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# Original article

# Genetic variants in the WNT signaling pathway are protectively associated with colorectal cancer in a Saudi population



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# ABSTRACT

The Wnt/ $\beta$ -catenin signaling pathway has been etiologically implicated in the development and progression of colorectal cancer. We studied thirteen single nucleotide polymorphisms (SNPs) located in SFRP3 (rs7775), CTNNB1 ( $\beta$ -catenin) [rs4135385, rs13072632], APC (rs454886, rs459552), LRP6 (rs2075241, rs2284396), DKK4 (rs3763511), DKK3 (rs6485350), TCF4 (rs12255372) and AXIN2 (rs3923086, rs3923087, rs4791171) in patients with colorectal cancer (n = 122) and controls (n = 110). Evaluation of WNT pathway SNPs showed protective association for rs4135385, located in  $\beta$ -catenin. Additionally, variants in SFRP3 (rs7775) and LRP6 (rs2284396) which did not show any association in the overall analysis were significantly associated with female and old aged colorectal cancer patients, respectively. © 2018 The Authors. Production and hosting by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

# 1. Introduction

Colorectal cancer (CRC) is the second most common cause of cancer related mortalities in Saudi Arabia, and the incidence is rising since past decade. Accumulated evidence in the past three decades suggests WNT signaling pathway genes to be mutated in very high proportion of sporadic colorectal tumors. Wnt ligands are a family of 19 glycoproteins which have a key role in early development and tissue homeostasis. Any changes in WNT signaling genes may cause disease including colorectal cancer (Mao et al., 2001; Segditsas and Tomlinson, 2006). The possible role of WNT genes in cancer has been reported few decades ago in mouse models. Variation in expression levels of WNT1 lead to tumor formation in transgenic mice (Nusse et al., 1984). Further studies reported that WNT genes promoted stabilization of  $\beta$ -catenin and  $\beta$ -catenin dependent transcription. Axin, APC and GSK3 $\beta$  forms

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β-catenin destruction complex. Canonical WNT pathway activity is dependent on this complex, which eradicates newly formed β-catenin protein through the ubiquitin–proteasome pathway in the off-state when WNT ligands are not bound to its receptors frizzled and LRP5/6 (Benham-Pyle et al., 2016). In the on-state, WNT ligands bind to its receptors resulting in cytoplasmic accumulation of β-catenin which than translocates into the nucleus leading to formation of a complex with TCF/LEF family of transcription factors. This complex formation drives transcriptional activation of genes involved in cell proliferation such as c-Myc and Cyclin D (Clevers, 2006).

The high rate of WNT pathway genes mutations in various cancers emphasizes the significance of WNT/ $\beta$ -catenin signaling pathway in cancer progression. Apart from APC that has been reported to play crucial role in colorectal cancer progression, The Cancer Genome Atlas Network has reported the involvement of several other WNT pathway genes (Anastas and Moon, 2013). Although mutations in genes such as FZD4, LRP5 and LRP6 that obstruct WNT signaling have been recognized in other diseases, similar WNT-pathway inactivating mutations have not been identified in cancer (Anastas and Moon, 2013). Most of the WNT pathway gene mutations reported in cancer are found to result in hyperactivation of WNT pathway.  $\beta$ -catenin missense and other mutations are very common in hepatocellular carcinoma and ovarian cancer, whereas deletions and truncation mutations in *AXIN1* are commonly

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observed in hepatocellular carcinoma and colorectal cancers (Giles et al., 2003;Anastas and Moon, 2013). Thus, in light of the previous reports that provide compelling evidence of the involvement of Wnt signaling pathway in the progression of colorectal cancer, we in the present study evaluated the association of SNPs in WNT signaling pathway genes with susceptibility to colorectal cancer in Saudi population. We investigated 13 germline polymorphisms in 8 genes involved in the Wnt signaling pathway to evaluate their risk association in patients with colorectal cancer.

### 2. Materials and methods

## 2.1. Study population

This study was approved by ethical review committee of King Khalid University Hospital, Riyadh, Saudi Arabia and written informed consent was obtained from all participants. The samples comprised of 122 colorectal cancer patients (age 18–82 years, mean age 57 years). Additionally, 110 gender and age matched non-cancer samples were recruited as controls in the present study. 5 ml blood was collected from patients and healthy individuals. Histology and TNM staging were analyzed to verify the diagnosis. Demographic information for the colorectal cancer and control subjects are presented in Table 1.

#### 2.2. Genotyping

The DNA was isolated from colorectal cancer patients and control blood samples using DNA extraction kit (Qiagen, Valencia, CA) according to the manual of manufacturer. A total of 13 SNPs located in eight genes involved in WNT signaling pathway were selected based on previous literature and genotyped using predesigned TaqMan assays using ABI 7500 real-time PCR machine (Applied Biosystems, USA) as previously described (Almutairi et al., 2015). The SNPs selected were located in SFRP3 (rs7775), APC (rs454886, rs459552), LRP6 (rs2075241, rs2284396), DKK4 (rs3763511), AXIN2 (rs3923086, rs3923087, rs4791171),  $\beta$ -catenin (rs4135385, rs13072632), DKK3 (rs6485350) and TCF4 (rs12255372) genes respectively. Around 10% of the samples were randomly used to reconfirm the results.

# 2.3. Statistical analysis

The Hardy–Weinberg equilibrium was assessed using  $\chi^2$  test for controls and cases. Pearson's goodness-of-fit chi-square ( $\chi^2$ ) values, odds ratios (OR), 95% confidence intervals (CI), and p values were calculated using SPSS *ver* 22 to find out the association between genotypes of all the SNPs with colorectal cancer risk as described by Alanazi et al. (2013).

## 3. Results

The demographic characteristics of selected samples are shown in Table 1.

#### Table 1

Demographic characteristics of CRC patients and control subjects.

Characteristics	Case	Control
Samples	122	110
Age		
<57	62	48
>57	60	62
Gender		
Male	74	57
Female	48	53

#### 3.1. Association of SNPs with colorectal cancer risk

The study group comprised of 122 patients with histopathologically confirmed colorectal cancer and 110 age and gender matched cancer-free controls (Table 1). To evaluate the role of WNT pathway genes in colorectal carcinogenesis, we examined 13 SNPs in eight genes of WNT signaling pathway (Table 2).

Ancestral allele was selected based on NCBI SNP database and used as a reference to calculate the odds to check the association of genotypes and alleles with colorectal cancer. The overall genotype frequencies of the analyzed SNPs and the odds ratio and significance are presented in Table 2. The allelic frequencies of all tested SNPs were in limits of Hardy-Weinberg equilibrium. The homozygous GG genotype of SNP rs4135385 in the β-catenin gene showed significant protective association (OR: 0.092, p = 0.03) (Table 2). We did not detect any statistically significant association with the risk of developing colorectal cancer for the other twelve SNPs examined in the overall study population (Table 2). However, when the samples were segregated based on gender and age at disease diagnosis, SNP rs7775 in SFRP3 gene showed significant protective association in female patients with minor allele Gly (OR (0.397, p = 0.02) as well as with heterozygous Arg/Gly genotype (OR 0.408, p = 0.04 (Table 3). None of the evaluated SNPs showed significant protective or risk association with colorectal cancer in males (Table 4) as well as in patients whose age at the time of disease diagnosis was below 57 years (Table 5). Interestingly, the CC genotype of LRP6 gene SNP rs2284396 showed significant protective association with colorectal cancer in patients who were above 57 years of age at the time of disease diagnosis (OR: 0.250, p = 0.021). In the allelic model as well similar protection against colorectal cancer was observed with the C allele of LRP6 SNP rs2284396 in individuals who were above 57 years of age (OR 0.561, p = 0.03) (Table 6).

### 4. Discussion

The present study evaluated the association of WNT signaling pathway gene variants with colorectal cancer susceptibility in Saudi population. Three of the 13 SNPs that were examined in this study showed significant decreased risk association with colorectal cancer. Two of the three protectively associated SNPs were found to be in the intron region and only SFRP3 gene SNP rs7775 was in the exon that codes for either Arg (CGC) or Gly (GGC). We found a strong association of the  $\beta$ -catenin gene rs4135385 with a decreased CRC risk. It was observed that individuals carrying GG genotype have approximately 11-fold lower risk of developing colorectal cancer relative to those having AA genotype at rs4135385 of β-catenin. This is in accordance with Wang et al. who investigated the rs4135385 and identified significant association of increased gastric cancer risk in Chinese patients having AG genotype compared to those having GG genotype (Wang et al., 2012). In our previous study as well we found significant risk association with rs4135385 in breast cancer while the other SNP rs13072632 in  $\beta$ -catenin was not associated (Alanazi et al., 2013). Zhang et al. reported that there is no association between rs4135385 and acute leukemia (Zhang et al., 2015).

LRP6 gene SNP rs2284396 showed decreased risk of colorectal cancer in above 57 years old patients with CC genotype and C allele. A fourfold decreased risk of developing CRC was observed in individuals with CC genotype compared to those having TT genotype at rs2284396. SNP rs2284396 as well as other SNPs in LRP6 didn't show any association in diabetes mellitus in Japanese population (Zenibayashi et al., 2008). However, Bai et al. reported an association of LRP6 SNP rs2284396 with Alzheimer's disease (Bai et al., 2016).

Genotype frequencies of WNT pathway gene polymorphism in colorectal cancer cases and controls.

