UC39	UC	PC	69	F	Ascending (x3)	- Mixed LGD/HGD (x2) - LGD (x4)	42	No	No
UC40	UC	PC	69	F	Ascending Transverse	- HGD - LGD (x4)	25	Yes	No
UC41	UC	PC	59	M	Sigmoid	- LGD	28	Yes	No

UC = ulcerative colitis, PSC = primary sclerosing cholangitis, MSI = microsatellite instability, PC = pan-colitis

Supplementary Table 4 – Primer sequences

Primer	Sequence (5'→3')
KRAS Forward	GAGTTTGTATTAAAAGGTACTGGTGGGA
KRAS Reverse	ATCAAAGAATGGTCCTGCAC
p53-exon6 Forward	AGAGACGACAGGGCTGGTT
p53-exon6 Reverse	TGGAGGGCCACTGACAAC
p53-exon7 Forward	TGCTTGCCACAGGTCTCC
p53-exon7 Reverse	GGTCAGAGGCAAGCAGAGG
p53-exon8 Forward	TTTTTAAATGGGACAGGTAGGA
p53-exon8 Reverse	CACCCTTGGTCTCCTCCAC
Bat-25 Forward	TCGCCTCCAAGAATGTAAGT
Bat-25 Reverse	TCTGCATTTTAACTATGGCTC
Bat-26 Forward	TGACTACTTTTGACTTCAGCC
Bat-26 Reverse	AACCATTCAACATTTTTAACCC

Supplementary Table 5 – Summary of SNVs and INDELs from WES

	Biopsy	Non synonymous SNVs	SNV frequency (per megabase)	Total INDELs	INDEL frequency (per megabase)
UC01	- Tumour 1	87	2.89	3	0.10
	- Tumour 2	68	2.56	2	0.08
	- Pseudopolyp 1	55	1.79	0	0
	- Pseudopolyp 2	66	2.16	2	0.07
	- Normal mucosa	42	1.37	2	0.07
UC02	- Tumour 1	1017	34.56	81	2.75
	- Tumour 2	1026	39.68	82	3.17
	- Normal mucosa 1	24	0.85	12	0.42
	- Normal mucosa 2	74	2.30	9	0.28
UC03	- Tumour 1	183	6.02	10	0.33
	- Tumour 2	161	5.53	11	0.38
	- Normal mucosa	42	1.63	1	0.04
UC04	- Tumour	70	2.07	5	0.15
UC05	- Tumour 1	118	1.15	14	0.14
	- Tumour 2	120	1.19	12	0.12
	- Normal mucosa	114	1.57	10	0.14
UC06	- Tumour 1	158	5.20	11	0.36
	- Tumour 2	162	5.36	10	0.33
	- Tumour 3	173	5.61	12	0.39
	- Tumour 4	180	5.92	11	0.36
	- HGD	101	3.31	8	0.26
	- LGD	124	3.98	13	0.42
	- Normal mucosa	79	2.59	11	0.36
UC07	- Tumour 1	77	2.44	17	0.54
	- Tumour 2	40	1.63	8	0.33
	- Tumour 3	45	1.60	14	0.50
	- Tumour 4	63	2.13	13	0.44
	- Tumour 5	57	1.99	14	0.49
	- LGD	71	2.23	17	0.53
	- Normal mucosa 1	48	1.61	12	0.40
	- Normal mucosa 2	46	1.43	15	0.47
	- Normal mucosa 3	38	1.25	15	0.49
UC08	- Tumour	80	2.38	5	0.15
UC09	- Tumour	962	28.72	115	3.43
CD01	- Tumour 1	132	4.30	8	0.16
	- Tumour 2	119	3.78	5	0.26
	- Normal mucosa	117	3.82	4	0.13
CD02	- Tumour 1	149	4.89	13	0.43
	- Tumour 2	154	4.73	15	0.46
	- Normal mucosa	25	0.80	7	0.23
CD03	- Tumour 1	80	3.06	9	0.34
	- Tumour 2	97	3.39	10	0.35
	- Normal mucosa	101	3.64	6	0.22

