

## 기관고유연구사업 최종보고서

연구분야(코드)		과제번호	1110300		지원 프로그램	창의 (일반연구)과제	
과제성격(기초,응용,개발)		실용화 대상여부	실용화/비실용화	공개가능여부 (공개,비공개)			
연구과제명	(국문) 한국인의 위암 1차 예방을 위한 식생활 관련 위험요인 규명 (영문) Dietary factors in the etiology of gastric cancer						
과제책임자	소 속	분자역학연구과	직 위	부 장			
	성 명	김 정 선	전 공	영양역학			
세부과제	구분	세부과제명			세부과제책임자		
					성명	소속(직위)	전 공
	1						
	2						
3							
총 연구기간	2011년 01월 ~ 2013년 12월(총3년)		참여연구원수 (단위: 명, MY)	5명			
연구기간 및 연구비 (단위:천원)	구분	연구기간	계	국립 암센터	기업부담금		
	계	2011.01~2013.12	370,000	370,000	소계	현금	현물
	제1차	2011.01~2011.12	130,000	130,000			
	제2차	2012.01~2012.12	120,000	120,000			
	제3차	2013.01~2013.12	120,000	120,000			
참여기업	명칭		전화		FAX		
<p>기관고유연구사업관리규칙에 따라 본 연구개발사업을 성실히 수행하였으며 아래와 같이 최종보고서를 제출합니다.</p> <p style="text-align: center;">2013년 10월 30일</p> <p style="text-align: center;">과제책임자    김 정 선 (서명)</p>							
국립 암 센터 원 장    귀 하							
(첨부서류)							

# 목 차

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## < 요약 문 >

<p>연구목표 (200자 이내)</p>	<p>&lt;최종목표&gt;</p> <ul style="list-style-type: none"> <li>- 한국인의 호발암종인 위암의 예방을 효율적으로 관리하기 위해 유전적 요인과 식생활을 포함하는 생활습관 요인의 영향, 미생물학적인 요인 및 상호작용의 규명을 통한 위암의 1차 예방 방안 제시하고자 함.</li> </ul> <p>&lt;당해연도목표&gt;</p> <ul style="list-style-type: none"> <li>- 신규 위암 환자로 진단받은 사람들 100명과 검진센터 건강한 사람들 200명의 식생활 (식품 또는 식품군)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집</li> </ul>												
<p>연구내용 및 방법 (500자 이내)</p>	<p>1) 연구 대상 및 기간</p> <ul style="list-style-type: none"> <li>- 환자군: 2011년 3월부터 2013년 10월까지 국립암센터 위암센터에서 신규 위암 환자로 진단된 위암 환자 400명</li> <li>- 대조군: 동기간에 확인된 환자군에 대해 연령, 성별로 1:2 짝짓기한 위암이 없는 수검자 800명</li> </ul> <p>2) 자료수집 내용 및 방법</p> <ul style="list-style-type: none"> <li>- 설문조사: 식이섭취, 음주, 흡연 등 암 위험요인, 인구통계학적 특성</li> <li>- serum / plasma             <ul style="list-style-type: none"> <li>· H. pylori 감염여부: ELISA kit 로 H.pylori IgG를 정량 측정함</li> <li>· H. pylori 아형 (Cag A, Vac A, babA, dupA) 확인: Western blot kit (Helico Blot 2.1 MP Biomedicals Asia Pacific, Singapore) 및 PCR를 이용하여 아형을 결정</li> </ul> </li> <li>- buffy coat에서 추출한 genomic DNA의 exome array 분석             <ul style="list-style-type: none"> <li>· Axiom 2.0 Reagent kit(Affymetrix, 901758)와 Axiom Exome 319 array plate(Affymetrix, 902106)를 이용하여 protocol을 따라 분석</li> </ul> </li> <li>- 내시경 검사에서 조직검사로 위염과 H. pylori 감염 여부 확인</li> </ul> <p>3) 자료의 분석</p> <ul style="list-style-type: none"> <li>- 각 군의 인구-사회학적 특성, 흡연, 음주, 질병 과거력 및 암 가족력 여부, virulence factor, 전적 다형성에 대한 단변수 분석은 chi-square 검정을 수행</li> <li>- 유전적, 환경적, 미생물학적 위험요인의 다변량분석 및 상호작용 검정은 logistic regression model을 이용하여 odds ratio 및 95% 신뢰구간을 산출</li> </ul>												
<p>연구개발에 따른 기대성과</p>	<p>&lt;정량적 성과<sup>1)</sup>&gt;</p> <table border="1" style="width: 100%; border-collapse: collapse; text-align: center;"> <thead> <tr> <th>구분</th> <th>달성치/목표치<sup>1)</sup></th> <th>달성도(%)</th> </tr> </thead> <tbody> <tr> <td>SCI 논문 편수</td> <td>5/5</td> <td>100</td> </tr> <tr> <td>IF 합</td> <td>10.757/10</td> <td>100</td> </tr> <tr> <td>기타 성과</td> <td></td> <td></td> </tr> </tbody> </table> <p>1) 총연구기간 내 목표연구성과로 기 제출한 값</p>	구분	달성치/목표치 <sup>1)</sup>	달성도(%)	SCI 논문 편수	5/5	100	IF 합	10.757/10	100	기타 성과		
구분	달성치/목표치 <sup>1)</sup>	달성도(%)											
SCI 논문 편수	5/5	100											
IF 합	10.757/10	100											
기타 성과													

		<정성적 성과> - 학술대회 발표를 통해 학술교류 - 대중매체를 통한 위암예방 교육 및 홍보		
색인어	국문	위암	영양평가	유전자-영양 상호작용
		헬리코박터 파이로리	유전자 다형성	영양역학
		위험요인		
	영문	gastric cancer	nutritional assessment	gene-nutrition interaction
		<i>Helicobacter pylori</i>	genetic polymorphism	nutritional epidemiology
		risk factor		

