

Table 1. Characteristics of gastric cancer patients

Characteristic		% (No.)
Age	Mean age (SD)	65.1 (11.8)
Gender	Female	35 (34)
	Male	65 (64)
Histology	Diff	49 (48)
	Undiff	51 (50)
Stage	IA/IB	18 (18)
	IIA/IIB	30 (29)
	IIIA/IIIB/IIIC	38 (37)
	IV	14 (14)
T	T1a/1b	14 (14)
	T2	14 (14)
	T3	28 (27)
	T4a/4b	44 (43)
N	N0	27 (26)
	N1	35 (34)
	N2	24 (24)
	N3	14 (14)
Distant Metastasis	Negative	86 (84)
	Positive	14 (14)
MSI	MSI	13 (13)
	Non-MSI	87 (85)
<i>LOH Ratio</i>	Mean Ratio (SD)	0.24 (0.3)
CIN	Positive	51 (50)
	Negative	47 (46)
	Not-informative	2 (2)
<i>KRAS</i>	Mutant	5 (5)
	Wild	95 (93)
<i>BRAF</i>	Mutant	0 (0)
	Wild	100 (98)
<i>PIK3CA</i>	Mutant	4 (3)
	Wild	96 (94)
H.pyroli	Positive	71 (70)
	Negative	29 (28)

Supplementary Table 2. Primer Sequences

Gene Name	Primer* (5' to 3')	Temperature (cycles)	product size (Restriction enzyme)	
COBRA				
DCC	F; AAGGTGTTGGTTGAAATATGGAGAA R; AAAAACCACCTTACCRATTACTTAAAAA	56 (5), 54 (10), 52 (30)	121 (<i>Hha</i> I)	
UNC5C	F; TTTAGTGGGGTTTTTAGTTGTTTG R; TATCCCAATCCCAATCCRCAAC	56 (5), 54 (10), 52 (30)	125 (<i>Hha</i> I)	
RT-PCR				
DCC	F; ACGAGGCGAGGAAGTCATCCAAC R; TGGGCATTTCCAGCCTCATTTTC	55 (35)	Reference 31	
UNC5C-All	F; AACTTCCGGTCTCATTGTCC R; TTTTCAACCATTCCACCTCAG	55 (35)	272	
UNC5C-001-004	F; TGCAAATGCTCGTGCTACCT R; TGTGGTCTTCTGATGAACCC	55 (35)	258	
UNC5C-002 specific	F; GTACCACAAAGAGCCGGAAG R; ATCTTGAGCCCGCTGTTTCT	55 (35)	351	
UNC5C-003 specific	F; TCAACTGAACAGAGAACCAGAG R; TCAGTGCACCAGAAAAAGCA	55 (35)	692	
UNC5C-004 specific	F; TCAACTGAACAGAGAACCAGAG R; CAGGGGTCAAAAGTGTCTGAG	55 (35)	703	
β-actin	F; TCACCATGGATGATGATATCGCC R; CCACACGCAGCTCATTGTAGAAGG	55 (35)	282	
LOH analysis				
D18S35	F; AGCTAGATTTTTACTTCTCTG R; CTGTTGTACATGCCTGAC	55 (35)	104	
DCC	D18S64	F; TTTTGCCACAAAAATTACCAA R; TGCACAGGAAGTTGCAAAGA	55 (35)	201
	D18S69	F; AGCAGTCTGGAAATCCTCTTTC R; GGTGGGATGCGTGAATTTTA	55 (35)	153
	D4S1559	F; CAGCCAAAGGTGAATCAGA R; GCGTTGAAACCATCCACA	55 (35)	259-269
UNC5C	D4S2380	F; ACCTTATTGTGCTATGGAAACA R; TCAGCCAAGATTACCTACCG	55 (35)	195
	D4S470	F; ACCAGGAGGGTCCTAATTCA R; CCTAGCTCCAGGGAATTTGT	55 (35)	146
Helicobacter pylori				
cagA	F; CKCTCRCCAAAAATTTTTCGGA R; TTTAGCAACTTGAGYRTAAATGGG	60 (45)	261, 159	

Supplementary Table 1. Association between alterations in netrin-1 receptors and clinicopathological features in gastric cancer