Supplementary Table 7 – Summary of *TP53* variants in CA-CRC

	Biopsy	TP53 variant	VAF(s)
UC01	- Tumour 1 - Tumour 2 - Pseudopolyp 1 - Pseudopolyp 2	- exon8:c.C844T:p.R282W;;exon7:c.G733A:p.G245S; exon7:c.T700C:p.Y234H - exon8:c.C844T:p.R282W;;exon7:c.G733A:p.G245S; exon7:c.T700C:p.Y234H	0.49; 0.42; 0.33 0.32; 0.88; 0.88
UC02	- Tumour 1 - Tumour 2 - Normal mucosa 1 - Normal mucosa 2		
UC03	- Tumour 1 - Tumour 2 - Normal mucosa	- exon7:c.G733C:p.G245R - exon7:c.G733C:p.G245R	0.24 0.47
UC04	- Tumour	- exon7:c.G743A:p.R248Q	0.54
UC05	- Tumour 1 - Tumour 2 - Normal mucosa	- exon7:c.675_676G - exon7:c.675_676G	0.36 0.52
UC06	- Tumour (x4) - HGD - LGD - Normal mucosa	- exon4:c.G202T:p.E68X	0.71, 0.61, 0.67, 0.4 0.45
UC07	- Tumour (x5) - LGD - Normal mucosa 1 - Normal mucosa 2 - Normal mucosa 3	- exon6:c.559+1G>A (splice site) - exon8:c.C916T:p.R306X	0.3, 0.4, 0.5, 0.33, 0.45 0.38
UC08	- Tumour	- exon6:c.376-1G>C (splice site)	0.5
UC09	- Tumour	- exon11:c.1146_1147C; exon7:c.560-2A>G (splice site)	0.2, 0.17
CD01	- Tumour 1 - Tumour 2 - Normal mucosa	- exon6:c.C569T:p.P190L - exon6:c.C569T:p.P190L	0.86 0.92
CD02	- Tumour 1 - Tumour 2 - Normal mucosa	- exon6:c.C569T:p.P190L - exon6:c.C569T:p.P190L	0.27 0.1
CD03	- Tumour 1 - Tumour 2 - Normal mucosa	- exon5:c.G524A:p.R175H - exon5:c.G524A:p.R175H	0.92 0.63

Supplementary table 8 – Functional analysis of putative CA-CRC driver genes

Gene	Gene function	Associated pathways	Cancer association	Description
<i>ARID1A</i>	Chromatin remodelling/transcription	Transcription machinery	Yes	A member of the SWI/SNF family of helicase/ATPases. Regulates gene transcription by altering the chromatin structure.
<i>ASTN2</i>	Neuronal migration	Calcium ion binding	No	Mediates recycling of the neuronal cell adhesion molecule ASTN1 to the anterior pole of the cell membrane in migrating neurons.
<i>CACNA1E</i>	Voltage dependent calcium channel	MAPK signalling, Calcium signalling	Uncertain	Mediates the entry of calcium ions into excitable cells, therefore is involved in a variety of calcium-dependent processes (e.g. gene expression, cell motility, cell division and cell death).
<i>CDC42EP1</i>	Actin cytoskeleton organisation	GTP/Rho binding, actin nucleation, ERK signalling	Uncertain	A CDC42 binding protein that mediates actin cytoskeleton reorganisation at the plasma membrane.
<i>CDH2</i>	Cell-cell adhesion	Cell adhesion molecules	Yes	Encodes N-cadherin (also known as cadherin-2 [CDH2] or neural cadherin [NCAD]), a transmembrane protein that functions to mediate cell-cell adhesion.
<i>CNN2</i>	Cell motility	Actin binding, calmodulin binding	No	Involved in regulating cytoskeleton functions and cell motility.
<i>COL6A3</i>	Structural, collagen	PI3K-Akt signalling Focal adhesion, ECM-receptor interaction	Uncertain	Encodes the alpha-3 chain of type VI collagen, a beaded filament collagen found in most connective tissues.
<i>GUCY1A2</i>	Purine metabolism	Purine metabolism, cGMP-PKG signaling	Uncertain	Catalyses the conversion of GTP to 3',5'-cyclic GMP and pyrophosphate.
<i>GXYLT1</i>	Xylosyltransferase	O-glycan biosynthesis	Uncertain	A glycosyltransferase which elongates the O-linked glucose attached to EGF-like repeats in the extracellular domain of Notch proteins by catalysing the addition of xylose.
<i>PAXIP1</i>	DNA damage response	DNA double strand break repair	Yes	Plays a critical role in maintaining genome stability, condensation of chromatin and progression through mitosis.
<i>POLG</i>	Mitochondrial polymerase	Metabolic pathways, DNA polymerase gamma complex	Yes	The catalytic subunit of the mitochondrial DNA polymerase (DNA polymerase gamma).
<i>PTTG1P</i>	PTTG1-binding membrane protein	RNA transport, receptor activity	No	A membrane protein, which binds to pituitary tumour-transforming 1 protein (PTTG1), and facilitates its translocation into the nucleus, thereby promoting the transcriptional activation of basic fibroblast growth factor.
<i>RP1L1</i>	Differentiation of photoreceptors	Cytoskeleton, microtubule-binding proteins	No	Binds microtubules and regulates microtubule polymerisation in the retina.
<i>SLC25A5</i>	Mitochondrial ATP/ADP transport	Calcium signalling, cellular senescence	No	Encodes adenine nucleotide translocator 2 (ANT2), a major constituent of the mitochondrial permeability-transition pore complex that catalyses the exchange of mitochondrial ATP with cytosolic ADP.
<i>SLC39A11</i>	Cellular zinc transporter	Solute carrier family, metal ion transporter	No	Increases cytosolic zinc concentrations via uptake across the plasma membrane or efflux from intracellular compartments
<i>TAS2R19</i>	Taste receptor/GI sensing	GPCR activity	No	Involved in the perception of salt and bitter tastes. May play a role in sensing the chemical composition of the gastrointestinal content.