Gene	SNP	Variant	Cases (Freq)	Controls	OR	CI	$\chi^2$ Value	P-Value
SFRP3	rs7775	Arg/Arg Arg/Gly Gly/Gly	96 (0.79) 24 (0.20) 2 (0.01)	77(0.70) 30(0.27) 3 (0.02)	Ref 0.642 0.535	0.347-1.187 0.087-3.281	2.02 0.47	0.15570 0.49239
		Arg Gly	216(0.89) 28 (0.11)	184(0.83) 36 (0.16)	0.663	0.389-1.127	2.32	0.12732
APC	rs454886	TT TC CC T	53 (0.45) 54 (0.46) 10 (0.9) 160(0.68)	53(0.49) 44 (0.40) 13 (0.11) 150(0.69)	Ref 1.227 0.769 Ref	0.707–2.129 0.310–1.907	0.53 0.32	0.46598 0.57058
		С	74 (0.32)	70 (0.31)	0.991	0.667-1.472	0.00	0.96455
APC	rs459552	Val/Val Val/Asp Asp/Asp Val Asp	88 (0.72) 30 (0.25) 4 (0.33) 206(0.84) 38 (0.16)	72 (0.65) 35 (0.32) 3 (0.02) 179(0.81) 41 (0.19)	Ref 0.701 1.091 Ref 0.805	0.393–1.251 0.236–5.033 0.496–1.308	1.45 0.01 0.77	0.22848 0.91117 0.38080
LRP6	rs2075241	GG GC CC G	92 (0.75) 24 (0.19) 6 (0.04) 208(0.85)	76 (0.70) 31 (0.29) 1 (0.009) 183(0.85)	Ref 0.640 4.957 Ref	0.346-1.181 0.584-42.073	2.05 2.61	0.15172 0.10600
I RP6	rs2284396	C TT	36 (0.14) 64 (0.53)	33 (0.15) 50 (0.46)	0.960 Ref	0.575-1.602	0.02	0.87526
		TC CC T	43 (0.35) 14 (0.11) 171(0.70)	40 (0.37) 19 (0.17) 140(0.64)	0.840 0.576 Ref	0.476-1.482 0.263-1.260	0.36 1.93	0.54661 0.16442
DIVILA		C	71 (0.3)	78 (0.36)	0.745 Def	0.504-1.102	2.17	0.14049
DKK4	132/02211	CT TT	37 (0.70) 32 (0.26) 4 (0.03) 206(0.83)	29 (0.26) 1 (0.009)	1.015 3.678 Ref	0.564–1.825 0.403–33.604	0.00 1.52	0.96124 0.21805
		T	40 (0.16)	31 (0.14)	1.184	0.712-1.969	0.42	0.51536
AXIN2	rs3923086	TT TG GG	48 (0.39) 52 (0.42) 21 (0.17)	41 (0.37) 50 (0.45) 19 (0.17)	Ref 0.888 0.944	0.503–1.570 0.447–1.994	0.17 0.02	0.68364 0.88007
		T G	148(0.61) 94 (0.38)	132(0.60) 88 (0.40)	Ref 0.953	0.656-1.384	0.06	0.79934
AXIN2	rs3923087	AA AG GG A	35 (0.28) 56 (0.45) 32 (0.26) 126(0.51)	37 (0.33) 50 (0.45) 23 (0.20) 124(0.56)	Ref 1.184 1.471 Ref	0.650-2.156 0.725-2.984	0.31 1.15	0.58049 0.28440
AXIN2	rs4791171	G AA	120(0.49) 40 (0.32)	96 (0.44) 38 (0.34)	1.230 Ref	0.854–1.773	1.24	0.26627
		AG GG A	55 (0.45) 27 (0.22) 135(0.55)	48 (0.43) 24 (0.22) 124(0.56)	1.089 1.069 Ref	0.604–1.962 0.527–2.167	0.08 0.03	0.77771 0.85370
		G	109(0.44)	96 (0.44)	1.043	0.723-1.505	0.05	0.82250
β-catenin	rs4135385	AA AG GG A	89 (0.74) 31 (0.26) 0 (0.0) 209(0.87)	74 (0.67) 32 (0.30) 4 (0.04) 180(0.81)	Ref 0.805 0.092 Ref	0.450-1.442 0.005-1.746	0.53 4.68	0.46618 <b>0.03059</b>
		G	31 (0.13)	40 (0.18)	0.667	0.401-1.111	2.44	0.11844
β-catenin	rs13072632	CT TT C	51 (0.42) 47 (0.39) 23 (0.19) 149(0.61) 02 (0.28)	46 (0.42) 51 (0.46) 13 (0.11) 143(0.65) 77 (0.25)	Ref 0.831 1.596 Ref	0.474-1.458 0.725-3.510	0.42 1.36	0.51900 0.24335
DKK3	rs6485350	AA	46 (0.39)	77 (0.35) 36 (0.33)	Ref	0.793-1.694	0.58	0.44519
		AG GG A	56 (0.47) 17 (0.14) 148(0.62)	50 (0.45) 24 (0.22) 122(0.55)	0.877 0.554 Ref	0.491–1.564 0.259–1.184	0.20 2.34	0.65563 0.12586
TCF4	rc10055070	G	90 (0.37) 47 (0.40)	98 (0.44)	0.757 Ref	0.521-1.100	2.14	0.14350
1074	1512200372	GT TT G	47 (0.40) 56 (0.47) 17 (0.14) 150(0.62)	49 (0.44) 46 (0.42) 15 (0.14) 144(0.65)	1.269 1.182 Ref	0.726–2.219 0.530–2.633	0.70 0.17	0.40279 0.68309
		Т	90 (0.37)	76 (0.34)	1.137	0.776-1.665	0.43	0.50982

SFRP3 gene showed significant protective association in female patients harbouring minor allele G. The G allele of rs7775 codes for Gly while the C allele codes for Arg. Women having Gly at codon 324 (rs7775) of SFRP3 have 2.5-fold lower risk of developing CRC relative to those have Arg at this locus. Our finding of the strong protection conferred by the GG genotype of rs7775 against

Distribution of WNT pathway gene SNPs genotype and allele frequencies in colorectal cancer cases and control population based on gender (female).

SNP	Variant	Cases (Freq)	Controls	OR	CI	$\chi^2$ Value	P-Value
rs7775	Arg/Arg	38 (0.79)	31 (0.59)	Ref			
	Arg/Gly	10 (0.20)	20 (0.38)	0.408	0.167-0.998	3.96	0.04670
	Gly/Gly Aro	0 (0.0) 86 (0.90)	2 (0.03) 82 (0.80)	0.164 Ref	0.008-3.534	2.37	0.12370
	Gly	10 (0.10)	24 (0.20)	0.397	0.179-0.882	5.38	0.02039
rs454886	TT	24 (0.55)	26 (0.49)	Ref			
	CT	17 (0.40)	21 ()0.40	0.877	0.376-2.045	0.09	0.76116
	CC	2(0.05)	6(0.11)	0.361 Pof	0.066-1.964	1.48	0.22454
	C	21 (0.24)	33 (0.31)	0.715	0.376-1.357	1.06	0.30354
rs459552	Val/Val	35 (0.73)	35 (0.67)	Ref			
13433332	Val/Asp	9 (0.19)	17 (0.32)	0.529	0.208-1.347	1.81	0.17882
	Asp/Asp	4 (0.08)	1 (0.01)	4.000	0.425-37.605	1.68	0.19457
	Val	79 (0.82)	87 (0.82)	Ref			
	Asp	17 (0.17)	19 (0.18)	0.985	0.479-2.028		0.96802
rs2075241	GG	41(0.85)	39 (0.73)	Ref			
	GC	5 (0.10)	13 (0.25)	0.366	0.119-1.122	3.25	0.07141
	C C	2 (0.04) 87(0.91)	I (0.02) 91(0.86)	1.902 Ref	0.166-21.830	0.28	0.59983
	C	9 (0.09)	15 (0.14)	0.628	0.261-1.509	1.10	0.29481
rs2284396	TT	26 (0.55)	24 (0.45)	Ref			
132204330	TC	13 (0.28)	21 (0.40)	0.571	0.235-1.387	1.54	0.21437
	CC	8 (0.17)	8 (0.15)	0.923	0.299-2.846	0.02	0.88919
	Т	65 (0.70)	69 (0.65)	Ref			
	С	29 (0.30)	37 (0.35)	0.832	0.460-1.505	0.37	0.54277
rs3763511	CC	32 (0.66)	39 (0.74)	Ref			
	CI	14(0.30)	14 (0.26)	1.219	0.508-2.926	0.20	0.65783
	C	2 (0.04) 78 (0.81)	92 (0.87)	Ref	0.282-131.125	2.50	0.12456
	T	18 (0.19)	14 (0.13)	1.516	0.709-3.245	1.16	0.28131
rs3923086	TT	19 (0.40)	19 (036)	Ref			
	TG	21 (0.44)	24 (0.45)	0.875	0.369-2.077	0.09	0.76204
	GG	8 (0.16)	10 (0.19)	0.800	0.259-2.468	0.15	0.69759
	T	59 (0.61) 27 (0.20)	62 (0.59)	Ref	0.502 1.552	0.19	0 66725
rs3923087	AA	14 (0 29)	44 (0.41) 18 (0.34)	0.884 Ref	0.305-1.335	0.18	0.00755
135325007	AG	21 (0.43)	23 (0.43)	1.174	0.470-2.932	0.12	0.73126
	GG	13 (0.27)	12 (0.23)	1.393	0.487-3.982	0.38	0.53591
	A	49 (0.51)	59 (0.56)	Ref			
	G	47 (0.49)	47 (0.44)	1.204	0.692-2.095	0.43	0.51104
rs4791171	AA	15 (0.32)	19 (0.36)	Ref	0.705 4.250	1.45	0 22001
	AG	26 (0.55) 6 (0.28)	19 (0.36)	1.733	0.705-4.259	1.45	0.22891
	A	56 (0.60)	57 (0.54)	Ref	0.130-1.025	1.55	0.24034
	G	38 (0.40)	49 (0.46)	0.789	0.450-1.384	0.68	0.40886
rs4135385	AA	34 (0.74)	34 (0.64)	Ref			
	AG	12 (0.26)	16 (0.30)	0.750	0.309-1.820	0.41	0.52428
	GG	0 (0.0)	3 (0.06)	0.143	0.007-2.871	2.88	0.08978
	A	80 (0.87)	84 (0.79) 22 (0.21)	Ref 0.573	0.266_1.233	2.06	0 15130
-12072622	6	12 (0.15)	22 (0.21)	0.575	0.200-1.255	2.00	0.15150
rs13072632	CT	22 (0.46) 16 (0.33)	22 (0.42)	Ker 0.640	0.270_1.515	1.03	0 30016
	TT	10 (0.21)	6 (0.11)	1.667	0.516-5.381	0.74	0.39075
	С	60 (0.63)	69 (0.65)	Ref			
	Т	36 (0.37)	37 (0.35)	1.119	0.630-1.988	0.15	0.70150
rs6485350	AA	19 (0.43)	16 (0.30)	Ref			
	AG	19 (0.43)	29 (0.55)	0.552	0.229-1.332	1.76	0.18429
	GG ∆	ь (U.14) 57 (0.65)	8 (U.15) 61 (0.58)	0.632 Ref	0.181-2.205	0.52	0.46971
	G	31 (0.35)	45 (0.42)	0.737	0.412-1.320	1.05	0.30470
rs12255372	GG	20 (0.42)	22 (0.42)	Ref			
1312233372	GT	18 (0.37)	25 (0.47)	0.792	0.336-1.865	0.29	0.59342
	TT	10 (0.21)	6 (0.11)	1.833	0.564-5.963	1.03	0.31075
	G	58 (0.60)	69 (0.65)	Ref	0.000 0.463	0.47	0.463-00
	Т	38 (0.40)	37 (0.35)	1.222	0.690-2.164	0.47	0.49198

colorectal cancers however in a small population size is significant and provides strong reason for examination of this SNP in larger studies in other ethnic groups. In our previous study we found that the CG and GG genotypes of rs7775 were protectively associated with breast cancers (Alanazi et al., 2013). Our results are in contrast with the findings of Shanmugam et al. (2007) who reported

Distribution of WNT pathway gene SNPs genotype and allele frequencies in colorectal cancer cases and control population based on gender (male).