		Alteration in Netrin-1 Receptors - % (No.)			P
		Neither (n=15)	Either (n=22)	Both Receptors (n=29)	
Age	Mean age (SD)	64.9 (11.9)	63.5 (12.3)	67.9 (9.6)	0.37 ^a
Gender	Female	40 (6)	27 (6)	28 (8)	0.65 ^b
	Male	60 (9)	73 (16)	72 (21)	
Histology	Diff	33 (5)	64 (14)	45 (13)	0.17 ^b
	Undiff	67 (10)	36 (8)	55 (16)	
Stage	IA/IB	27 (4)	27 (6)	3 (1)	0.006^c
	IIA/IIB	20 (3)	55 (12)	24 (7)	
	IIIA/IIIB/IIIC	33 (5)	18 (4)	48 (14)	
	IV	20 (3)	0 (0)	24 (7)	
T	T1a/1b	13 (2)	27 (6)	3 (1)	0.017^b
	T2	13 (2)	27 (6)	7 (2)	
	T3	13 (2)	27 (6)	40 (11)	
	T4a/4b	60 (9)	18 (4)	52 (15)	
N	N0	40 (6)	36 (8)	10 (3)	0.01^d
	N1	33 (5)	36 (8)	24 (7)	
	N2	20 (3)	23 (5)	38 (11)	
	N3	7 (1)	5 (1)	28 (8)	
Distant Metastasis	Negative	80 (12)	100 (22)	76 (22)	0.05^b
	Positive	20 (3)	0 (0)	24 (7)	
MSI	MSI	7 (1)	9 (2)	7 (2)	0.95 ^b
	MSS	93 (14)	91 (20)	93 (27)	
LOH Ratio	Mean Ratio (SD)	0.01 (0.04)	0.17 (0.25)	0.37 (0.31)	< 0.0001^a
CIN*	Positive (n=33)	7 (1)	50 (10)	76 (22)	< 0.0001^b
	Negative (n=31)	93 (14)	50 (10)	24 (7)	
KRAS/BRAF/PIK3CA	Mutant	0 (0)	5 (1)	7 (2)	0.58 ^b
	Wild	100 (15)	95 (21)	93 (27)	
H.pyroli	Positive	53 (8)	73 (16)	76 (22)	0.28 ^b
	Negative	47(7)	27 (6)	24 (7)	

* 2 cases are not informative of CIN status

a P values were calculated by Wilcoxon/Kruskal–Wallis test

b P values were calculated by Pearson's chi-square test

c P value was calculated between Stage I/II vs III/IV by Pearson's chi-square test

d Pvalue was calculated between N0 vsN1-3 by Pearson's chi-square test

Table 3. Association between epigenetic/genetic alterations of the UNC5C gene and clinicopathological features in gastric cancers.