Supplementary table 9 – Meta-analysis of putative CA-CRC driver genes

Gene	Mutant cases CA-CRC (n=10) Current study	Mutant cases CA-CRC (n=30) Robles <i>et al</i> , 2016	Mutant cases CA-CRC (n=47) Yaegar <i>et al</i> , 2016	Mutant cases S-CRC (n=189)	Fraction mutant in CA-CRC	Fraction mutant in S-CRC	<i>p</i> value	Adjusted <i>p</i> value (<i>q</i> value)
<i>TP53</i>	8	19	42	110	0.79	0.58	0.0007	0.0048
<i>KRAS</i>	4	6	19	82	0.33	0.43	0.1459	0.1772
<i>APC</i>	4	4	10	141	0.21	0.75	2.48E-17	0.0000
<i>SMAD4</i>	0	4	8	18	0.14	0.10	0.3028	0.3418
<i>TAS2R19</i>	5	0	NR	0	0.13	0.00	0.0001	0.0023
<i>FBXW7</i>	3	2	NR	21	0.13	0.11	0.7859	0.8090
<i>ASTN2</i>	3	2	NR	6	0.13	0.03	0.0263	0.0418
<i>TRRAP</i>	0	3	NR	3	0.10	0.02	0.0190	0.0317
<i>SRRM4</i>	0	3	NR	0	0.10	0.00	0.0008	0.0048
<i>RIMS2</i>	0	4	NR	4	0.10	0.02	0.0332	0.0506
<i>NRG1</i>	0	4	NR	3	0.10	0.02	0.0190	0.0317
<i>IL16</i>	0	4	NR	1	0.10	0.01	0.0036	0.0125
<i>DOCK3</i>	0	4	NR	0	0.10	0.00	0.0008	0.0048
<i>COL6A3</i>	4	0	NR	12	0.10	0.06	0.4910	0.5208
<i>CNN2</i>	4	0	NR	0	0.10	0.00	0.0008	0.0048
<i>CACNA1E</i>	3	1	NR	2	0.10	0.01	0.0093	0.0218
<i>ARID1A</i>	3	1	NR	9	0.10	0.05	0.2501	0.2918
<i>PIK3CA</i>	2	3	3	25	0.09	0.13	0.4260	0.4660
<i>SLC39A11</i>	3	0	NR	0	0.08	0.00	0.0050	0.0125
<i>SLC25A5</i>	3	0	NR	0	0.08	0.00	0.0050	0.0125
<i>RRBP1</i>	0	3	NR	0	0.08	0.00	0.0050	0.0125
<i>RP1L1</i>	3	0	NR	4	0.08	0.02	0.1042	0.1351
<i>RADIL</i>	0	3	NR	0	0.08	0.00	0.0050	0.0125
<i>PTTG1IP</i>	3	0	NR	0	0.08	0.00	0.0050	0.0125
<i>POLG</i>	3	0	NR	1	0.08	0.01	0.0175	0.0317
<i>PAXIP1</i>	3	0	NR	0	0.08	0.00	0.0050	0.0125
<i>GXYLT1</i>	3	0	NR	1	0.08	0.01	0.0175	0.0317
<i>GUCY1A2</i>	3	0	NR	3	0.08	0.02	0.0677	0.0911
<i>EP300</i>	0	3	NR	2	0.08	0.01	0.0385	0.0539
<i>CDH2</i>	3	0	NR	5	0.08	0.03	0.1468	0.1772
<i>CDC42EP1</i>	3	0	NR	2	0.08	0.01	0.0385	0.0539
<i>CACNA1D</i>	0	3	NR	1	0.08	0.01	0.0175	0.0317
<i>IDH1</i>	0	0	5	0	0.06	0.00	0.0029	0.0125
<i>BRAF</i>	0	1	1	5	0.02	0.03	1.0000	1.0000
<i>NRAS</i>	1	0	0	17	0.01	0.09	0.0157	0.0317