n775Name Argicia Argicia Argicia Argicia Argicia Argicia (1001)1001 10010110 100100.452-275 0.052 0.052-2760.10 0.452-275 0.0700.101 0.452-2550 0.0010.101 0.452-2550 0.0010.101 0.452-2550 0.0010.101 0.452-2550 0.0010.101 0.452-2550 0.0010.101 0.452-2550 0.0010.101 0.10210.102 0.10210.101 0.	SNP	Variant	Cases (Freq)	Controls	OR	CI	$\chi^2$ Value	P-Value
Arg(c)y    14 (19)    100.18)    1.110    0.422-273    0.05    0.81946      Cby(c)y    160.01)    100.11    1.7    0.542-2555    0.17    0.0015      rs/64886    TT    390.30    120.011    1.7    0.542-2555    0.17    0.0015      rs/64886    TT    390.401    7.01    1.64    0.345-2555    0.17    0.23784      rs/64895    S(0.11)    7.01.51    1.64    0.342-1254    0.15    0.23794    0.01    0.93154      rs/64895    S(0.11)    7.01.51    Ref    7.01.51    Ref    7.01.51    0.01    0.321-174    0.22    0.0055    0.0055    0.0055    0.007-50.05    0.007-50.	rs7775	Arg/Arg	58 (0.78)	46(0.81)	Ref			
chy (cyby 2 (0.03)    10(0.13)    1.286    0.139-16.044    0.14    0.0770      rs45    1000.080    1000.080    1000.080    Rd    0.07    0.08015      rs45    201.030    270.400    Rd    7    0.08015    0.07    0.08015      r    950.64    700.88    Rd    7    0.08015    0.001    0.02154      r    950.64    700.89    700.89    Rd    7    0.0316    0.021 <th< td=""><td></td><td>Arg/Gly</td><td>14 (0.19)</td><td>10(0.18)</td><td>1.110</td><td>0.452-2.728</td><td>0.05</td><td>0.81946</td></th<>		Arg/Gly	14 (0.19)	10(0.18)	1.110	0.452-2.728	0.05	0.81946
Arg    130,038)    120,013    1		Gly/Gly	2 (0.03)	1(0.01)	1.586	0.139-18.044	0.14	0.70770
rds    10    11/1    11		Arg	130(0.88)	102(0.89)	Ref	0 5 42 2 5 5 5	0.17	0.00015
rsf 54886    rt    200,39)    270,47)    Rd      C    370,50)    230,400    230,400    201,401    1.35    0.37    0.31    0.316    0.316    0.316    0.316    0.316    0.316    0.316    0.316    0.317    0.316    0.317    0.326    0.376    0.327    0.396    0.397    0.396		Gly	18(0.12)	12(0.11)	1.177	0.342-2.333	0.17	0.68015
Li    34(13)    24(14)    148    0.16-3.13    0.13    0.25714      C    50(0.5)    77(0.32)    1.161    0.39-333    0.3    0.3714      rs    50(0.5)    77(0.32)    1.161    0.39-1.346    0.32    0.5779      rs    50(0.5)    87(0.2)    0.814    0.322-1.736    0.28    0.05951      App(AS)    0.000    2(0.31)    87(0.7)    87    0.28    0.05951      App(AS)    0.000    2(0.31)    87(0.81)    87(0.81)    0.39-1.322    1.23    0.28893      rs    0.000    8(0.31)    0.76    0.342-125.445    2.81    0.09919      rs    1.100.021    18(0.32)    28(0.46)    874    0.15    0.08919      rs    70.001.021    18(0.32)    10(0.20)    0.373    0.13    0.13    0.13    0.03      rs    1.100.021    1.140    0.592-2.196    0.15    0.08    0.7334    0.15    0.76      rs    3.00.021    1	rs454886	TT	29(0.39)	27(0.47)	Ref	0.510, 0.105		0.00000
Ind    Barlan    Constrained    Constrained    Constrained    Constrained    Constrained      rs429552    Valual    2300.27)    270.05)    Ref    0.007.3.05    2.78    0.00555      rs429552    Valual    2300.27)    270.05)    Ref    0.007.3.05    2.78    0.00555      rs42075241    CC    1200.080    270.07)    Ref    0.007.3.055    2.78    0.00555      rs2075241    CC    190.05)    18(0.33)    0.766    0.354.1.256    0.46    0.04971      rs2075241    CC    210.020    200.84)    Ref    0.057    Ref    0.05997      rs22244995    CC    210.013    18(0.16)    1.140    0.592-2.196    0.15    0.09399      rs22244995    TT    300.401    100.23    Ref    0.157    0.157      rs2224995    TT    300.402    100.201    Ref    0.157    0.157      rs300.527    700.531    410.727    Ref    0.007    0.007    0.007			37(0.50)	23(0.40)	1.498	0./16-3.135	1.15	0.28289
r+459552    Valuation    Silo (25)    Silo (25) <th< td=""><td></td><td>T</td><td>8(0.11)</td><td>7(0.13)</td><td>1.064 Ref</td><td>0.340-3.333</td><td>0.01</td><td>0.91514</td></th<>		T	8(0.11)	7(0.13)	1.064 Ref	0.340-3.333	0.01	0.91514
rs49552    rs4    rs4    rs4    rs4    rs4    rs4    rs4      rs49552    Val (bg)    21(0.23)    370.05    Ref    0.007-3.05    2.78    0.0395      rs40752    Val    21(0.14)    22(0.19)    0.691    0.359-1.32    1.23    0.28955      rs2075241    GG    510(0.05)    18(0.33)    0.766    0.354-1.266    0.46    0.09340      rs2075241    GG    110(0.25)    18(0.33)    0.766    0.354-1.266    0.46    0.059      rc224495    GG    210(0.81)    18(0.61)    1.40    0.592-2.196    0.15    0.89397      rc224495    TC    30(0.40)    190.331    Ref    77    0.15    0.89397      rc2    210(1.81    110(20)    0.373    0.12-1.136    0.10    0.3727      rc376351    C    510.0257    rd    0.03    0.737    0.73    0.73    0.73    0.73    0.73    0.73    0.73    0.73    0.73    0.73    0.73		C	53(0.36)	37(0.32)	1.161	0.693-1.946	0.32	0.57079
jh99992    vial vial Asp/Ap    2100.25 (0.33)    2100.35 (0.33)    vial vial (0.33)    0.382+173 (0.07-3.005)    0.28 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.382+173 (0.35)    0.332+135 (0.35)    0.332+136 (0.35)    0.332+136 (0.35)	*** 450552	Va1/Va1	E2(0.72)	27(0.65)	Dof			
Name    Notion    20031    0.140    0.007-3.005    2.78    0.00555      Nap    21(0.14)    22(0.31)    0.691    0.0359-1.322    1.23    0.28355      152075241    GC    51(0.026)    18(0.32)    0.766    0.354-1.556    0.46    0.499719      152075241    GC    121(0.82)    92(0.84)    Ref    0.592-2.195    0.15    0.69397      152284396    TT    38(0.52)    26(0.46)    Ref    0.005-2.312    0.04    0.4224      152075241    GC    83(0.52)    26(0.46)    Ref    0.123-1136    3.14    0.07444      1500721    71(0.63)    Ref    0.006-1.100    1.99    0.152      153763311    CC    55(0.73)    1.10(2.01    0.4861    0.311-1.008    0.01    0.24523      153763311    CC    55(0.73)    81(0.42)    1.401    0.311-1.008    0.01    0.24523      15376331    CC    55(0.43)    1.0021    1.60    0.494-1.347    0.00    0.55557 <td>15455552</td> <td>Val/Asn</td> <td>21(0.28)</td> <td>18(0.32)</td> <td>0.814</td> <td>0 382-1 736</td> <td>0.28</td> <td>0 59481</td>	15455552	Val/Asn	21(0.28)	18(0.32)	0.814	0 382-1 736	0.28	0 59481
via    127(0.86)    92(0.81)    Ref      Asp    21(0.14)    22(0.91)    0.661    0.359-1.332    1.23    0.26833      rt2075241    GG    15(0.82)    92(0.81)    Ref    0.354-1556    0.46    0.493719      rt2075241    GG    15(0.82)    92(0.64)    Ref    0.352-2196    0.15    0.89391      rt2075241    10(0.82)    92(0.64)    Ref    0.555-2312    0.04    0.64    0.83291      rt2075241    10(0.07)    71(0.63)    Ref    0.356-2312    0.04    0.83291      rt2075241    10(0.07)    71(0.63)    Ref    0.356-2312    0.04    0.83291      rt2075241    10(0.07)    71(0.63)    Ref    0.331-17008    0.09    0.3572      rt3753511    GT    18(0.24)    10(0.2)    1.491    0.313-17008    0.00    0.73629      rt3753511    GT    18(0.61)    10(0.2)    1.491    0.31-17008    0.10    0.3592392      rt37635211    17(0.15)    0.99		Asp/Asp	0(0.0)	2(0.03)	0.140	0.007-3.005	2.78	0.09555
space <th< td=""><td></td><td>Val</td><td>127(0.86)</td><td>92(0.81)</td><td>Ref</td><td></td><td></td><td></td></th<>		Val	127(0.86)	92(0.81)	Ref			
is2073241GGS1(0.69)37(0.67)RefGC10(0.5)0(0.0)6.530.34-1.5560.460.493/90G27(0.18)18(0.15)1.1400.52-1.25.4452.810.493/90152284396T30(0.40)18(0.16)1.1400.52-1.25.4453.140.693/97152284396TC30(0.40)19(0.34)1.0800.53-2.3120.440.842.241522843961166(0.72)71(0.63)Ref1.231.310.0764166(0.72)71(0.63)Ref1.231.310.0764.25173763511C55(0.73)41(0.72)Ref1.231.310.0764.2517376351106(0.22)1.002)0.8950.404-1.9820.080.7834.45173923086T22(0.15)1.002)0.9850.404-1.9820.080.7834.45173923086T22(0.15)1.002)0.9850.404-1.9120.080.895.75173923087AA22(0.15)1.002)0.9850.432-1.9230.070.7959173923087AA21(0.22)10(0.30)Ref1.230.6387.3230.070.7959173923087AA21(0.22)1.002)0.9850.432-1.9360.070.79591749171AA22(0.51)1.003Ref1.230.63870.413-1.920.638717499171AA21(0.22)1.0303Ref1.230.63850.413-1.920.638717499171 <td< td=""><td></td><td>Asp</td><td>21(0.14)</td><td>22(0.19)</td><td>0.691</td><td>0.359-1.332</td><td>1.23</td><td>0.26833</td></td<>		Asp	21(0.14)	22(0.19)	0.691	0.359-1.332	1.23	0.26833
r4    r6    r10(25)    r10(33)    0.766    0.334-125.465    0.46    0.47919      r5    22(0.82)    92(0.84)    Ref    0.001    6.553    0.512-126.46    0.0019      r5    22(0.16)    1140    0.592-2196    0.15    0.604    0.842      r5    30(0.52)    26(0.46)    Ref    0.012    0.044    0.842      r5    30(0.62)    71(0.63)    Ref    0.044    0.842    0.044    0.842      r5    50(7)    110(20)    0.856    0.406-1.160    0.95    0.75	rs2075241	GG	51(0.69)	37(0.67)	Ref			
CC    1005    000    653    0.342-125.445    2.81    0.0399      C    27(0.18)    18(0.16)    1.140    0.592-136    0.04    0.5939      rs2284396    T    38(0.52)    28(0.46)    Ref		GC	19(0.26)	18(0.33)	0.766	0.354-1.656	0.46	0.49719
G    121(0.82)    92(0.84)    Ref      C    27(0.18)    18(0.15)    1.140    0.592-2.196    0.505    0.4224      TC    30(0.40)    19(0.34)    1080    0.505-2.312    0.04    0.84224      TC    30(0.60)    11(0.20)    0.373    0.123-1.136    3.14    0.07644      T    106(0.72)    71(0.63)    Ref    0.068    0.406-1.160    1.99    0.5572      r3763511    C    50.73)    41(0.72)    Ref    0.08    0.786364      TT    12(0.24)    170(0.51)    Ref    0.01    0.74629      TC    12(0.83)    97(0.85)    Ref    0.02    0.95557      r3323086    TT    22(0.45)    0.905    0.423-1.936    0.407    0.905      r3323087    AA    210(23)    19(0.33)    Ref    0.33673    0.34    0.35872      r3323087    AA    210(23)    19(0.33)    Ref    0.34    0.35873      r47391171    AA    22		CC	4(0.05)	0(0.0)	6.553	0.342-125.445	2.81	0.09349
r2284396    r    230(18)    110(10)    1.40    0.95    0.15    0.05939      r2284396    T    30(0.40)    19(0.34)    1.080    0.55-2.132    0.04    0.84224      C    6(0.08)    11(0.20)    0.373    0.123-1.136    3.14    0.0586      r    108(0.72)    71(0.63)    Ref		G	121(0.82)	92(0.84)	Ref			
rs2284396    TT    380.52)    28(0.46)    Ref      CC    300.40)    19(0.34)    1.080    0.505-2.312    0.4    0.48224      CC    6(0.08)    11(0.20)    0.373    0.23-1.136    3.14    0.07644      T    106(0.22)    71(0.63)    Ref    1.99    0.515-2.312    0.6    0.575-2.312    0.6    0.575-2.312    0.575-2.312    0.6    0.575-2.312    0.6    0.575-2.312    0.575-2.312    0.6    0.575-2.312    0.6    0.575-2.312    0.6    0.575-2.312    0.6    0.575-2.312    0.575-2.312    0.375-2.375    0.375-2.		C	27(0.18)	18(0.16)	1.140	0.592-2.196	0.15	0.69397