※ 요약문의 총분량은 2page 이내로 제한함

## Project Summary

<b>Title of Project</b>	Dietary factors in the etiology of gastric cancer
<b>Key Words</b>	gastric cancer, nutritional assessment, gene–nutrition interaction, <i>Helicobacter pylori</i> , genetic polymorphism, nutritional epidemiology
<b>Project Leader</b>	Jeongsoen Kim
<b>Associated Company</b>	National Cancer Center
<p>This study was aimed to investigate the effects of lifestyle and genetic factors as well as <i>H. pylori</i> infection, cigarette on the risk of gastric carcinogenesis. We have recruited 405 cases and 807 controls from National Cancer Center in a hospital–based case–control study design from March 2011 until present (as of Oct. 18th, 2013). The clinical information and genetic materials were obtained under the approval of the Institutional Review Board of the National Cancer Center in Korea, and written informed consent was obtained from each subject.</p> <p>The questionnaire data and blood samples were obtained at the initial recruitment of both cases and controls. All participants were asked to complete a self–administered questionnaire about their sociodemographic characteristics (e.g., age, family history of gastric cancer, income, and education), smoking habits, alcohol intake, and personal medical history. <i>H. pylori</i> infection status was determined by a rapid urease test and a histological evaluation. For the analysis of genetic variants, Affymetrix Axiom™ exome array was performed using Axiom®2.0 Reagent Kit (Affymetrix Axiom®2.0 Assay User Guide) according to manufacturer’s protocol.</p> <p>The demographic characteristics, environmental factors, and gene frequencies in cases and controls were compared using <math>\chi^2</math> statistics. The risk of gastric cancer was estimated by multivariate logistic regression with adjustments for all confounding variables and was expressed as odds ratios (ORs) with 95% confidence intervals (CIs).</p> <p>For the research outcomes three articles have been published and two articles are in press.</p> <ul style="list-style-type: none"> <li>– Gastric cancer epidemiology in Korea, Journal of Gastric Cancer, 2011;11(3):135–140.</li> <li>– Dietary flavonoid intake and smoking–related cancer risk: A meta–analysis, PLoS One 2013;8:e75604</li> <li>– Association of polymorphisms in the MCP–1 and CCR2 genes with the risk of cancer: A meta–analysis, Cytokine 2013;64:213–220</li> <li>– Effects of polymorphisms of innate immunity genes and environmental factors on the risk of noncardia gastric cancer Cancer Research and Treatment, in press</li> <li>– Gene–diet interactions in gastric cancer risk: A systematic review World Journal of Gastroenterology, in press</li> </ul>	

## 1. 연구의 최종목표

### 1) 연구의 최종 목표

- 한국인의 호발암종인 위암의 예방을 효율적으로 관리하기 위해 유전적 요인과 식생활을 포함하는 생활습관 요인의 영향, 미생물학적인 요인 및 상호작용의 규명을 통한 위암의 1차 예방 방안 제시하고자 함

### 2) 2013년도 목표

- 신규 위암 환자로 진단받은 사람들 100명과 검진센터 건강한 사람들 200명의 식생활 (식품 또는 식품군)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집

## 2. 연구의 내용 및 결과

### 가. 연구수행 방법

#### 1) 연구 대상 및 기간

- 환자군

· 2011년 3월부터 2013년 10월까지 국립암센터 위암센터에서 신규 위암 환자로 진단된 위암 환자 400명

· 국립암센터 위암센터에서 위암 치료를 위해 내원한 환자들 중 입적기준 (inclusion criteria)에 해당되면서 배제기준 (exclusion criteria)에 해당되지 않는 대상자들

#### ▷ 입적 기준(Inclusion criteria)

- 국립암센터에서 위암치료를 위해 내원한 20세 이상의 한국인 환자
- 위암을 새로 진단 받은 지 3개월 이내의 환자
- 연구에 참여하기로 동의한 환자

#### ▷ 배제 기준(Exclusion criteria)

- 본 연구에 동의하지 않은 환자
- 이전에 위암의 과거력이 있는 환자
- 진행성 위암으로 식이 습관의 변화가 있는 환자
- 위암의 원격장기의 전이가 있는 환자
- 위암으로 위출구 폐색이 있는 환자
- 위암으로 인한 출혈이 있었던 환자
- 5년 이내에 다른 암 (자궁경부의 carcinoma in situ 제외)으로 진단된 환자
- 다른 심각한 정신 동반 질환 환자
- 정신 병력이 있는 환자

- 임신 또는 수유 중인 환자
- 이전에 헬리코박터 감염 치료 경력이 있는 환자
- 대조군
- 동기간에 확인된 환자군에 대해 연령, 성별로 1:2 짝짓기한 위암이 없는 수검자 800명
- 국립암센터 암예방검진센터에서 위내시경 검사를 받아 위암 환자가 아닌 것으로 확인된 20세 이상 대상자 (이전에 헬리코박터 감염 치료 경력이 있는 환자 제외)

## 2) 자료 수집 내용 및 방법

### (1) 설문조사

- 훈련된 설문조사원이 식이섭취, 음주, 흡연 등 암 위험요인, 인구통계학적 특성을 면담을 통해 설문함

### (2) 생체시료

- 혈액채취는 훈련된 임상병리사가 7ml 채취하여 1~2시간 내에 buffy coat, RBC, plasma, serum 등으로 분리·분주하여 -80°C 냉동 보관함
- 내시경 검사 시에 정상 점막에서 약 2mm 크기의 조직을 5조각은 위염과 헬리코박터 검사를 시행하고, 2조각은 채취하여 헬리코박터 virulence factor에 대한 PCR용 검체로 보관함