NR = not reported

Supplementary table 11 - Copy number validation by FISH

Sample	Chr	1	2	3	4	5	6	7	CN by WES
CD01	8	3 (2%)	11 (8%)	41 (31%)	20 (15%)	48 (36%)	8 (6%)	1 (1%)	3
CD01	18	15 (15%)	22 (21%)	36 (35%)	28 (27%)	2 (2%)	-	-	2
CD02	8	7 (7%)	16 (17%)	38 (40%)	35 (36%)	-	-	-	4
CD03	5	-	-	1 (1%)	40 (38%)	55 (53%)	8 (8%)	-	4 / 5
CD03	8	-	17 (14%)	46 (39%)	44 (37%)	11 (9%)	-	-	4
UC02	8	-	18 (18%)	83 (81%)	1 (1%)	-	-	-	3
UC05	8	-	25 (71%)	10 (29%)	-	-	-	-	2
UC06	5	-	9 (8%)	29 (27%)	17 (16%)	47 (44%)	4 (4%)	-	4 / 5
UC06	8	-	1 (1%)	13 (13%)	72 (72%)	5 (5%)	6 (6%)	3 (3%)	3 / 4
UC06	18	4 (4%)	30 (34%)	51 (58%)	3 (3%)	-	-	-	2 / 3
UC07	5	-	16 (19%)	66 (79%)	1 (1%)	1 (1%)	-	-	3
UC07	8	16 (16%)	84 (84%)	-	-	-	-	-	2 / 3
UC07	18	29 (30%)	57 (59%)	10 (10%)	1 (1%)	-	-	-	2 / 3
UC10	8	-	53 (85%)	9 (15%)	-	-	-	-	2
UC10	18	58 (59%)	39 (40%)	1 (1%)	-	-	-	-	1