rd    30(0.40)    19(0.34)    1.080    0.052-3.12    0.04    0.84224      r    106(0.72)    71(0.63)    Ref	rs2284396	TT	38(0.52)	26(0.46)	Ref			
		TC	30(0.40)	19(0.34)	1.080	0.505-2.312	0.04	0.84224
r    100,023    100,033    Ref    0.406-1.160    1.99    0.15872      rs3263511    CC    55(0.73)    41(0.72)    Ref			6(0.08)	II(0.20)	0.3/3 Pof	0.123-1.136	3.14	0.07644
		ſ	42(0.28)	41(0.37)	0.686	0.406-1.160	1 99	0 15872
FS /05311    CC    53(0/3)    41(0/2)    Ref      TT    2(0.03)    1(0.02)    1.491    0.131-17.008    0.10    0.78844      T    2(0.03)    1(0.02)    1.491    0.131-17.008    0.10    0.78842      T    22(0.15)    17(0.15)    0.981    0.494-1.947    0.00    0.5557      rs3923086    TC    22(0.15)    17(0.15)    0.905    0.423-1.936    0.07    0.79995      GG    13(0.42)    26(0.45)    0.005    0.397-3.022    0.03    0.88972      T    89(0.61)    70(0.61)    Ref    -    -    -    -    -    -    0.0397-3.022    0.03    0.88973    -    -    -    -    0.03993    0.594-4.103    0.82    .0684    .03973-3.022    0.03    0.89936    - <td< td=""><td></td><td>6</td><td>12(0.20)</td><td>11(0.57)</td><td>0.000</td><td>0.100 1.100</td><td>1.55</td><td>0.15072</td></td<>		6	12(0.20)	11(0.57)	0.000	0.100 1.100	1.55	0.15072
	rs3763511	CT CT	55(0.73)	41(0.72) 15(0.26)	Ket 0.805	0 404 1 092	0.09	0 79264
		TT	2(0.03)	10.020	0.895	0.404-1.982	0.08	0.78504
T    22(0.15)    17(0.15)    0.881    0.494-1.947    0.00    0.9557      rs3923066    TT    29(0.40)    22(0.39)    Ref		C	128(0.85)	97(0.85)	Ref	0.151-17.000	0.10	0.74025
rs3923086    TT    29(0.40)    22(0.39)    Ref		Т	22(0.15)	17(0.15)	0.981	0.494-1.947	0.00	0.95557
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	rs3923086	TT	29(0.40)	22(0.39)	Ref			
GG    13(0.18)    9(0.16)    1.06    0.37-3.022    0.03    0.8572      G    57(0.39)    44(0.39)    1.019    0.616-1.684    0.01    0.94182      rs3923087    AA    21(0.28)    19(0.33)    Ref	100020000	TG	31(0.42)	26(0.45)	0.905	0.423-1.936	0.07	0.79595
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		GG	13(0.18)	9(0.16)	1.096	0.397-3.022	0.03	0.85972
G    57(0.39)    44(0.39)    1.09    0.616-1.684    0.01    0.94182      rs3923087    AA    21(0.28)    19(0.33)    Ref		Т	89(0.61)	70(0.61)	Ref			
rs3923087    AA    210(28)    19(0.33)    Ref      AG    350.471    27(0.47)    1.173    0.528-2.606    0.15    0.69536      GG    19(0.25)    11(0.20)    1.563    0.594-4.113    0.82    0.36473      A    77(0.51)    65(0.57)    Ref		G	57(0.39)	44(0.39)	1.019	0.616-1.684	0.01	0.94182
AG    35(0.47)    27(0.47)    1.173    0.528-2.606    0.15    0.669536      A    77(0.51)    65(0.57)    Ref    0.32    0.36473      G    73(0.49)    49(0.43)    1.28    0.771-2.053    0.84    0.3584      rs4791171    AA    25(0.33)    19(0.33)    Ref    0.346-1.671    0.47    0.494444      GG    29(0.53)    67(0.59)    Ref    0.346-1.671    0.47    0.494444      GG    29(0.53)    67(0.59)    Ref    0.32201    0.33201    0.33201      rs4135385    AA    55(0.74)    40(0.70)    Ref    0.33201    0.336-1.884    0.14    0.71243      rs4135385    AA    55(0.74)    40(0.70)    Ref    0.33201    0.336-1.884    0.14    0.71243      G    19(0.26)    16(0.28)    0.864    0.396-1.884    0.14    0.71243      rs4135385    AA    55(0.74)    40(0.70)    Ref    0.322    0.331    1.36    0.24430	rs3923087	AA	21(0.28)	19(0.33)	Ref			
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		AG	35(0.47)	27(0.47)	1.173	0.528-2.606	0.15	0.69536
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		GG	19(0.25)	11(0.20)	1.563 Bef	0.594-4.113	0.82	0.36473
rs4791171  AA  25(0.33)  19(0.33)  Ref    rs4791171  AG  29(0.39)  29(0.51)  0.760  0.346-1.671  0.47  0.49444    GG  21(0.28)  9(0.16)  1.773  0.664-4.737  1.32  0.25099    GG  71(0.47)  47(0.41)  1.281  0.784-2.095  0.98  0.32301    rs4135385  AA  55(0.74)  40(0.70)  Ref		A G	77(0.51) 73(0.49)	49(0.43)	1 258	0 771_2 053	0.84	0 35884
rs4/911/1    AA    25(0.33)    19(0.33)    Ref      AG    29(0.39)    29(0.51)    0.760    0.346-1.671    0.47    0.49444      GG    21(0.28)    9(0.16)    1.773    0.664-4.737    1.32    0.25099      A    79(0.53)    67(0.59)    Ref	1001101	3	75(0.13)	13(0.13)	1.250	0.771 2.055	0.01	0.55001
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	rs4/911/1	AA AC	25(0.33)	19(0.33)	Ker 0.760	0346-1671	0.47	0 49444
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		GG	21(0.28)	9(0.16)	1 773	0.664-4.737	1 32	0.25099
G    71(0.47)    47(0.41)    1.281    0.784-2.095    0.98    0.32301      rs4135385    AA    55(0.74)    40(0.70)    Ref		A	79(0.53)	67(0.59)	Ref		102	0120000
rs4135385    AA    55(0.74)    40(0.70)    Ref      AG    19(0.26)    16(0.28)    0.864    0.396-1.884    0.14    0.71243      AG    19(0.26)    16(0.28)    0.243    0.10-6.125    1.36    0.2433      A    129(0.87)    96(0.84)    Ref		G	71(0.47)	47(0.41)	1.281	0.784-2.095	0.98	0.32301
AG    19(0.26)    16(0.28)    0.864    0.396-1.884    0.14    0.71243      GG    0(0.0)    1(0.02)    0.243    0.010-6.125    1.36    0.24430      A    129(0.87)    96(0.84)    Ref    0.010-6.125    1.36    0.24430      G    19(0.13)    18(0.16)    0.786    0.391-1.577    0.46    0.49641      rs13072632    CC    29(0.40)    24(0.42)    Ref    0.00    0.94646      TT    13(0.42)    25(0.44)    1.026    0.482-2.183    0.00    0.94646      TT    13(0.18)    8(0.14)    1.345    0.478-3.780    0.32    0.57366      C    89(0.61)    73(0.64)    Ref    0.0687-1.893    0.26    0.61154      T    57(0.39)    41(0.36)    1.140    0.687-1.893    0.26    0.61154      S    S    0.20(0.35)    Ref    0.02    0.026    0.599    0.593-2.870    0.44    0.50745      GG    11(0.14)    16(0.28)    0.50	rs4135385	AA	55(0.74)	40(0.70)	Ref			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		AG	19(0.26)	16(0.28)	0.864	0.396-1.884	0.14	0.71243
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		GG	0(0.0)	1(0.02)	0.243	0.010-6.125	1.36	0.24430
G    19(0.13)    18(0.16)    0.786    0.391-1.577    0.46    0.49641      rs13072632    CC    29(0.40)    24(0.42)    Ref		А	129(0.87)	96(0.84)	Ref			
rs13072632    CC    29(0.40)    24(0.42)    Ref      CT    31(0.42)    25(0.44)    1.026    0.482-2.183    0.00    0.94646      TT    13(0.18)    8(0.14)    1.345    0.478-3.780    0.32    0.57366      C    89(0.61)    73(0.64)    Ref		G	19(0.13)	18(0.16)	0.786	0.391-1.577	0.46	0.49641
CT    31(0.42)    25(0.44)    1.026    0.482-2.183    0.00    0.94646      TT    13(0.18)    8(0.14)    1.345    0.478-3.780    0.32    0.57366      C    89(0.61)    73(0.64)    Ref	rs13072632	CC	29(0.40)	24(0.42)	Ref			
TT  13(0.18)  8(0.14)  1.345  0.478–3.780  0.32  0.57366    C  89(0.61)  73(0.64)  Ref  7 <td></td> <td>CT</td> <td>31(0.42)</td> <td>25(0.44)</td> <td>1.026</td> <td>0.482-2.183</td> <td>0.00</td> <td>0.94646</td>		CT	31(0.42)	25(0.44)	1.026	0.482-2.183	0.00	0.94646
rs6485350    AA    27(0.36)    41(0.36)    1.140    0.687-1.893    0.26    0.61154      rs6485350    AA    27(0.36)    20(0.35)    Ref		TT	13(0.18)	8(0.14)	1.345	0.478-3.780	0.32	0.57366
rs6485350  AA  27(0.36)  20(0.35)  Ref    AG  37(0.49)  21(0.37)  1.305  0.593-2.870  0.44  0.50745    GG  11(0.14)  16(0.28)  0.509  0.195-1.331  1.92  0.16632    A  91(0.60)  61(0.54)  Ref  1.365  0.456-1.221  1.36  0.24377    rs12255372  GG  27(0.37)  27(0.47)  Ref  1.310  0.851-3.846  2.39  0.12172    TT  38(0.53)  21(0.37)  1.810  0.851-3.846  2.39  0.12172    TT  7(0.10)  9(0.16)  0.778  0.253-2.390  0.19  0.66042    G  92(0.64)  75(0.66)  Ref  1.087  0.649-1.819  0.10  0.75103		τ T	89(0.61) 57(0.39)	/3(0.64)	Ker 1 140	0.687-1.803	0.26	0.61154
rs6485350  AA  27(0.36)  20(0.35)  Ref    AG  37(0.49)  21(0.37)  1.305  0.593-2.870  0.44  0.50745    GG  11(0.14)  16(0.28)  0.509  0.195-1.331  1.92  0.1663    A  91(0.60)  61(0.54)  Ref		1	57(0.59)	41(0.50)	1.140	0.087-1.895	0.20	0.01134
rs12255372  GG  27(0.47)  16(0.28)  0.509  0.195-1.331  1.92  0.166028    A  91(0.60)  61(0.54)  Ref  1.365  0.446  0.24377    rs12255372  GG  27(0.37)  27(0.47)  Ref  1.360  0.851-3.846  2.39  0.12172    TT  38(0.53)  21(0.37)  1.810  0.851-3.846  2.39  0.12172    GG  92(0.64)  75(0.66)  Ref  1.087  0.649-1.819  0.10  0.75103	rs6485350	AA AC	27(0.36)	20(0.35)	Ket	0 502 2 970	0.44	0 50745
rs12255372    GG    27(0.37)    27(0.47)    Ref    1.810    0.456-1.221    1.36    0.24377      rs12255372    GG    27(0.37)    27(0.47)    Ref    0.746    0.456-1.221    1.36    0.24377      GT    38(0.53)    21(0.37)    1.810    0.851-3.846    2.39    0.12172      TT    7(0.10)    9(0.16)    0.778    0.253-2.390    0.19    0.66042      G    92(0.64)    75(0.66)    Ref    75103    1.087    0.649-1.819    0.10    0.75103		л <del>о</del> СС	11(0.49)	21(0.57) 16(0.28)	0.503	0.595-2.070	0.44 1 92	0.50745
G    59(0.40)    53(0.46)    0.746    0.456-1.221    1.36    0.24377      rs12255372    GG    27(0.37)    27(0.47)    Ref		A	91(0.60)	61(0.54)	Ref	0.135 1.351	1.52	0.10052
rs12255372 GG 27(0.37) 27(0.47) Ref GT 38(0.53) 21(0.37) 1.810 0.851-3.846 2.39 0.12172 TT 7(0.10) 9(0.16) 0.778 0.253-2.390 0.19 0.66042 G 92(0.64) 75(0.66) Ref T 52(0.36) 39(0.34) 1.087 0.649-1.819 0.10 0.75103		G	59(0.40)	53(0.46)	0.746	0.456-1.221	1.36	0.24377
GT    38(0.53)    21(0.47)    Ref      TT    38(0.53)    21(0.37)    1.810    0.851-3.846    2.39    0.12172      TT    7(0.10)    9(0.16)    0.778    0.253-2.390    0.19    0.66042      G    92(0.64)    75(0.66)    Ref    7    75(0.36)    816      T    52(0.36)    39(0.34)    1.087    0.649-1.819    0.10    0.75103	rs12255272	GG	27(0 37)	27(0.47)	Ref			
TT7(0.10)9(0.16)0.7780.253-2.3900.190.66042G92(0.64)75(0.66)RefT52(0.36)39(0.34)1.0870.649-1.8190.100.75103	1312233372	GT	38(0.53)	21(0.37)	1.810	0.851-3.846	2.39	0.12172
G 92(0.64) 75(0.66) Ref T 52(0.36) 39(0.34) 1.087 0.649-1.819 0.10 0.75103		TT	7(0.10)	9(0.16)	0.778	0.253-2.390	0.19	0.66042
T 52(0.36) 39(0.34) 1.087 0.649–1.819 0.10 0.75103		G	92(0.64)	75(0.66)	Ref			
		Т	52(0.36)	39(0.34)	1.087	0.649-1.819	0.10	0.75103