### (3) 엑솜 어레이 (Exome array)

- 분석은 DNA Link에 의뢰하여 수행하였고 Affymetrix사 Axiom<sup>®</sup> Exome 319 Array 제품으로 엑솜(exome)을 포획하였다. Affymetrix Axiom Exome 319 array 분석방법은 다음과 같다.
- Axiom 2.0 Reagent kit(Affymetrix, 901758)와 Axiom Exome 319 array plate(Affymetrix, 902106)를 이용하여 제조사의 protocol을 따라 다음과 같이 진행하였다.
- Genomic DNA 200ng을 Denaturation master mix를 넣고 denaturation한 후 Axiom 2.0 Amp Soln 225 $\mu$ l와 Axiom 2.0 Amp Enzyme 5 $\mu$ l를 넣고 37°C에서 23 $\pm$ 1 시간 동안 amplification하였다. Amplification된 샘플에 Axiom 10X Frag buffer 45.7 $\mu$ l와 Axiom Frag Dilunt 10.3 $\mu$ l, Axiom Frag Enzyme 1 $\mu$ l를 넣고 40°C 에서 20분동안 incubation하여 25에서 125 base pair로 fragmentation하였다. 위의 product에 238 $\mu$ l의 Axiom Precip Soln1과 2 $\mu$ l의 Axiom Precip Soln2를 첨가한 후 600 $\mu$ l의 isopropanol을 첨가하고 -20°C에서 overnight하였다. 4°C에서 3200Xg로 40분동안 centrifuge하여 침전시키고 Resuspension soln 35 $\mu$ l를 넣어주었다. 70.5 $\mu$ l의 Axiom Hyb Buffer와 0.5 $\mu$ l의 axiom Hyb Soln1, 9 $\mu$ l의 Axiom Hyb Soln2를 첨가하였다. 최종 product의 size(25-125bp)를 E-Gel을 이용하여 확인하였다. GeneTitan MC Instrument(Affymetrix, Santa Clara, CA, USA)와 Axiom Exome 319 array plate(Affymetrix, 902106)를 이용하여 Hybridization과 Wash, Scan과정을 진행하였다. Scan이 완료되면 Genotyping Console<sup>™</sup> Software (Affymetrix, Santa Clara, CA, USA)을 이용하여 분석하였다.

### 3) 자료 분석

- 각 군의 인구-사회학적 특성, 흡연, 음주, 질병 과거력 및 암가족력 여부, virulence factor, 유전적 다형성에 대한 단변수 분석은 chi-square 검정을 수행하였다.
- 유전적, 환경적, 미생물학적 위험요인의 다변량분석 및 상호작용 검정은 logistic regression model을 이용하여 odds ratio 및 95% 신뢰구간을 산출하였다.
- 통계분석은 모수 통계분석을 주로 사용하였고 모수 통계방법이 적용되지 않는 경우는 비모수 통계방법을 사용하였다.
- 모수 통계방법으로는 dominant model, recessive model, allele-based test의 경우 Chi-square 검정을 수행하였고 additive model인 경우에는 Cochran-Armitage Trend test를 수행하였다.
- 모수 통계분석을 적용할 수 없는 경우는 dominant model, recessive model, additive model, allele-based test의 경우 Jonckheere-Terpstra test를 수행하였다.



4) 연구 사업의 추진 체계

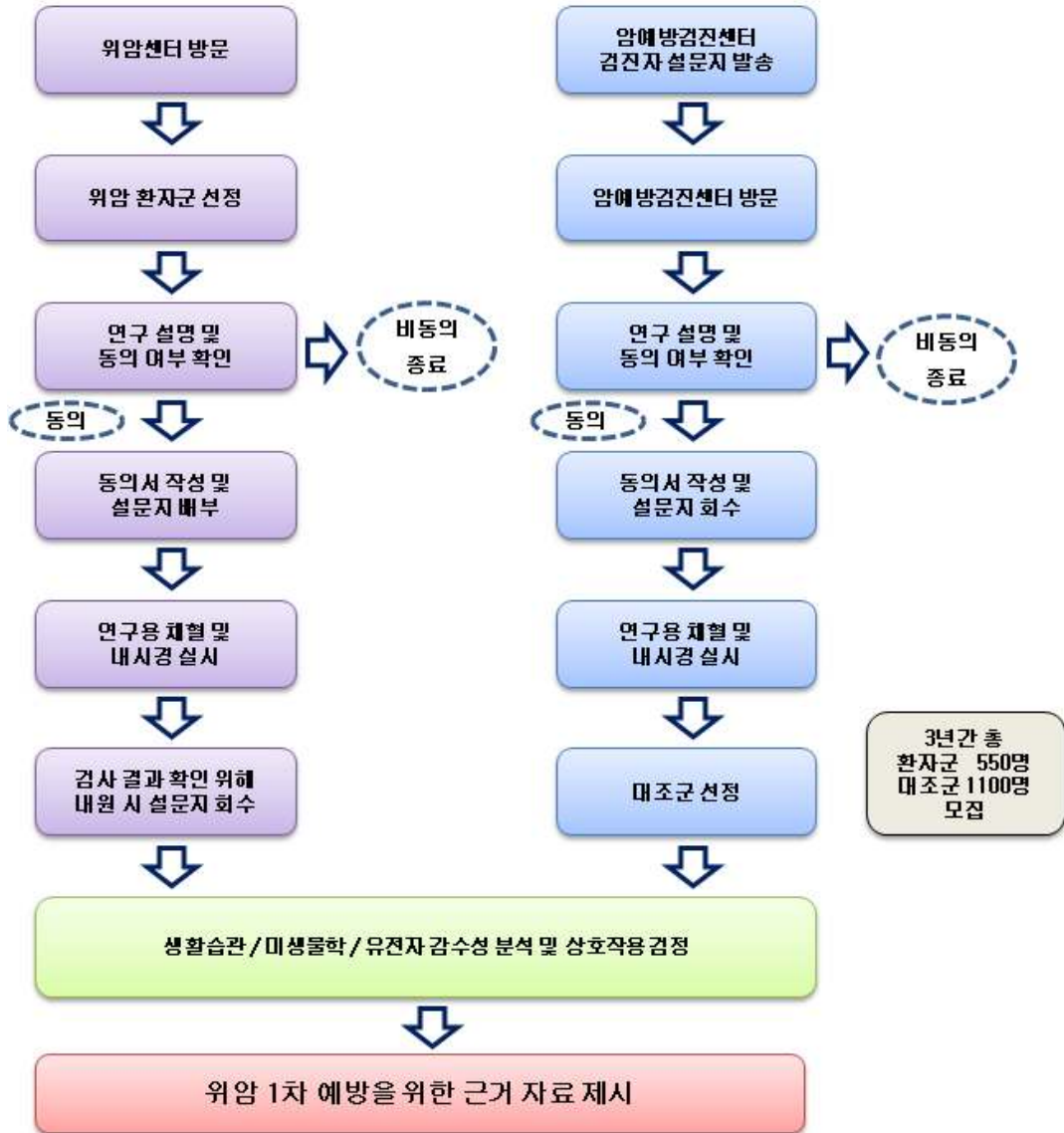


Figure 1. 연구사업의 추진체계

## 나. 연구수행 내용 및 결과

### ▷ 연구대상자

· 2011년 3월 31일부터 2013년 10월 18일까지 국립암센터 위암센터에서 신규위암 환자로 진단된 위암 환자 중 본 연구에 동의한 405명이 환자군으로 모집되었고 동기간에 국립암센터 암예방검진센터에서 암 검진을 받아 위암환자가 아닌 것으로 진단된 검진자 중 본 연구에 동의한 807명이 대조군으로 모집되었다. 대상자 중 설문지가 누락된 환자군 18명과 대조군 27명을 제외한 환자군 387명, 대조군 780명의 자료가 최종 통계분석에 활용되었다.