Supplementary table 12 – Copy number analysis of colorectal cancer driver genes

Gene	ARID1A		CTNNB1		PIK3CA		FBXW7		APC		KRAS		TP53		ERBB2	
Locus	1p36.11		3p22.1		3q26.32		4q.31.3		5q22.2		12p12.1		17p13.1		17q12	
Allele	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
CD01_C1	2	0	1	1	1	1	1	1	1	1	20	0	2	0	2	0
CD01_C2	2	0	2	1	1	1	1	1	1	1	8	0	2	0	2	0
CD02_C1	1	0	2	0	2	0	1	1	1	1	2	1	2	1	2	1
CD02_C2	1	0	1	0	1	0	1	1	1	1	2	1	2	1	2	1
CD03_C1	1	1	1	1	2	0	1	0	1	0	2	0	2	0	2	0
CD03_C2	1	1	1	1	2	0	1	0	1	0	2	0	2	0	2	0
UC01_C1	2	2	1	1	4	1	2	0	1	1	2	2	1	1	1	1
UC01_C1	2	1	1	0	3	1	2	1	1	1	2	1	1	1	1	1
UC03_C1	2	0	1	0	2	0	2	0	2	1	2	0	1	1	1	1
UC03_C1	1	0	2	0	1	1	3	0	2	1	2	1	1	1	1	1
UC04_C	1	1	2	0	2	1	2	1	2	2	2	1	1	0	2	1
UC05_C1	1	1	2	0	1	1	2	1	1	1	1	1	1	0	2	0
UC05_C2	1	1	3	0	2	1	2	1	1	1	1	1	1	0	2	0
UC06_C1	2	0	2	2	2	1	1	1	2	0	2	2	2	0	2	0
UC06_C2	2	0	2	2	2	1	1	1	1	0	2	1	2	0	2	0
UC06_C3	2	0	2	2	2	1	1	1	1	0	2	1	2	0	2	0
UC06_C4	2	0	2	2	2	1	1	1	1	0	2	1	2	0	2	0
UC07_C1	1	1	2	1	2	1	1	1	1	1	1	1	2	0	2	0
UC07_C2	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1
UC07_C3	1	1	2	1	2	1	1	1	1	1	1	1	2	0	2	0
UC07_C4	1	1	2	1	2	1	1	1	1	1	1	1	2	0	2	0
UC07_C5	1	1	2	1	2	1	1	1	1	1	1	1	2	0	2	0
UC08_C	2	1	2	2	2	2	2	1	2	0	3	2	2	0	2	0
UC10_C1	1	0	1	1	1	1	1	0	1	0	1	1	1	0	1	0
UC10_C2	1	0	1	1	1	1	1	0	1	0	1	1	1	0	1	0
UC11_C	1	0	1	1	0	0	0	1	0	1	3	1	3	1	1	1
UC12_C	1	1	1	1	1	1	1	1	2	0	1	1	2	2	1	1
UC14_C	2	1	2	2	2	2	1	0	1	0	1	1	1	1	1	1
UC17_C	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
UC18_C	12	8	2	2	2	2	2	0	1	1	2	0	2	2	2	2
UC19_C	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1
UC20_C	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
UC21_C	1	0	3	1	2	2	4	0	2	1	2	0	2	2	2	2
UC22_C	0	1	1	1	1	1	1	1	1	0	1	1	2	2	2	2