that variations in rs7775 significantly increased risk for CRC in German patients (Shanmugam et al., 2007). Few other studies found no association of this SNP with colorectal cancer (Berndt

et al., 2009) and osteoarthritis (Loughlin et al., 2004). Thus, it may be possible that rs7775 brings about different outcome in cooperation with other SNPs and warrants a detailed investigation

Distribution of WNT pathway gene SNPs genotype and allele frequencies in colorectal cancer cases and control population based on age (<57).

n7775    Arg(Cry Arg(Cy Cy/Cy    400.78 (10.11)    370.77 (10.11)    Ref.    0.335	SNP	Variant	Cases (Freq)	Controls	OR	CI	$\chi^2$ Value	P-Value
numbernumbernumbernumbernumbernumbernumbernumbernumbernumber(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)number(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)number(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)number(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)number(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)(ika)number(ika)	rs7775	Arg/Arg	48(0.78)	37(0.77)	Ref			
chy/strip    1001/1    20.41    0.835    0.834415    0.63    0.62786      rsf45886    T    250.41    240.02    Ref    0.77    0.78    0.78      rsf45886    T    250.44    240.02    Ref    0.79    0.79    0.79      rsf458952    Yallyap    700.02    880.79    0.70    2.69    0.10    0.7797      rsf39552    Vallyap    30.05    70.02    0.375    0.376-2.027    0.10    0.7797      rsf39552    Vallyap    30.05    30.06    0.21    0.135-1.556    0.23    0.629      rsf39552    Vallyap    30.057    30.061    0.37    0.376-2.037    0.10    0.379      rsf3952    Vallyap    30.057    70.077    Ref    0.10    0.02    0.63    0.69    0.63    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69    0.69		Arg/Gly	13(0.21)	9(0.19)	1.113	0.430-2.885	0.05	0.82488
Nag    160,08)    150,12 <td></td> <td>Gly/Gly</td> <td>1(0.01)</td> <td>2(0.41)</td> <td>0.385</td> <td>0.034-4.415</td> <td>0.63</td> <td>0.42786</td>		Gly/Gly	1(0.01)	2(0.41)	0.385	0.034-4.415	0.63	0.42786
ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<ci<		Arg	109(0.88)	83(0.86)	Ref			
refs2886T C C C C C C C C C C C C 		Gly	15(0.12)	13(0.14)	0.879	0.396-1.947	0.10	0.74980
rr CC <td>rs454886</td> <td>TT</td> <td>25(0.44)</td> <td>24(0.50)</td> <td>Ref</td> <td></td> <td></td> <td></td>	rs454886	TT	25(0.44)	24(0.50)	Ref			
CC T C70.12) 78.00.4140.08)r439552Val(val) 		СТ	25(0.44)	20(0.42)	1.200	0.533-2.703	0.19	0.65979
rd c70 30(3.4)86(0.7) 2000Ref		CC	7(0.12)	4(0.08)				
r. 495952Val/Val Val/Val490(0.9)28(0.28)1.2630.703 - 2.3690.610.43480r. 495952Val/Val Ag/Ag170.027)14(0.29)0.8750.376 - 2.0370.100.75972Ag/Ag130.032)20(0.15)Ref0.435 - 1.6560.230.62998r. 40923(0.18)20(0.17)Ref0.230.6690.869Age23(0.18)10(0.27)Ref0.231 - 2.3740.360.869C100(0.4)10(0.27)2.3120.231 - 2.3140.310.4686C100(0.4)10(0.27)1.1670.533 - 2.5560.150.58273C100(0.4)10(0.27)1.1670.334 - 1.8230.100.51274C100(0.11)100(0.11)1.1670.394 - 1.8230.100.51274C100(0.12)100(0.11)1.1670.394 - 1.8230.100.91071C100(0.12)100(0.11)1.0740.31 - 1.830.100.91071C100(0.12)100(0.11)1.0740.31 - 1.830.100.91071C100(0.12)100(0.10)0.7560.464 - 1.2170.000.92731C100(0.11)100(0.11)1.037Ref1.0371.037C100(0.11)100(0.11)0.371 - 2.8990.000.9472C100(0.11)1.037Ref1.0371.0371.037C100(0.11)1.037Ref1.0371.0371.037C </td <td></td> <td>Т</td> <td>75(0.66)</td> <td>68(0.71)</td> <td>Ref</td> <td></td> <td></td> <td></td>		Т	75(0.66)	68(0.71)	Ref			
refs2552Nulkay Valkay Nulkay31(0.63)RefNulkay Nulkay17(0.27)14(0.05)0.7300.156-3.8130.150.6590Nulkay Nulkay10(0.02)78(0.08)0.210.156-3.8130.150.6590Nulkay Nulkay10(0.02)78(0.08)0.435-1.6560.230.6591R2075241GG48(0.76)10(0.21)0.8240.316-2.7340.030.67714CG10(0.11)10(0.21)0.8240.316-2.7340.030.67714CG10(0.11)10(0.21)0.8240.316-2.7340.010.67714CG10(0.11)10(0.21)0.8160.333-2.5560.150.6992152244396T280(0.8)660.09)Ref0.010.57718CG10(0.11)10(0.21)10(0.21)0.341-1.8230.010.5771815325610(1.01)10(0.21)10(0.21)0.3691.660.96153276851110(1.01)10(0.21)0.7560.046-12.5170.040.8415323086T10(0.15)15(0.16)0.5690.046-12.5170.040.8415323086T27(0.03)37(0.40)0.660.5590.700.4415323086T27(0.35)27(0.44)0.660.5690.559-1.6530.700.4415323086T27(0.35)27(0.44)0.660.5690.559-1.6530.700.8415323086T27(0.35)27(0.44)0.66<		С	39(0.34)	28(0.29)	1.263	0.703-2.269	0.61	0.43469
Name Anylow<	rs459552	Val/Val	43(0.68)	31(0.65)	Ref			
Ang/App Val3(0.6b) (10)3(0.6b) (20)0.721 (20)0.38-3813 (20)0.150.69920 (20)r2075241GG (GC (C) (C		Val/Asp	17(0.27)	14(0.29)	0.875	0.376-2.037	0.10	0.75747
NameNameNameNameNameNameNameNameNameName12/075241GC18(0.76)70(0.71)RefNameNameNameName12/075241GC12(0.14)10(0.2)2.3120.231-23.1450.540.540.5612/07524112(0.14)12(0.37)7.1670.331-2560.550.560.58212/22439512/07.16112(0.31)1.1670.331-2560.350.570.57214812/22439512/07.16113(0.31)1.1670.331-2570.300.582730.57214812/22439512/07.16138(0.81)66(0.68)Ref0.010.010160.582730.010.58273413/73551112/07.1134(0.71)84(0.71)0.410710.4100.581-1.3880.010.59714813/73551110/01.1110/0210.7560.425-2.0020.010.68440.614-1.51713/73551110/01.1110/0210.7560.455-2.0020.010.49417215/735110/01.1110/0210.7560.271-2.8990.700.49417215/735116/01.1110/01.110.6880.391-1.6350.620.68915/735216/01.1115/01.110.6890.391-1.6350.620.68915/735316/02.1110/01.110.5690.591-1.6510.010.58915/735316/01.1110/01.110.5690.591-1.6510.100.59215/7353 <td></td> <td>Asp/Asp</td> <td>3(0.05)</td> <td>3(0.06)</td> <td>0.721</td> <td>0.136-3.813</td> <td>0.15</td> <td>0.69920</td>		Asp/Asp	3(0.05)	3(0.06)	0.721	0.136-3.813	0.15	0.69920
r2075241GG48(0.7)0.707Refr2075241GG48(0.7)10(0.21)0.9250.360-2.3740.630.67118CC100(0.86)84(0.87)Ref0.333-2.5560.150.68982r2284396TT19(0.31)1.070.333-2.5560.150.68982r2284397TT19(0.16)6(0.13)1.1670.533-2.5560.150.68982r3763511C45(0.5)6(0.6)Ref0.341-1.8230.300.791r3763511C45(0.7)84(0.7)84(0.7)0.581-1.8380.010.97141r3763511C45(0.7)30(0.21)0.9880.441-1.5170.000.978418r1710(0.15)10(0.10)0.5990.449-1.5170.000.978418r1710(0.15)10(0.2)0.7880.449-2.0020.100.91095r3763511C45(0.2)10(0.2)0.5990.459-2.0020.010.91095r3923086TT19(0.21)18(0.37)Ref70.020.94942r3923086TT722(0.35118(0.37)Ref0.010.91094r3923087AA15(0.24)16(0.31)Ref0.020.9200.91r3923086TT722(0.35116(0.31)Ref0.020.920r3923087AA15(0.24)16(0.31)Ref0.020.9200.91r3923087AA15(0.24)16(0.31)Ref0.02		Val	103(0.82)	76(0.79)	Ref			
r2075241GG GC 		Asp	23(0.18)	20(0.21)	0.849	0.435-1.656	0.23	0.62996
SC    12(0.19)    10(0.21)    2.312    0.330-2.374    0.30    0.57118      CC    108(0.56)    84(0.87)    Ref	rs2075241	GG	48(0.76)	37(0.77)	Ref			
rd    30.04)    10.02    2.312    0.231-34.54    0.4    0.4606      C    180.14)    12(0.13)    1.167    0.533-556    0.5992      rs2284396    T    32(0.52)    24(0.50)    Ref		GC	12(0.19)	10(0.21)	0.925	0.360-2.374	0.03	0.87118
G184(0.87)84(0.87)Refr12284395C18(0.65)24(0.50)Refr2284395T32(0.52)24(0.50)Refr18(0.10)6(0.13)1.2500.334-1.8230.00r83(0.82)30(0.31)1.0340.38-1.9380.01r83(0.32)30(0.31)1.0340.43-1.8380.01r83(0.32)30(0.31)1.0340.43-1.3880.04r70(27)13(0.27)0.9880.423-2.3080.04r107(0.85)81(0.84)Ref100(21)0.97560.464-12.517r107(0.85)81(0.84)Ref100(21)0.97560.464-2.517r107(0.85)81(0.84)Ref100(21)0.371-2.8990.00r27(0.13)18(0.37)Ref100(21)0.371-2.8990.00r27(0.13)18(0.37)Ref100(21)0.371-2.8990.00r7627(0.51)140(22)9(0.19)0.371-2.8990.00r7627(0.51)140(22)0.593-4.4330.620.472r7630(0.41)1.4450.593-4.4330.620.472r77(0.50)Ref1211.4450.462-2.611.42r7627(0.57)24(0.50)Ref1.4451.420.758r7627(0.57)24(0.52)Ref1.4451.420.758r7627(0.57)24(0.52)R		CC	3(0.04)	1(0.02)	2.312	0.231-23.145	0.54	0.46406