· 위암환자와 건강한 정상인 사이의 유전자를 비교하기 위한 엑솜 어레이(Exome array) 대상자는 위암 환자군 237명(여성 70명, 남성 167명)과 대조군인 건강한 성인 678명(여성 389명, 남성 289명)을 포함한 총 915명이 분석에 활용되었다.

### ▷ 일반적 특징

· Table 1은 연구대상자의 일반적인 특성을 비교한 결과이다. 연구대상자의 연령은 환자군 55.4±1.1.19세, 대조군 50.2±6.8세로 환자군의 연령이 유의적으로 더 높게 나타났다( $p<.001$ ). 성별의 분포는 환자군 남자 266명 (68.6%), 여자 122명 (27.8%)으로 대조군 남자 334명 (42.8%), 여자 446명 (57.2%)에 비해 환자군 남자의 분포가 유의적으로 높게 나타났다( $p<.001$ ). 환자군은 대조군과 비교하여 대학이상의 교육을 받은 대상자수가 적었고 ( $p<.001$ ), 흡연 및 음주 경험이 있는 대상자수가 더 많았다 (흡연: $p<.001$ , 음주: $p=0.030$ ), 환자군은 대조군과 비교하여 신체활동을 더 적게 하는 것으로 나타났고( $p=0.004$ ) 현재 단순 업무에 종사하고 있는 경우가 많았다 ( $p<.001$ ).

### ▷ 정기검진 여부 비교

· Table 2는 병·의원에서 검진 받은 경험을 비교한 결과이다. 위내시경 검사를 받아본 경험이 있는 경우는 환자군 66.8%, 대조군 86.9%로 환자군에서 유의적으로 더 낮게 경험한 것으로 나타났다 ( $p<.001$ ). 위 조영 검사( $p<.001$ ), 대장내시경( $p<.001$ ), 대장 조영 검사( $p<.001$ ), 대변 배양 검사( $p<.001$ ), 상복부초음파 검사( $p<0.004$ )의 모든 검사에서 대조군이 유의적으로 낮게 경험해 본 것으로 나타났다.

### ▷ 조직검사 결과 비교

· Table 3은 환자군과 대조군의 CLO test 와 *Helicobacter pylori* 균 검사 결과를 비교한 표이다. 환자군은 대조군과 비교하여 CLO test 양성반응이 76.6%, *Helicobacter pylori* 양성반응이 80.1%로 두 검사 결과 모두 통계적으로 유의적인 차이가 나타났다 ( $p<.001$ ).

▷ 일상적인 식생활 비교

· Table 4는 연구대상자의 식생활을 비교한 결과이다. 식생활과 관련된 총 12가지 질문 중에서 음식을 짜게 먹느냐는 질문에 그렇다고 응답한 대상자가 환자군 33.5%, 대조군 10.9%로 환자군이 음식을 더 짜게 먹는 것으로 나타나났다( $P<.001$ ). 외식할 때 음식이 짜다고 느끼는지를 묻는 질문에 환자군 41.2%, 대조군 57.8%가 그렇다고 응답하여 두 군간 유의적 차이가 나타났다( $P<.001$ ). 과일은 일주일에 5일 이상 먹느냐는 질문에 그렇다고 응답한 비율이 환자군 35.1%, 대조군 47.2%로 유의적인 차이가 나타났다( $P<.001$ ), 굽다가 탄 고기가 있으면 그 고기를 먹느냐는 질문에 환자군 11.9%, 대조군 6.6%가 그렇다고 응답하여 환자군에서 탄 고기를 유의적으로 더 자주 먹는 것으로 나타났다( $p=0.004$ ). 이외의 다른 질문에서는 통계적으로 유의적인 차이가 나타나지 않았다.

Table 1. General characteristics of study subjects

	Case	Control	n(%) or mean±sd <i>p</i> <sup>†</sup>
Age (years)	55.4 ± 11.1	50.2 ± 6.8	<.001
Sex			
Male	266(68.6)	334(42.8)	<.001
Female	122(31.4)	446(57.2)	
Body mass index (kg/m <sup>2</sup> )			
<23	156(40.2)	333(42.7)	0.716
23–25	112(28.9)	214(27.4)	
≥25	120(30.9)	233(29.9)	
Family history (yes)	191(49.2)	386(49.7)	0.365
Supplement use (yes)	213(54.9)	424(54.7)	0.138
Marital status			
Married	327(84.3)	661(84.7)	0.879
Single	15(3.9)	33(4.2)	
Others	46(11.9)	86(11.0)	
Education			
≤ Middle school	143(36.9)	111(14.2)	<.001
High school	155(40.0)	311(40.0)	
≥ College	87(22.4)	322(41.3)	
N/A	3(0.8)	35(4.6)	
Smoking status			
non-smoker	149(38.4)	474(60.8)	<.001
ex-smoker	114(29.4)	173(22.2)	
current smoker	124(32.0)	133(17.1)	
N/A	1(0.3)	0(0.0)	
Alcohol consumption			
non-drinker	114(29.5)	269(34.5)	0.030
ex-drinker	39(10.1)	49(6.3)	
current drinker	234(60.5)	462(59.2)	
Physical activity (MET–min/week)			
<792	102(30.5)	180(24.7)	0.004
792–1980	88(26.4)	177(24.4)	
1980–3600	53(15.9)	186(25.6)	
≥3600	91(27.3)	184(25.3)	
Job			
Housewives	48(12.5)	210(27.0)	<.001
Professional administrator	63(16.4)	138(17.7)	
Office workers	43(11.2)	72(9.2)	
Sales, Service	68(17.7)	210(27.0)	
Others (Laborer, Unemployed)	163(42.3)	149(19.1)	

<sup>†</sup> *p* values were calculated by t-test and chi-square test.