		UNC5 Methylation Status - % (No.)			4q LOH Status - % (No.)				UNC5C Alteration Status - % (No.)						
		Unmethylation	Methylation	P	Not-informative	Negative	Positive	P	Not-informative	Negative	Positive Total	Positive			P
		(n=67)	(n=31)									(n=19)	(n=56)	(n=23)	
		(n=67)	(n=31)		(n=19)	(n=56)	(n=23)		(n=19)	(n=39)	(n=40)	(n=17)	(N=13)	(N=10)	
Age	Mean age (SD)	64.3 (12.6)	66.7 (9.7)	0.49 ^a	60.2 (12.6)	65.4 (12.3)	68.3 (8.2)	0.42 ^a	60.2 (12.6)	64.8 (13.3)	67.8 (8.9)	67.0 (10.0)	67.2 (8.3)	69.8 (8.2)	0.36 ^a
Gender	Female	36 (24)	32 (10)	0.73 ^b	47 (9)	36 (20)	22 (5)	0.23 ^b	47 (9)	33 (13)	30 (12)	41 (7)	38 (5)	0 (0)	0.75 ^b
	Male	64 (43)	68 (21)		53 (10)	64 (36)	78 (18)		53 (10)	67 (26)	70 (28)	59 (10)	62 (8)	100 (10)	
Histology	Diff	48 (32)	52 (16)	0.72 ^b	58 (11)	39 (22)	65 (15)	0.036^b	58 (11)	41 (16)	52 (21)	35 (6)	54 (7)	80 (8)	0.31 ^b
	Undiff	520(35)	48 (15)		42 (8)	61 (34)	35 (8)		42 (8)	59 (23)	48 (19)	65 (11)	46 (6)	20 (2)	
Stage	IA/IB	22 (15)	10 (3)	0.17 ^b	26 (5)	21 (12)	4 (1)	0.29 ^b	26 (5)	28 (11)	5 (2)	6 (1)	8 (1)	0 (0)	0.03^b
	IIA/IIB	33 (22)	23 (7)		21 (4)	29 (16)	39 (9)		21 (4)	33 (13)	30 (12)	18 (3)	38 (5)	40 (4)	
	IIIA/IIIB/IIIC	31 (21)	52 (16)		37 (7)	38 (21)	39 (9)		37 (7)	28 (11)	48 (19)	59 (10)	31 (4)	50 (5)	
	IV	13 (9)	16 (5)		16 (3)	13 (7)	17 (4)		16 (3)	10 (4)	18 (7)	18 (3)	23 (3)	10 (1)	
T	T1a/1b	18 (12)	6 (2)	0.20 ^b	21 (4)	16 (9)	4 (1)	0.49 ^b	21 (4)	21 (8)	5 (2)	6 (1)	8 (1)	0 (0)	0.15 ^b
	T2	16 (11)	10 (3)		11 (2)	14 (8)	17 (4)		11 (2)	18 (7)	13 (5)	6 (1)	15 (2)	20 (2)	
	T3	22 (15)	39 (12)		26 (5)	25(14)	35 (8)		26 (5)	23 (9)	33 (13)	29 (5)	23 (3)	50 (5)	
	T4a/4b	43 (29)	45 (14)		42 (8)	45 (25)	43 (10)		42 (8)	38 (15)	50 (20)	59 (10)	54 (7)	30 (3)	
N	N0	31 (21)	16 (5)	0.06 ^b	32 (6)	32 (18)	9 (2)	0.19 ^b	32 (6)	38 (15)	13 (5)	18 (3)	15 (2)	0 (0)	0.03^b
	N1	39 (26)	26 (8)		42 (8)	30 (17)	39 (9)		42 (8)	33 (13)	33 (13)	24 (4)	38 (5)	40 (4)	
	N2	19 (13)	35 (11)		11 (2)	25 (14)	38 (8)		11 (2)	21 (8)	35 (14)	35 (6)	31 (4)	40 (4)	
	N3	10 (7)	23 (7)		16 (3)	13 (7)	17 (4)		16 (3)	8 (3)	20 (8)	24 (4)	15 (2)	20 (2)	
Distant Metastasis	Negative	87 (58)	84 (26)	0.72 ^b	84 (16)	88 (49)	83 (19)	0.57 ^b	84 (16)	90 (35)	39	94 (16)	100 (13)	100 (10)	0.35 ^b
	Positive	13 (9)	16 (5)		16 (3)	13 (7)	17 (4)		16 (3)	10 (4)	0	6 (1)	0 (0)	0 (0)	
MSI	MSI	7 (5)	26 (8)	0.013^b	21 (4)	14 (8)	4 (1)	0.21 ^b	21 (4)	10 (4)	5	24 (4)	0 (0)	10 (1)	0.75 ^b
	Non-MSI	93 (62)	74 (23)		79 (15)	86 (48)	96 (22)		79 (15)	90 (35)	35	76 (13)	100 (13)	90 (9)	
LOH Ratio	Mean Ratio (SD)	0.21 (0.28)	0.31 (0.35)	0.19 ^a	0.32 (0.36)	0.15 (0.25)	0.40 (0.29)	< .0001 ^a	0.32 (0.36)	0.11 (0.22)	0.33 (0.30)	0.24 (0.29)	0.37 (0.25)	0.45 (0.36)	0.0001^a
CIN*	Positive	49 (32)	58 (18)	0.42 ^b	58 (11)	37 (20)	83 (19)	0.0003^b	58 (11)	30 (11)	28	53 (9)	85 (11)	80 (8)	0.004^b
	Negative	51 (33)	42 (13)		42 (8)	63 (34)	17 (4)		42 (8)	70 (26)	12	47 (8)	15 (2)	20 (2)	
KRAS/BRAF/PIK3CA	Mutant	6 (4)	13 (4)	0.24 ^b	5 (1)	13 (7)	0 (0)	0.08 ^b	5 (1)	8 (3)	4	24 (4)	0 (0)	0 (0)	0.72 ^b
	Wild	94 (63)	87 (27)		95 (18)	88 (49)	100 (23)		95 (18)	92 (36)	36	76 (13)	100 (13)	100 (10)	
H.pyroli	Positive	72 (48)	71 (22)	0.95 ^b	68 (13)	70 (39)	78 (18)	0.44 ^b	68 (13)	67 (26)	9	24 (4)	15 (2)	30 (3)	0.28 ^b
	Negative	28 (19)	29 (9)		32 (6)	30 (17)	22 (5)		32 (6)	33 (13)	31	76 (13)	85 (11)	70 (7)	