c    18(0.14)    12(0.3)    1.67    0.53.255    0.15    0.69822      n2284396    T    22(0.50)    Ref    0.39    0.39    0.30    0.53279      C    19(0.31)    18(0.37)    0.792    0.341.1232    0.30    0.392      C    38(0.68)    66(0.69)    Ref    0.0101    0.0101      r3753511    CC    45(0.71)    34(0.71)    Ref    0.010    0.9781      TT    19(0.15)    15(0.16)    0.959    0.435-2.062    0.01    0.91095      r3753511    CC    45(0.71)    16(0.10)    0.959    0.459-2.002    0.01    0.91095      r37323082    T    72(0.13)    18(0.37)    Ref    0.00    0.94172      r53923087    AA    15(0.24)    18(0.33)    Ref    0.3071-2.893    0.00    0.94172      r53923087    AA    15(0.24)    18(0.33)    Ref    0.70    0.91    0.927      r53923087    AA    15(0.24)    18(0.33)		G	108(0.86)	84(0.87)	Ref			
ris2284396T C<		C	18(0.14)	12(0.13)	1.167	0.533-2.556	0.15	0.69982
rd    90.01)    180.07)    0.72    0.349    0.30    0.352/9      r    830.08)    66(0.6)    Ref    0.399-3017    0.15    0.010      rs3763511    CC    45(0.71)    34(0.71)    Ref    7    0.027    0.038    0.423-2.308    0.01    0.93783      r    17(0.27)    13(0.27)    0.788    0.423-2.308    0.00    0.93783      r    19(0.15)    13(0.16)    0.399    0.459-2.002    0.01    0.91783      r    19(0.15)    110(0.2)    0.756    0.046-12.517    0.04    0.9478      r    19(0.15)    110(0.2)    0.767    0.459-2.002    0.01    0.9187      r    19(0.15)    110(0.2)    0.776    0.459-2.002    0.00    0.9447      r    70(0.68)    9(1.94)    1.037    0.77    7    0.00    0.9477      r    70(0.40)    30(0.40)    9692    0.591-1.633    0.02    0.9472      r    70(70,13)    16(0.3	rs2284396	TT	32(0.52)	24(0.50)	Ref			
CC T C    100.16) 30(0.3)    60.13) 60(0.6) 80(0.3)    1.280 80(0.3)    0.399-3.917    0.15    0.7014 80(0.3)      153763511    C    30(0.3)    30(0.3)    1.034    0.399-3.917    0.01    0.010      153763511    C    470(0.27)    13(0.27)    0.988    0.426-2.308    0.00    0.97781      15376351    C    107(0.5)    110021    0.958    0.426-2.308    0.00    0.97781      150    19(0.15)    15(0.16)    0.959    0.426-2.308    0.01    0.94442      150    19(0.15)    15(0.16)    0.959    0.459-2.002    0.01    0.94472      150    19(0.15)    15(0.16)    0.959    0.301-6.25    0.70    0.44417      150    10(0.2)    9(0.19)    1.037    0.37    2.80    0.20    0.88712      153    22(0.35)    21(0.44)    0.962    0.559-1.633    0.02    0.88721      153    40(0.2)    142(0.20)    8(0.17)    2.318    0.598-3.433    0.62    0.43258		TC	19(0.31)	18(0.37)	0.792	0.344-1.823	0.30	0.58279
T C 		CC	10(0.16)	6(0.13)	1.250	0.399-3.917	0.15	0.70148
c    39(0.32)    30(0.31)    1.034    0.91.1838    0.01    0.9010      rs3763511    C    40(71)    34(0.71)    0.988    0.423-2.308    0.00    0.9781      r    10.01)    10.02)    0.761    0.046-12.517    0.04    0.84438      c    10(0.05)    18(0.04)    Ref    0.01    0.91095      r    13(0.15)    15(0.16)    0.959    0.030-1.625    0.70    0.040472      r    22(0.35)    21(0.44)    0.698    0.300-1.625    0.70    0.84722      r    76(0.60)    57(0.60)    Ref		Т	83(0.68)	66(0.69)	Ref			
rs3763511CC C TT T(0.01)49(071) 10202Ref 0.756U 0.046-12.5170.04 0.0490.93784rs323086TT T T27(013)15(016)0.9590.459-2.0020.010.91095rs323086TT C C C27(013)15(016)0.9590.459-2.0020.010.91095rs323086TT C C C C27(013)15(016)0.9590.300-1.5250.700.404172rs323086TT C C C16(060)77(060)Ref T T T T C77(060)RefTTrs323087A C C16(025)8(0.17)1.4320.589-3.4330.620.43288rs323087A C C C16(025)8(0.17)1.4220.589-3.4330.620.43288rs4791171AA C C A C26(04)140241.4420.846-2.4681.820.16358rs4791171AA C C C C21(0.44)20(04)1.4220.391-2.1070.050.38258rs4791171AA C C C CAC C C21(0.35)T(0.35)RefTTrs4191171AA C C C CAC C C21(0.35)17(0.35)RefTT0.050.391-2.1070.050.3825.380rs4191171AA C C C C C C C C C C16(0.31)RefTT0.100.5520.570.420.500.42rs4191171AA C <td></td> <td>C</td> <td>39(0.32)</td> <td>30(0.31)</td> <td>1.034</td> <td>0.581-1.838</td> <td>0.01</td> <td>0.91001</td>		C	39(0.32)	30(0.31)	1.034	0.581-1.838	0.01	0.91001
CT    170.27    130.27    0.988    0.423-3.208    0.00    0.97781      C    107(0.85)    81(0.84)    Per    0.044-12.517    0.04    0.84438      T    19(0.15)    15(0.16)    0.959    0.459-2.002    0.01    0.91095      T3322086    TT    27(0.13)    18(0.37)    Ref	rs3763511	СС	45(0.71)	34(0.71)	Ref			
Tr C    1001    1002    0.756    0.046-12.517    0.04    0.84438      T    190.15)    150.16)    0.599    0.459-2.002    0.01    0.91085      rs3923086    TT    27(0.13)    18(0.37)    Ref    7    0.00    0.94472      CG    14(0.22)    9(0.19)    1.037    0.371-2.899    0.00    0.94472      CG    16(0.23)    9(0.49)    0.962    0.559-1.653    0.02    0.88712      rs3923087    AG    15(0.24)    16(0.33)    Ref    7    0.01    0.17521      AG    32(0.51)    24(0.50)    1.422    0.589-3.433    0.62    0.43258      GG    16(0.23)    8(0.17)    2.133    0.708-6.428    1.84    0.17521      AG    32(0.51)    7(0.68)    Ref    7    0.05    0.82058      GG    64(0.51)    40(0.42)    1.445    0.391-2.107    0.5    0.82058      rs4791171    GG    27(0.44)    23(0.49)    0.907		СТ	17(0.27)	13(0.27)	0.988	0.423-2.308	0.00	0.97781
C    107(0.85)    81(0.84)    Ref      r53923086    TT    27(0.13)    18(0.37)    Ref      TG    22(0.35)    21(0.44)    0.698    0.300-1.62.90    0.00    0.94472      TG    22(0.35)    21(0.44)    0.698    0.300-1.62.90    0.00    0.94472      TG    22(0.35)    21(0.44)    0.698    0.300-1.62.90    0.00    0.94472      TG    20(0.01)    39(0.40)    39(0.40)    0.599-1.653    0.02    0.88712      r53923087    AA    15(0.24)    16(0.33)    Ref		TT	1(0.01)	1(0.02)	0.756	0.046-12.517	0.04	0.84438
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		C	107(0.85)	81(0.84)	Ref			
rs3923086    TT    27(0.13)    18(0.37)    Ref      rs3923086    TT    22(0.35)    21(0.42)    9(0.19)    1.037    0.371-2.899    0.00    0.94472      rs    76(0.60)    S7(0.60)    Ref		Т	19(0.15)	15(0.16)	0.959	0.459-2.002	0.01	0.91095
TG    22(0.35)    21(0.44)    0.698    0.300-1.625    0.70    0.40417      T    76(0.60)    57(0.60)    Ref    0.371-2.899    0.00    0.94472      T    76(0.60)    57(0.60)    Ref    1.02    0.859-1.653    0.62    0.43258      AG    32(0.51)    24(0.50)    1.422    0.589-3.433    0.62    0.43258      GG    62(0.49)    56(0.58)    Ref    1.84    0.17521      A    62(0.49)    56(0.58)    Ref    1.84    0.17521      G    64(0.51)    40(0.42)    1.445    0.846-2.483    1.82    0.17692      K4791171    AG    27(0.44)    23(0.48)    0.907    0.391-2.107    0.05    0.82058      GG    13(0.21)    8(0.17)    1.256    0.424-3.714    0.10    0.559-1.653      K4791171    AG    53(0.43)    39(0.40)    1.091    0.635-1.874    0.10    0.559-1.53      K4791171    AG    53(0.43)    39(0.40)    1.091	rs3923086	TT	27(0.13)	18(0.37)	Ref			
GG140.2290.0191.030.371-2.8990.000.4472760.607760.607867		TG	22(0.35)	21(0.44)	0.698	0.300-1.625	0.70	0.40417
T    76(0.60)    57(0.60)    Ref      rs3923087    AA    15(0.24)    16(0.33)    Ref		GG	14(0.22)	9(0.19)	1.037	0.371-2.899	0.00	0.94472
		Т	76(0.60)	57(0.60)	Ref			
rs3923087    AA    15(0,24)    16(0.3)    Ref      AG    32(0,51)    24(0,50)    1,122    0.589-3,433    0.62    0.43258      GG    16(0.25)    8(0,17)    2,132    0.708-6,428    1,84    0.17521      A    62(0,49)    56(0,58)    Ref		G	50(0.40)	39(0.40)	0.962	0.559-1.653	0.02	0.88712
AG    32(051)    24(050)    1.422    0.589-3.433    0.62    0.43258      A    62(0.49)    56(0.58)    Ref	rs3923087	AA	15(0.24)	16(0.33)	Ref			
GG    16(0.25)    8(0.17)    2.133    0.708-6.428    1.84    0.7211      G    64(0.51)    40(0.42)    1.445    0.846-2.468    1.82    0.17698      rs4791171    AA    22(0.35)    17(0.35)    Ref		AG	32(0.51)	24(0.50)	1.422	0.589-3.433	0.62	0.43258
A    62(0.49)    56(0.58)    Ref      rs4791171    AA    22(0.35)    17(0.35)    Ref      rs4791171    AA    22(0.35)    17(0.35)    Ref      GG    13(0.21)    8(0.17)    1.266    0.391-2.107    0.05    0.82058      GG    13(0.21)    8(0.17)    1.266    0.424-3.714    0.10    0.75223      rs4135385    AA    42(0.70)    33(0.69)    Ref		GG	16(0.25)	8(0.17)	2.133	0.708-6.428	1.84	0.17521