METs are multiples of the resting metabolic rate and calculated using short form (version 2.0 April 2004) of the International Physical Activity Questionnaire (IPAQ).

Table 2. Comparison of regular check-ups for the study subjects.

	Case	Control	n(%) $p^{\dagger}$
Esophagogastroduodenoscopy (yes)	259(66.8)	647(86.9)	<.001
Upper gastrointestinal series (yes)	86(22.2)	185(33.3)	<.001
Colonoscopy (yes)	134(34.5)	288(46.5)	<.001
Colon study (yes)	8(2.1)	36(6.9)	<.001
Stool culture (yes)	64(16.5)	157(27.9)	<.001
Abdomen ultrasonography (yes)	102(26.4)	197(35.2)	0.004

$^{\dagger}$   $p$  values were calculated by chi-square test

Table 3. Comparison of CLO test and *H. pylori* for the study subjects

	Case	Control	n(%) $p^{\dagger}$
CLO test			
negative	90(23.4)	373(46.7)	<.001
positive	295(76.6)	426(53.3)	
<i>H.pylori</i>			<.001
negative	77(19.9)	374(47.0)	
positive	310(80.1)	421(53.0)	

$^{\dagger}$   $p$  values were calculated by chi-square test

Table 4. Dietary habit of study subjects.

	Case	Control	n(%) <i>p</i> <sup>†</sup>
Having three meals a day, five or more days a week			
Yes	309(79.6)	593(76.1)	0.177
No	79(20.4)	186(23.9)	
Taking more than ten minutes at a meal on the average			
Yes	273(70.4)	582(74.7)	0.114
No	115(29.6)	197(25.3)	
Eating meat or egg five or more times a week			
Yes	136(35.1)	241(30.9)	0.157
No	252(65.0)	538(69.1)	
Eating fish or shellfish three or more times a week			
Yes	130(33.5)	240(30.9)	0.358
No	258(66.5)	538(69.2)	
Eating tofu or soy milk three times a week			
Yes	165(42.5)	366(47.0)	0.150
No	223(57.5)	413(53.0)	
Eating vegetables (except kimchi), seaweeds, mushrooms at every meal			
Yes	178(45.9)	397(51.0)	0.102
No	210(54.1)	382(49.0)	
Eating fruits five or more days a week			
Yes	136(35.1)	368(47.2)	<.001
No	252(65.0)	411(52.8)	
Eating milk or dairy products five or more days a week			
Yes	98(25.3)	226(29.1)	0.173
No	290(74.7)	552(71.0)	
Having three or more side dishes (except soup and kimchi) at every meal			
Yes	316(81.4)	596(76.5)	0.055
No	72(18.6)	183(23.5)	
Evaluating salty for restaurant foods			
Yes	160(41.2)	449(57.8)	<.001
No	228(58.8)	328(42.2)	
Eating salty food			
Yes	130(33.5)	85(10.9)	<.001
Sometimes	218(56.2)	542(69.6)	
No	40(10.3)	152(19.5)	
Eating charred meat			
Never	177(45.6)	410(52.6)	0.004
Sometimes	163(42.0)	308(39.5)	
Often	46(11.9)	51(6.6)	
N/A	2(0.5)	10(1.3)	

† *p* values were calculated by chi-square test

## ▷ 영양소 섭취 비교

· Table 5는 영양소 평균 섭취량에 대한 환자군과 대조군의 비교 결과이다. 단백질, 식물성 단백질, 지방, 식물성 지방, 동물성 지방, 식이섬유, 칼슘, 식물성 칼슘, 동물성 칼슘, 인, 철분, 식물성 철분, 동물성 철분, 비타민 A, 레티놀, 베타 카로틴, 비타민 B1, 비타민 B2, 비타민 B6, 비타민 C, 엽산, 비타민 E, 콜레스테롤, 칼륨, 나이아신 섭취량이 대조군과 비교하여 환자군에서 유의적으로 더 낮게 섭취하는 것으로 나타났다. 열량과 탄수화물은 환자군에서 유의적으로 높게 섭취하는 것으로 나타났다.

· Table 6은 환자군과 대조군 두 군간 영양소 섭취 사이의 관련성을 분석한 결과이다. 영양소들 중에서 열량, 단백질, 동물성 단백질, 지방, 식물성 지방, 동물성 지방, 탄수화물, 식이섬유, 칼슘, 식물성 칼슘, 동물성 칼슘, 인, 철분, 식물성 철분, 동물성 철분, 아연, 비타민 A, 칼륨, 레티놀, 베타 카로틴, 비타민 B1, 비타민 B2, 비타민 B6, 니아신, 비타민 C, 엽산, 비타민 E, 콜레스테롤 에서 통계적으로 유의한 차이가 나타났다. 단백질( $p$  for trend=0.012), 동물성 단백질( $p$  for trend=0.006), 지방( $p$  for trend=0.005), 식물성 지방( $p$  for trend=0.002), 동물성 지방( $p$  for trend=0.029), 식이섬유( $p$  for trend=0.001), 칼슘( $p$  for trend=0.002), 식물성 칼슘( $p$  for trend=0.020), 동물성 칼슘( $p$  for trend=0.011), 인( $p$  for trend=0.008), 철분( $p$  for trend<.001), 식물성 철분( $p$  for trend<.001), 동물성 철분( $p$  for trend=0.004), 아연( $p$  for trend=0.010), 비타민 A( $p$  for trend=0.002), 칼륨( $p$  for trend<.001), 레티놀( $p$  for trend=<.001), 비타민 B1( $p$  for trend=0.045), 비타민 B2( $p$  for trend<.001), 비타민 B6( $p$  for trend<.001), 나이아신( $p$  for trend=0.009), 비타민 C( $p$  for trend<.001), 엽산( $p$  for trend<.001), 비타민 E( $p$  for trend<.001), 콜레스테롤( $p$  for trend<.001) 섭취가 많을수록 암 발생 위험을 낮추는 것으로 나타났다. 열량( $p$  for trend<.001), 탄수화물( $p$  for trend=0.006)은 섭취가 많을수록 암 발생 위험을 증가시키는 것으로 나타났다.