* 2 cases are not informative of CIN status

a P value were calculated between unmethylation and methylation, 4qLOH negative and positive, and UNC5C alteration negative and positive(total) by Wilcoxon/Kruskal-Wallis test

b P values were calculated by Pearson's chi-square test

Table 2. Association between epigenetic/genetic alterations of the DCC gene and clinicopathological features in gastric cancers.

		DCC Methylation Status - % (No.)			18q LOH Status - % (No.)				DCC Alteration Status - % (No.)						
		Unmethylation	Methylation	P	Not-informative	Negative	Positive	P*	Not-informative	Negative	Positive Total	Positive			P**
		(n=54)	(n=44)									(n=15)	(n=47)	(n=36)	
												(n=22)	(n=19)	(n=17)	
Age	Mean age (SD)	63.6 (12.5)	67.0 (10.7)	0.48 ^a	68.9 (11.4)	64.8 (11.4)	63.9 (12.4)	0.76 ^a	68.9 (11.4)	63.5 (12.9)	64.8 (11.3)	66.3 (9.5)	60.7 (12.7)	67.4 (11.4)	0.98 ^a
Gender	Female	39 (21)	30 (13)	0.33 ^b	40 (6)	38 (18)	28 (10)	0.32 ^b	40 (6)	44 (11)	29 (17)	32 (7)	32 (6)	24 (4)	0.19 ^b
	Male	61 (23)	70 (31)		60 (9)	62 (29)	72 (26)		60 (9)	56 (14)	71 (41)	68 (15)	68 (13)	76 (13)	
Histology	Diff	41 (22)	59 (26)	0.071 ^b	47 (7)	55 (26)	42 (15)	0.22 ^b	47 (7)	52 (13)	48 (28)	59 (13)	32 (6)	53 (9)	0.76 ^b
	Undiff	59 (32)	41 (18)		53 (8)	45 (21)	58 (21)		53 (8)	48 (12)	52 (30)	41 (9)	68 (13)	47 (8)	
Stage	IA/IB	20 (11)	16 (7)	0.83 ^b	13 (2)	19 (9)	19 (7)	0.15 ^b	13 (2)	24 (6)	17 (10)	14 (3)	21 (4)	18 (3)	0.70 ^b
	IIA/IIB	26 (14)	34 (15)		27 (4)	30 (14)	31 (11)		27 (4)	24 (6)	33 (19)	36 (8)	32 (6)	29 (5)	
	IIIA/IIIB/IIC	39 (21)	36 (16)		53 (8)	43 (20)	25 (9)		53 (8)	40 (10)	33 (19)	45 (10)	26 (5)	24 (4)	
	IV	15 (8)	14 (6)		7 (1)	9 (4)	25 (9)		7 (1)	12 (3)	17 (10)	5 (1)	21 (4)	29 (5)	
T	T1a/1b	15 (8)	14 (6)	0.24 ^b	7 (1)	17 (8)	14 (5)	0.94 ^b	7 (1)	16 (4)	16 (9)	18 (4)	21 (4)	6 (1)	0.54 ^b
	T2	13 (7)	16 (7)		13 (2)	15 (7)	14 (5)		13 (2)	16 (4)	14 (8)	14 (3)	11 (2)	18 (3)	
	T3	20 (11)	36 (16)		33 (5)	28 (13)	25 (9)		33 (5)	16 (4)	31 (18)	41 (9)	16 (3)	35 (6)	
	T4a/b	52 (28)	34 (15)		47 (7)	40 (19)	47 (17)		47 (7)	52 (13)	40 (23)	27 (6)	53 (10)	41 (7)	