G    64(0.51)    40(0.42)    1.445    0.846-2.468    1.82    0.17698      rs4791171    AA    22(0.35)    17(0.35)    Ref		A	62(0.49)	56(0.58)	Ref			
rs4791171  AA  22(0.35)  17(0.35)  Ref    AG  27(0.44)  23(0.48)  0.907  0.391-2.107  0.05  0.82058    GG  13(0.21)  8(0.17)  1.256  0.424-3.714  0.17  0.68052    A  71(0.57)  57(0.60)  Ref		G	64(0.51)	40(0.42)	1.445	0.846-2.468	1.82	0.17698
AG    27(0.44)    23(0.48)    0.907    0.391-2.107    0.05    0.82058      AG    13(0.21)    8(0.17)    1.256    0.424-3.714    0.17    0.650      A    71(0.57)    57(0.60)    Ref	rs4791171	AA	22(0.35)	17(0.35)	Ref			
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		AG	27(0.44)	23(0.48)	0.907	0.391-2.107	0.05	0.82058
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		GG	13(0.21)	8(0.17)	1.256	0.424-3.714	0.17	0.68052
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		A	71(0.57)	57(0.60)	Ref			
rs4135385  AA  42(0.70)  33(0.69)  Ref    AG  18(0.30)  13(0.27)  1.088  0.467-2.537  0.04  0.84532    AG  00(0)  2(0.04)  0.158  0.467-2.537  0.246  0.11648    A  102(0.85)  79(0.82)  Ref		G	53(0.43)	39(0.40)	1.091	0.635-1.874	0.10	0.75223
AG    18(0.30)    13(0.27)    1.088    0.467-2.537    0.04    0.84532      GG    0(0.0)    2(0.04)    0.158    0.007-3.396    2.46    0.11648      A    102(0.85)    79(0.82)    Ref    0.29    0.59143      rs13072632    CC    23(0.37)    16(0.33)    Ref    0.29    0.59143      TT    12(0.19)    7(0.16)    1.193    0.325-1.738    0.45    0.50348      TT    12(0.19)    7(0.16)    1.193    0.385-3.690    0.09    0.75985      C    73(0.59)    57(0.59)    Ref    0.45    0.01    0.93989      T    51(0.41)    39(0.41)    1.021    0.594-1.756    0.01    0.93989      rs6485350    AA    25(0.42)    18(0.37)    Ref    0.46    0.44    0.31    0.31    0.31    0.31    0.3168      GG    25(0.42)    18(0.37)    0.400    0.425-2.356    0.00    1    0.32504    0.33168    0.3168    0.3168	rs4135385	AA	42(0.70)	33(0.69)	Ref			
GG A    0(0.0)    2(0.04)    0.158    0.007-3.396    2.46    0.11648      A    102(0.85)    79(0.82)    Ref		AG	18(0.30)	13(0.27)	1.088	0.467-2.537	0.04	0.84532
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		GG	0(0.0)	2(0.04)	0.158	0.007-3.396	2.46	0.11648
G    18(0.15)    17(0.18)    0.820    0.397-1.693    0.29    0.59143      rs13072632    CC    23(0.37)    16(0.33)    Ref		A	102(0.85)	79(0.82)	Ref			
rs13072632  CC  23(0.37)  16(0.33)  Ref    CT  27(0.44)  25(0.52)  0.751  0.325-1.738  0.45  0.50348    TT  12(0.19)  7(0.16)  1.193  0.385-3.690  0.09  0.75985    C  73(0.59)  57(0.59)  Ref  0.01  0.93989    rs6485350  AA  25(0.42)  18(0.37)  1.021  0.594-1.756  0.01  0.93989    rs6485350  AA  25(0.42)  18(0.37)  1.001  0.425-2.356  0.00  1    GG  25(0.42)  18(0.37)  1.000  0.425-2.356  0.00  1    AG  25(0.42)  18(0.37)  1.000  0.425-2.356  0.00  1    GG  10(0.16)  12(0.25)  0.600  0.213-1.689  0.94  0.33168    A  75(0.62)  54(0.56)  Ref  1  10  1.00  0.446-1.333  0.87  0.35204    rs12255372  GG  22(0.35)  23(0.48)  Ref  1  1  1.150  0.446-1.333  0.07  0.79157		G	18(0.15)	17(0.18)	0.820	0.397-1.693	0.29	0.59143
CT    27(0.44)    25(0.52)    0.751    0.325-1.738    0.45    0.50348      TT    12(0.19)    7(0.16)    1.193    0.385-3.690    0.09    0.75985      C    73(0.59)    57(0.59)    Ref    0.01    0.93989      rs6485350    AA    25(0.42)    18(0.38)    Ref    0.01    0.93989      rs6485350    AA    25(0.42)    18(0.37)    1.000    0.425-2.356    0.00    1      AG    25(0.42)    18(0.37)    1.000    0.213-1.689    0.04    0.33168      AG    25(0.42)    18(0.37)    1.000    0.213-1.689    0.00    1      AG    25(0.42)    18(0.37)    1.000    0.213-1.689    0.04    0.33168      A    75(0.62)    54(0.56)    Ref    0.033168    0.07    0.35204      Fs12255372    GG    22(0.35)    23(0.48)    Ref    0.07    0.07    0.07      TT    11(0.18)    10(0.21)    1.150    0.860-4.750    2.63	rs13072632	CC	23(0.37)	16(0.33)	Ref			
TT    12(0.19)    7(0.16)    1.193    0.385-3.690    0.09    0.75985      C    73(0.59)    57(0.59)    Ref    0    0.09    0.93989      rs6485350    AA    25(0.42)    18(0.38)    Ref    0.00    0.00    0.00    0.93989      rs6485350    AA    25(0.42)    18(0.37)    1.000    0.425-2.356    0.00    1      AG    25(0.42)    18(0.37)    1.000    0.213-1.689    0.94    0.33168      AG    75(0.62)    54(0.56)    Ref    0.033168    0.075    0.00    0.213-1.689    0.94    0.33168      AG    75(0.62)    54(0.56)    Ref    0.033168    0.071    0.446-1.333    0.87    0.35204      rs12255372    GG    22(0.35)    23(0.48)    Ref    0.071    0.446-1.333    0.07    0.79157      GT    29(0.47)    15(0.31)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-		СТ	27(0.44)	25(0.52)	0.751	0.325-1.738	0.45	0.50348
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$		TT	12(0.19)	7(0.16)	1.193	0.385-3.690	0.09	0.75985
T    51(0.41)    39(0.41)    1.021    0.594-1.756    0.01    0.93989      rs6485350    AA    25(0.42)    18(0.38)    Ref		C	73(0.59)	57(0.59)	Ref			
rs6485350    AA    25(0.42)    18(0.38)    Ref      AG    25(0.42)    18(0.37)    1.000    0.425-2.356    0.00    1      GG    10(0.16)    12(0.25)    0.600    0.213-1.689    0.94    0.33168      A    75(0.62)    54(0.56)    Ref		Т	51(0.41)	39(0.41)	1.021	0.594-1.756	0.01	0.93989
AG    25(0.42)    18(0.37)    1.000    0.425-2.356    0.00    1      GG    10(0.16)    12(0.25)    0.600    0.213-1.689    0.94    0.33168      A    75(0.62)    54(0.56)    Ref	rs6485350	AA	25(0.42)	18(0.38)	Ref			
GG    10(0.16)    12(0.25)    0.600    0.213-1.689    0.94    0.33168      A    75(0.62)    54(0.56)    Ref    0.35204    0.000    0.446-1.333    0.87    0.35204      rs12255372    GG    22(0.35)    23(0.48)    Ref    0.10459    0.10459      TT    29(0.47)    15(0.31)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref    0.010459    0.010459    0.010459      T    51(0.41)    35(0.36)    1.218    0.704-2.107    0.50    0.48137		AG	25(0.42)	18(0.37)	1.000	0.425-2.356	0.00	1
A    75(0.62)    54(0.56)    Ref      G    45(0.38)    42(0.44)    0.771    0.446-1.333    0.87    0.35204      rs12255372    GG    22(0.35)    23(0.48)    Ref    54(0.51)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref    51(0.41)    35(0.36)    1.218    0.704-2.107    0.50    0.48137		GG	10(0.16)	12(0.25)	0.600	0.213-1.689	0.94	0.33168
G    45(0.38)    42(0.44)    0.771    0.446-1.333    0.87    0.35204      rs12255372    GG    22(0.35)    23(0.48)    Ref         0.87    0.35204      rs12255372    GG    22(0.35)    23(0.48)    Ref         0.10459      TT    29(0.47)    15(0.31)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref          T    51(0.41)    35(0.36)    1.218    0.704-2.107    0.50    0.48137		Α	75(0.62)	54(0.56)	Ref			
rs12255372    GG    22(0.35)    23(0.48)    Ref      GT    29(0.47)    15(0.31)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref    7    0.50    0.48137		G	45(0.38)	42(0.44)	0.771	0.446-1.333	0.87	0.35204
GT    29(0.47)    15(0.31)    2.021    0.860-4.750    2.63    0.10459      TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref	rs12255372	GG	22(0.35)	23(0.48)	Ref			
TT    11(0.18)    10(0.21)    1.150    0.408-3.243    0.07    0.79157      G    73(0.59)    61(0.64)    Ref    7    7    51(0.41)    35(0.36)    1.218    0.704-2.107    0.50    0.48137		GT	29(0.47)	15(0.31)	2.021	0.860-4.750	2.63	0.10459
G    73(0.59)    61(0.64)    Ref      T    51(0.41)    35(0.36)    1.218    0.704-2.107    0.50    0.48137		TT	11(0.18)	10(0.21)	1.150	0.408-3.243	0.07	0.79157
<u>1 51(0.41) 35(0.36) 1.218 0.704-2.107 0.50 0.48137</u>		G	73(0.59)	61(0.64)	Ref	0.004 0.405	0.50	
		Т	51(0.41)	35(0.36)	1.218	0.704-2.107	0.50	0.48137