Table 5. Comparison of nutrient intakes for the study subjects.

	mean±sd		
	Case (n=387)	Control (n=783)	<i>p</i>
Energy (kcal)	2042.6 ± 720.6	1851.1 ± 877.9	<.001
Protein (g)	70.3 ± 12.2	72.5 ± 13.5	0.012
vegetable	42.7 ± 6.8	42.6 ± 6.8	0.813
animal	27.4 ± 12.8	29.8 ± 13.9	0.010
Fat (g)	36.3 ± 12.4	39.8 ± 13.8	<.001
vegetable	15.8 ± 6.2	17.3 ± 7.3	0.001
animal	20.5 ± 10.6	22.5 ± 11.3	0.004
Carbohydrate (g)	342.8 ± 34.7	335.2 ± 37.2	<.001
Fiber (g)	20.3 ± 6.7	21.8 ± 7.1	<.001
Calcium (mg)	492.3 ± 193.4	548.6 ± 237.2	<.001
vegetable	322.5 ± 128.6	341.0 ± 140.8	0.022
animal	169.8 ± 130.0	210.8 ± 174.2	<.001
Phosphorus (mg)	1023.2 ± 173.1	1063.6 ± 205.4	0.001
Iron (mg)	12.4 ± 3.6	13.4 ± 4.2	<.001
vegetable	9.6 ± 3.2	10.3 ± 3.6	<.001
animal	2.8 ± 1.4	3.1 ± 1.5	0.003
Zinc (mg)	9.1 ± 4.7	9.1 ± 1.8	0.163
Vitamin A ( $\mu$ g RE)	552.3 ± 306.2	609.1 ± 337.8	0.001
Retinol ( $\mu$ g)	78.8 ± 49.3	99.0 ± 61.5	<.001
$\beta$ -Carotene ( $\mu$ g)	2807.9 ± 1779.6	3060.4 ± 1922.9	0.004
Vitamin B1 (mg)	1.2 ± 0.2	1.2 ± 0.3	0.001
Vitamin B2 (mg)	1.0 ± 0.3	1.1 ± 0.3	<.001
Vitamin B6 (mg)	1.9 ± 0.4	2.0 ± 0.6	<.001
Vitamin C (mg)	108.0 ± 3.3	130.8 ± 70.0	<.001
Folate ( $\mu$ g)	657.8 ± 268.7	729.2 ± 300.4	<.001
Vitamin E (mg)	9.3 ± 2.9	10.4 ± 3.4	<.001
Cholesterol (mg)	201.3 ± 110.7	225.5 ± 115.7	0.001
Sodium (mg)	3668.6 ± 1560.0	3573.3 ± 1421.2	0.543
Potassium (mg)	2610.3 ± 772.3	2854.2 ± 846.8	<.001
Niacin (mg)	17.1 ± 3.3	17.8 ± 3.8	0.001

Nutrients were adjusted for total energy intake by using the residual method.



Table 6. Odds ratios of gastric cancer risk according to nutrient intake

Nutrients		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*
Energy (kcal)	<1383.1	196	57	1.00(ref.)	1.00(ref.)
	1383.1-<1713.6	194	87	1.50(1.00-2.26)	1.43(0.94-2.18)
	1713.6-<2144.2	196	106	1.90(1.28-2.81)	1.77(1.18-2.66)
	2144.2-<	194	137	2.69(1.83-3.95)	2.62(1.76-3.90)
	P for trend <sup>†</sup>			<.001	<.001
Protein (g)	<63.4	195	119	1.00(ref.)	1.00(ref.)
	63.4-<70.7	195	94	0.85(0.60-1.21)	0.88(0.61-1.27)
	70.7-<77.8	195	98	0.90(0.63-1.27)	0.97(0.66-1.42)
	77.8-<	195	76	0.63(0.44-0.91)	0.63(0.44-0.91)
	P for trend			0.020	0.012
vegetable	<38.3	195	86	1.00(ref.)	1.00(ref.)
	38.3-<41.7	196	104	1.13(0.78-1.62)	1.13(0.78-1.65)
	41.7-<45.5	194	82	0.82(0.56-1.19)	0.80(0.54-1.18)
	45.5-<	195	115	1.02(0.71-1.46)	1.12(0.77-1.63)
	P for trend			0.794	0.896
animal	<20.3	195	120	1.00(ref.)	1.00(ref.)
	20.3-<28.1	195	100	0.90(0.64-1.27)	0.85(0.59-1.22)
	28.1-<37.3	195	100	0.97(0.69-1.37)	0.91(0.63-1.30)
	37.3-<	195	67	0.63(0.43-0.92)	0.58(0.39-0.86)
	P for trend			0.023	0.006
Fat (g)	<30.1	195	121	1.00(ref.)	1.00(ref.)
	30.1-<39.2	195	129	1.29(0.93-1.81)	1.20(0.85-1.70)
	39.2-<45.7	195	72	0.73(0.51-1.05)	0.58(0.38-0.87)
	45.7-<	195	65	0.68(0.47-1.00)	0.70(0.48-1.01)
	P for trend			0.006	0.005
vegetable	<12.4	195	122	1.00(ref.)	1.00(ref.)
	12.4-<16.1	195	107	0.97(0.69-1.37)	0.96(0.67-1.36)
	16.1-<20.7	195	101	0.95(0.68-1.35)	0.89(0.63-1.28)
	20.7-<	195	57	0.55(0.37-0.80)	0.54(0.36-0.80)
	P for trend			0.003	0.002
animal	<14.8	195	126	1.00(ref.)	1.00(ref.)
	14.8-<20.8	195	91	0.83(0.58-1.17)	0.79(0.55-1.13)
	20.8-<28.5	195	99	0.95(0.67-1.34)	0.83(0.58-1.20)
	28.5-<	195	71	0.71(0.49-1.03)	0.64(0.44-0.94)
	P for trend			0.119	0.029
Carbohydrate (g)	<313.7	195	68	1.00(ref.)	1.00(ref.)
	313.7-<337.9	195	82	1.21(0.82-1.78)	1.18(0.79-1.77)
	337.9-<361.2	195	118	1.74(1.20-2.53)	1.79(1.22-2.63)
	361.2-<	195	119	1.44(0.99-2.10)	1.54(1.05-2.27)
	P for trend			0.020	0.006
Fiber (g)	<17.0	195	134	1.00(ref.)	1.00(ref.)
	17.0-<20.6	195	99	0.72(0.51-1.01)	0.81(0.56-1.15)
	20.6-<25.4	195	80	0.52(0.36-0.75)	0.59(0.41-0.86)
	25.4-<	195	74	0.45(0.31-0.65)	0.58(0.39-0.85)
	P for trend			<.001	0.001