Supplementary Table 13 – CNA frequency in CA-CRC vs. S-CRC

	Fraction in CA-CRC	Fraction in S-CRC	OR	Fisher's Test <i>p</i> value	Adjusted <i>p</i> (<i>q</i> value)
Gain on 1p	0.097	0.030	3.437	0.063	0.174
Loss on 1p	0.274	0.190	1.607	0.211	0.445
Gain on 1q	0.384	0.170	2.892	0.005	0.027
Loss on 1q	0.039	0.100	0.469	0.395	0.701
Gain on 2p	0.178	0.080	2.375	0.077	0.201
Loss on 2p	0.109	0.030	3.437	0.063	0.174
Gain on 2q	0.121	0.100	1.268	0.585	0.801
Loss on 2q	0.150	0.030	5.442	0.005	0.027
Gain on 3p	0.182	0.060	3.402	0.017	0.061
Loss on 3p	0.132	0.090	1.451	0.558	0.777
Gain on 3q	0.107	0.100	0.987	1.000	1.000
Loss on 3q	0.051	0.050	0.988	1.000	1.000
Gain on 4p	0.034	0.010	2.164	0.441	0.717
Loss on 4p	0.554	0.250	3.666	0.000	0.005
Gain on 4q	0.066	0.040	1.997	0.394	0.701
Loss on 4q	0.514	0.240	3.459	0.000	0.008
Gain on 5p	0.428	0.140	4.506	0.000	0.003
Loss on 5p	0.077	0.100	0.721	0.779	0.964
Gain on 5q	0.040	0.070	0.700	1.000	1.000
Loss on 5q	0.547	0.170	5.869	0.000	0.000
Gain on 6p	0.371	0.140	3.662	0.001	0.011
Loss on 6p	0.073	0.070	1.076	1.000	1.000
Gain on 6q	0.290	0.140	2.620	0.019	0.063
Loss on 6q	0.151	0.100	1.565	0.408	0.707
Gain on 7p	0.456	0.470	0.920	0.866	1.000
Loss on 7p	0.045	0.010	4.421	0.136	0.303
Gain on 7q	0.400	0.410	0.965	1.000	1.000
Loss on 7q	0.060	0.010	4.421	0.136	0.303
Gain on 8p	0.301	0.280	1.101	0.851	1.000
Loss on 8p	0.271	0.500	0.380	0.010	0.041
Gain on 8q	0.459	0.460	0.964	1.000	1.000
Loss on 8q	0.001	0.120	0.000	0.012	0.047
Gain on 9p	0.296	0.180	1.961	0.086	0.217
Loss on 9p	0.096	0.080	1.248	0.758	0.964
Gain on 9q	0.275	0.150	2.114	0.068	0.182
Loss on 9q	0.063	0.090	0.825	1.000	1.000
Gain on 10p	0.218	0.050	5.400	0.001	0.011
Loss on 10p	0.154	0.090	1.791	0.250	0.476
Gain on 10q	0.129	0.020	7.118	0.005	0.027
Loss on 10q	0.211	0.130	1.694	0.222	0.456
Gain on 11p	0.141	0.090	1.791	0.250	0.476
Loss on 11p	0.144	0.090	1.791	0.250	0.476
Gain on 11q	0.088	0.070	1.473	0.514	0.743
Loss on 11q	0.361	0.110	4.373	0.000	0.005
Gain on 12p	0.175	0.210	0.798	0.680	0.899
Loss on 12p	0.230	0.090	2.939	0.023	0.073
Gain on 12q	0.132	0.180	0.656	0.503	0.743
Loss on 12q	0.240	0.070	4.393	0.001	0.014
Gain on 13q	0.625	0.560	1.307	0.495	0.743
Loss on 13q	0.019	0.040	0.634	1.000	1.000
Gain on 14q	0.090	0.050	2.079	0.261	0.485
Loss on 14q	0.284	0.300	0.887	0.853	1.000
Gain on 15q	0.011	0.020	0.000	1.000	1.000
Loss on 15q	0.438	0.320	1.743	0.109	0.265
Gain on 16p	0.232	0.180	1.330	0.512	0.743
Loss on 16p	0.181	0.050	3.954	0.010	0.041
Gain on 16q	0.165	0.180	0.973	1.000	1.000
Loss on 16q	0.149	0.060	2.834	0.047	0.141
Gain on 17p	0.036	0.050	0.482	0.702	0.912
Loss on 17p	0.564	0.560	1.061	1.000	1.000
Gain on 17q	0.109	0.120	0.811	1.000	1.000
Loss on 17q	0.374	0.150	3.336	0.002	0.014
Gain on 18p	0.110	0.090	1.130	0.770	0.964
Loss on 18p	0.356	0.610	0.344	0.003	0.024
Gain on 18q	0.014	0.010	2.164	0.441	0.717
Loss on 18q	0.611	0.660	0.768	0.477	0.743
Gain on 19p	0.153	0.110	1.441	0.428	0.717
Loss on 19p	0.165	0.040	5.193	0.003	0.024
Gain on 19q	0.321	0.150	2.680	0.013	0.047
Loss on 19q	0.087	0.050	1.519	0.461	0.733
Gain on 20p	0.447	0.580	0.594	0.128	0.302
Loss on 20p	0.110	0.320	0.238	0.004	0.026
Gain on 20q	0.815	0.720	1.831	0.183	0.396
Loss on 20q	0.005	0.150	0.000	0.004	0.026
Gain on 21q	0.104	0.020	5.547	0.022	0.070
Loss on 21q	0.283	0.220	1.330	0.544	0.771
Gain on 22q	0.048	0.030	1.635	0.629	0.846
Loss on 22q	0.477	0.260	2.557	0.008	0.038

Supplementary Table 14 – CNAs linear regression by grade

Grade	Coefficient	Lower 95% CI	Upper 95% CI
LGD	0.1319026	-0.002374498	0.2661796
U	0.2043117	0.027711592	0.3809118
HGD	0.3656963	0.213739674	0.5176529
CA-CRC	0.4353876	0.299164891	0.5716103