N	N0	30 (16)	23 (10)	0.66 ^b	20 (3)	28 (13)	28 (10)	0.29 ^b	20 (3)	32 (8)	26 (15)	23 (5)	32 (6)	24 (4)	0.19 ^b
	N1	37 (20)	32 (14)		47 (7)	38 (18)	25 (9)		47 (7)	44 (11)	28 (16)	32 (7)	26 (5)	24 (4)	
	N2	20 (11)	30 (13)		20 (3)	26 (12)	25 (9)		20 (3)	20 (5)	28 (16)	32 (7)	21 (4)	29 (5)	
	N3	13 (7)	16 (7)		13 (2)	9 (4)	22 (8)		13 (2)	4 (1)	19 (11)	14 (3)	21 (4)	24 (4)	
Distant Metastasis	Negative	85 (46)	86 (38)	0.87 ^b	93 (14)	91 (43)	75 (27)	0.041^b	93 (14)	88 (22)	83 (48)	95 (21)	79 (15)	71 (12)	0.55 ^b
	Positive	15 (8)	14 (6)		7 (1)	9 (4)	25 (9)		7 (1)	12 (3)	17 (10)	5 (1)	21 (4)	29 (5)	
MSI Status	MSI	6 (3)	23 (10)	0.013^b	33 (5)	9 (4)	11 (4)	0.69 ^b	33 (5)	4 (1)	12 (7)	14 (3)	0 (0)	24 (4)	0.25 ^b
	Non-MSI	94 (51)	77 (34)		67 (10)	91 (43)	89 (32)		67 (10)	96 (24)	88 (51)	86 (19)	100 (19)	76 (13)	
LOH Ratio	Mean Ratio (SD)	0.23 (0.30)	0.26 (0.31)	0.55 ^a	0.22 (0.29)	0.10 (0.15)	0.44 (0.36)	< .0001 ^a	0.22 (0.29)	0.05 (0.10)	0.33 (0.33)	0.16 (0.18)	0.44 (0.34)	0.44 (0.39)	< .0001 ^a
CIN*	Positive	46 (25)	57 (25)	0.39 ^b	47 (7)	38 (18)	74 (25)	0.0017^b	47 (7)	24 (6)	66 (37)	55 (12)	76 (13)	71 (12)	0.0005^b
	Negative	54 (27)	43 (19)		53 (8)	62 (29)	26 (9)		53 (8)	76 (19)	34 (19)	45 (10)	24 (4)	29 (5)	
RAS/BRAF/PIK3C	Mutant	6 (3)	11 (5)	0.30 ^b	27 (4)	6 (3)	3 (1)	0.45 ^b	27 (4)	4 (1)	5 (3)	9 (2)	5 (1)	0 (0)	0.82 ^b
	Wild	94 (51)	89 (38)		73 (11)	94 (44)	97 (35)		73 (11)	96 (24)	95 (55)	91 (20)	95 (18)	100 (17)	
H.pyroli	Positive	72 (39)	70 (31)	0.85 ^b	80 (12)	66 (31)	75 (27)	0.37 ^b	80 (12)	60 (15)	74 (43)	73 (16)	79 (15)	71 (12)	0.20 ^b
	Negative	28 (15)	30 (13)		20 (3)	34 (16)	25 (9)		20 (3)	40 (10)	26 (15)	27 (6)	21 (4)	29 (5)	

* 2 cases are not informative of CIN status

a P value were calculated between unmethylation and methylation, 18qLOH negative and positive, and DCCalteration negative and positive(total) by Wilcoxon/Kruskal–Wallis test

b P values were calculated between unmethylation and methylation, 18qLOH negative and positive, and DCCalteration negative and positive(total) by Pison's chi-square test