continued

Nutrients		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*	
Calcium (mg)	<386.1	194	123	1.00(ref.)	1.00(ref.)	
	386.1-<499.6	196	101	0.80(0.57-1.13)	0.89(0.62-1.26)	
	499.6-<620.2	195	94	0.72(0.51-1.02)	0.89(0.61-1.31)	
	620.2-<	195	69	0.48(0.33-0.69)	0.58(0.40-0.84)	
	P for trend <sup>†</sup>			<.001	0.002	
	vegetable	<249.4	195	120	1.00(ref.)	1.00(ref.)
		249.4-<317.8	195	100	0.77(0.54-1.09)	0.87(0.61-1.25)
		317.8-<400.5	195	82	0.61(0.43-0.88)	0.70(0.48-1.01)
		400.5-<	195	85	0.56(0.39-0.80)	0.68(0.47-1.00)
		P for trend			0.001	0.020
animal	<90.3	195	128	1.00(ref.)	1.00(ref.)	
	90.3-<155.7	195	92	0.79(0.56-1.12)	0.79(0.55-1.13)	
	155.7-<279.1	195	101	0.86(0.61-1.21)	0.93(0.65-1.33)	
	279.1-<	195	66	0.52(0.36-0.76)	0.58(0.39-0.85)	
	P for trend			0.001	0.011	
Phosphorus (mg)	<920.0	195	111	1.00(ref.)	1.00(ref.)	
	920.0-<1030.2	195	109	1.03(0.73-1.45)	1.05(0.73-1.50)	
	1030.2-<11176.8	195	94	0.81(0.57-1.15)	0.8490.58-1.21)	
	1176.8-<	195	73	0.58(0.40-0.84)	0.65(0.44-0.95)	
	P for trend			0.002	0.008	
Iron (mg)	<10.8	195	149	1.00(ref.)	1.00(ref.)	
	10.8-<12.6	195	87	0.55(0.39-0.77)	0.58(0.41-0.83)	
	12.6-<14.5	195	85	0.54(0.38-0.77)	0.60(0.41-0.88)	
	14.5-<	195	66	0.35(0.24-0.51)	0.48(0.33-0.68)	
	P for trend			<.001	<.001	
	vegetable	<8.0	195	126	1.00(ref.)	1.00(ref.)
		8.0-<9.7	195	115	0.76(0.54-1.07)	0.86(0.60-1.22)
		9.7-<11.8	195	76	0.48(0.33-0.69)	0.59(0.40-0.86)
		11.8-<	195	70	0.40(0.27-0.58)	0.52(0.35-0.77)
		P for trend			<.001	<.001
animal	<2.0	195	122	1.00(ref.)	1.00(ref.)	
	2.0-<2.9	195	116	1.03(0.74-1.45)	1.01(0.71-1.43)	
	2.9-<3.8	195	81	0.77(0.54-1.10)	0.74(0.51-1.08)	
	3.8-<	195	68	0.65(0.45-0.94)	0.62(0.42-0.92)	
	P for trend			0.008	0.004	
Zinc (µg)	<8.0	195	104	1.00(ref.)	1.00(ref.)	
	8.0-<8.8	195	120	1.17(0.83-1.64)	1.13(0.79-1.61)	
	8.8-<9.8	195	84	0.79(0.55-1.14)	0.85(0.58-1.25)	
	9.8-<	195	79	0.64(0.44-0.93)	0.68(0.46-1.00)	
	P for trend			0.003	0.010	
Vitamin A (mg)	<401.0	195	137	1.00(ref.)	1.00(ref.)	
	401.0-<538.9	195	96	0.66(0.47-0.94)	0.73(0.51-1.04)	
	538.9-<736.2	195	77	0.54(0.38-0.78)	0.57(0.40-0.83)	
	736.2-<	195	77	0.45(0.31-0.64)	0.58(0.39-0.84)	
	P for trend			<.001	0.002	