Distribution of WNT pathway gene SNPs genotype and allele frequencies in colorectal cancer cases and control population based on age (>57).

SNP	Variant	Cases (Freq)	Controls	OR	CI	$\chi^2$ Value	P-Value
rs7775	Arg/Arg	48 (0.80)	40 (0.65)	Ref			
	Arg/Gly	11 (0.18)	21(0.34)	0.437	0.188-1.013	3.82	0.05064
	Gly/Gly	1 (0.02)	1 (0.01)	0.833	0.051-13.750	0.02	0.89844
	Arg	107(0.89)	101 (0.81)	Ref			
	Gly	13 (0.11)	23 (0.19)	0.534	0.256-1.110	2.89	0.08935
rs454886	TT	28(0.47)	29 (0.47)	Ref			
	CT	29 (0.48)	24 (0.39)	1.251	0.591-2.649	0.34	0.55739
	CC T	3 (0.05)	9 (0.14)	0.345 Rof	0.085-1.409	2.33	0.12679
	C	35 (0.29)	42 (0.33)	0.804	0.468-1.382	0.62	0.42925
rc450552	Val/Val	45 (0.76)	(1) (0.66)	Pof			
13433332	Val/Asn	13 (0.22)	21 (0.34)	0 564	0 251-1 269	1 94	0 16397
	Asp/Asp	1 (0.02)	0(0.0)	2.736	0.108-69.043	0.90	0.34233
	Val	103(0.87)	103(0.83)	Ref			
	Asp	15 (0.13)	21 ()0.17	0.714	0.349-1.463	0.85	0.35605
rs2075241	GG	44 (0.75)	39 (0.65)	Ref			
	GC	12 (0.20)	21 (0.35)	0.506	0.221-1.162	2.62	0.10546
	CC	3 (0.05)	00.0	6.213	0.311-124.055	2.58	0.10827
	G	100(0.85)	99 (0.82)	Ref			
	C	18 (0.15)	21 (0.18)	0.849	0.426-1.689	0.22	0.63980
rs2284396	TT	32 (0.53)	26 (0.43)	Ref			
	TC	24 (0.40)	22 (0.36)	0.886	0.408-1.926	0.09	0.76063
	CC	4 (0.07)	13 (0.21)	0.250	0.073-0.859	5.27	0.02165
	I C	88 (0.73)	74 (0.60) 48 (0.40)	Ker 0.561	0.225 0.066	4 20	0.02607
0500514	C	32 (0.27)	48 (0.40)	0.501	0.323-0.900	4.55	0.03007
rs3763511	CC	42 (0.70)	46 (0.74)	Ref	0.452 2.220	0.00	0.04059
	TT	15(0.25) 3(0.05)	0(0.20)	7 659	0.455-2.550	0.00	0.94958
	C	99 (0.82)	108(0.87)	Ref	0.504 152.042	5.17	0.07455
	Т	21 (0.18)	16 (0.13)	1.432	0.707-2.899	1.00	0.31691
rs3923086	TT	21 (0.36)	23 (0.37)	Ref			
	TG	30 (0.52)	29 (0.47)	1.133	0.519-2.475	0.10	0.75405
	GG	7 (0.12)	10 (0.16)	0.767	0.247-2.380	0.21	0.64528
	Т	72 (0.62)	75 (0.60)	Ref			
	G	44 (0.38)	49 (0.40)	0.935	0.556-1.573	0.06	0.80113
rs3923087	AA	20 (0.33)	21 (0.34)	Ref			
	AG	24 (0.40)	26 (0.42)	0.969	0.424-2.215	0.01	0.94091
	GG	16 (0.27)	15 (0.24)	1.120	0.440-2.848	0.06	0.81187
	A C	64 (0.53) 56(0.47)	56 (0.55)	1.062	0.642-1.758	0.06	0.81350
		50(0.47)	50 (0.45)	1.002	0.042-1.758	0.00	0.81550
rs4791171	AA	18 (0.30)	21 (0.33)	Ref	0.570. 2.004	0.40	0 52670
	AG CC	28 (0.47) 14 (0.23)	25 (0.40)	1.307	0.370-2.994	0.40	0.52679
	A	64 (0.53)	67 (0.54)	Ref	0.555 2.051	0.00	0.50022
	G	56 (0.47)	57 (0.46)	1.029	0.622-1.701	0.01	0.91284
rs4135385	AA	47 (0 78)	41 (0.66)	Ref			
131133303	AG	13 (0.22)	19 (0.31)	0.597	0.263-1.356	1.53	0.21550
	GG	0 (0.0)	2 (0.03)	0.175	0.008-3.745	2.24	0.13485
	Α	107(0.89)	101(0.81)	Ref			
	G	13 (0.11)	23 (0.19)	0.534	0.256-1.110	2.89	0.08935
rs13072632	CC	28 (0.47)	30 (0.48)	Ref			
	CT	20 (0.34)	26 (0.42)	0.824	0.379-1.794	0.24	0.62595
	TT	11 (0.19)	6 (0.10)	1.964	0.641-6.021	1.42	0.23310
	C T	76 (0.64) 42 (0.36)	38 (0.09) 38 (0.31)	1 251	0 731_2 130	0.67	0 /13/2
			10 (0.31)	1.2J1	0.731-2.133	0.07	0.71342
rs6485350	AA	21 (0.36)	18 (0.29)	Ket	0 272 1 0 4 0	0.21	0 64972
	AG GG	51 (0.53) 7 (0.11)	52 (0.52) 12 (0.19)	0.830	0.575-1.848	1.48	0.04873
	A	73 (0.62)	68 (0 55)	Ref	0.102-1.340	1.70	0.22300
	G	45 (0.38)	56 (0.45)	0.749	0.448-1.250	1.23	0.26793
rs12255372	GG	25 (0.43)	26 (0.42)	Ref			
	GT	27 (0.47)	31 (0.50)	0.906	0.426-1.924	0.07	0.79687
	TT	6 (0.10)	5 (0.09)	1.248	0.338-4.614	0.11	0.73956
	G	77 (0.67)	83 (0.67)	Ref			
	Т	39 (0.33)	41 (0.33)	1.025	0.599-1.754	0.01	0.92722

to demonstrate its role in colorectal carcinogenesis as well as other diseases.

Significant risk association of developing colorectal cancer was not observed with 12 of the 13 SNPs examined in AXIN2, APC, SFRP3, LRP6, DKK3, DKK4, and TCF4 as well as with one of the SNPs in  $\beta$ -catenin gene (rs13072632) in the overall study population (Table 2). Fernández-Rozadilla and colleagues examined a set of 37 SNPs in Wnt and BMP pathways different than those in our study except for rs459552 in APC and observed no association with colorectal cancer in Spanish population (Fernandez-Rozadilla et al., 2010). It may be conceived that individually these SNPs might be posing little or no risk and may be exerting its effect in combination with other genetic variants or factors. Alternatively, other SNPs in these genes or possibly other genes in the Wnt pathway may have a greater role to play in the initiation of colorectal cancers.

In the present study, we performed pathway based genetic association and identified three SNPs in critical genes in Wnt signaling to be significantly associated with reduced colorectal cancer risk. Genetic variants in SFRP3 (rs7775),  $\beta$ -catenin (rs4135385) and LRP6 (rs2284396) genes correlated with considerable protection against colorectal cancer in our population. Though, the sample size is small in our study, the findings are noteworthy that need to be validated in larger and ethnically diverse groups for the identified potential genetic markers to be used for colorectal cancer screening.

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