continued

Nutrients		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*
Sodium (mg)	<2624.7	195	102	1.00(ref.)	1.00(ref.)
	2624.7-<3436.5	195	99	0.96(0.67-1.37)	1.00(0.68-1.41)
	3436.5-<4337.9	195	79	0.76(0.53-1.11)	0.84(0.50-1.08)
	4337.9-<	195	107	0.89(0.63-1.26)	0.92(0.64-1.33)
	P for trend <sup>†</sup>			0.407	0.450
Potassium (mg)	<2291.8	194	151	1.00(ref.)	1.00(ref.)
	2291.8-<2728.7	196	85	0.55(0.39-0.78)	0.62(0.43-0.89)
	2728.7-<3317.5	195	88	0.56(0.40-0.79)	0.65(0.45-0.92)
	3317.5-<	195	63	0.35(0.24-0.51)	0.44(0.30-0.64)
	P for trend			<.001	<.001
Retinol (µg)	<54.1	195	137	1.00(ref.)	1.00(ref.)
	54.1-<88.1	195	119	0.93(0.67-1.30)	0.92(0.65-1.29)
	88.1-<131.2	195	82	0.70(0.49-0.99)	0.73(0.51-1.05)
	131.2-<	195	49	0.40(0.27-0.59)	0.42(0.28-0.63)
	P for trend			<.001	<.001
β-carotene(µg)	<1898.5	195	127	1.00(ref.)	1.00(ref.)
	1898.5-<2573.8	195	92	0.67(0.47-0.95)	0.70(0.48-1.00)
	2573.8-<3711.4	195	93	0.67(0.47-0.95)	0.71(0.50-1.02)
	3711.4-<	195	75	0.45(0.31-0.65)	0.56(0.38-0.82)
	P for trend			<.001	0.005
Vitamin B1 (mg)	<1.1	195	120	1.00(ref.)	1.00(ref.)
	1.1-<1.2	195	110	1.09(0.77-1.53)	1.10(0.77-1.56)
	1.2-<1.4	195	82	0.84(0.59-1.20)	0.82(0.56-1.19)
	1.4-<	195	75	0.73(0.51-1.06)	0.81(0.56-1.19)
	P for trend			0.045	0.116
Vitamin B2 (mg)	<0.9	195	136	1.00(ref.)	1.00(ref.)
	0.9-<1.06	195	109	0.88(0.63-1.23)	0.96(0.68-1.37)
	1.06-<1.2	195	78	0.62(0.44-0.89)	0.75(0.51-1.11)
	1.2-<	195	64	0.47(0.32-0.68)	0.52(0.36-0.75)
	P for trend			<.001	<.001
Vitamin B6 (mg)	<1.7	195	137	1.00(ref.)	1.00(ref.)
	1.7-<1.9	195	92	0.69(0.49-0.97)	0.73(0.51-1.04)
	1.9-<2.2	195	88	0.62(0.44-0.88)	0.72(0.59-1.05)
	2.2-<	195	70	0.42(0.29-0.60)	0.54(0.38-0.77)
	P for trend			<.001	<.001
Niacin (mg)	<15.3	195	121	1.00(ref.)	1.00(ref.)
	15.3-<17.3	195	106	1.00(0.71-1.42)	1.04(0.73-1.49)
	17.3-<19.0	195	85	0.81(0.57-1.16)	0.81(0.55-1.20)
	19.0-<	195	75	0.65(0.45-0.94)	0.67(0.47-0.96)
	P for trend			0.010	0.009
Vitamin C (mg)	<83.6	195	144	1.00(ref.)	1.00(ref.)
	83.6-<117.6	195	111	0.78(0.56-1.09)	0.92(0.65-1.30)
	117.6-<151.1	195	76	0.46(0.32-0.66)	0.60(0.40-0.89)
	151.1-<	195	56	0.35(0.24-0.52)	0.47(0.32-0.68)
	P for trend			<.001	<.001

continued

Nutrients		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*
Folate ( $\mu\text{g}$ )	<523.9	195	133	1.00(ref.)	1.00(ref.)
	523.9-<678.9	195	101	0.74(0.53-1.05)	0.79(0.55-1.12)
	678.9-<820.1	195	91	0.62(0.44-0.89)	0.69(0.47-1.01)
	820.1-<	195	62	0.37(0.25-0.54)	0.54(0.37-0.78)
	P for trend <sup>†</sup>			<.001	<.001
Vitamin E (mg)	<8.0	195	136	1.00(ref.)	1.00(ref.)
	8.0-<9.7	195	108	0.85(0.61-1.19)	0.93(0.65-1.31)
	9.7-<12.2	195	80	0.63(0.44-0.90)	0.69(0.48-1.00)
	12.2-<	195	63	0.44(0.30-0.64)	0.53(0.36-0.78)
	P for trend			<.001	<.001
Cholesterol (mg)	<142.3	195	120	1.00(ref.)	1.00(ref.)
	142.3-<213.9	195	129	1.20(0.86-1.67)	1.15(0.82-1.63)
	213.9-<281.5	195	72	0.67(0.47-0.98)	0.65(0.44-0.95)
	281.5-<	195	66	0.59(0.41-0.86)	0.58(0.39-0.85)
	P for trend			<.001	<.001

\* Adjusted for age, bmi, supplement use, smoking, alcohol.

<sup>†</sup> Test for trend calculated with median intake of each category of intake as a continuous variable.

▷ 식품군별 섭취 비교

· Table 7은 총 16개 군으로 분류한 식품군별 평균 섭취량에 대한 환자군과 대조군의 비교 결과이다. 환자군은 대조군과 비교하여 종실류, 버섯류, 과일류, 우유 및 유제품, 음료류를 더 낮게 섭취하는 것으로 나타났고 곡류, 당류, 채소류, 생선류, 유지류는 더 높게 섭취하는 것으로 나타났다. 이 결과는 통계적으로 유의적인 차이를 보였다 (곡류:  $p<.001$ , 당류:  $p=0.005$ , 종실류:  $p=0.036$ , 채소류:  $p=0.027$ , 버섯류:  $p=0.054$ , 과일류:  $p<.001$ , 생선류:  $p=0.028$ , 우유 및 유제품:  $<.001$ , 유지류:  $p=0.026$ , 음료류:  $p=0.014$ ).

· Table 8은 환자군과 대조군 두 군간 식품군별 섭취 사이의 관련성을 분석한 결과이다. 곡류, 당류, 채소류, 육류, 유지류는 섭취량이 증가될수록 암 발생 위험이 증가되었고( $p$  for trend: 곡류 $<.001$ , 당류 $=0.010$ , 채소류 $=0.005$ , 육류 $=0.002$ , 유지류 $=0.023$ ), 종실류, 과일류, 우유 및 유제품의 경우 섭취량이 높을수록 암 발생 위험을 낮추는 것으로 나타났다 ( $p$  for trend: 종실류 $=0.007$ , 과일류 $=0.028$ , 우유 및 유제품 $=0.025$ ).

Table 7. Comparison of food intakes for the study subjects

	Case (n=387)	Control (n=780)	mean±sd (g/d) $p^{\dagger}$
Cereals	731.2 ± 234.6	599.0 ± 229.0	<.001
Potatoes	40.8 ± 39.0	42.7 ± 49.7	0.699
Sugars	7.0 ± 6.6	5.7 ± 6.3	0.005
Legumes	62.3 ± 67.4	62.7 ± 81.1	0.558
Seeds	4.8 ± 8.4	5.9 ± 14.4	0.036
Vegetables	358.9 ± 236.6	324.3 ± 228.7	0.027
Mushrooms	8.8 ± 11.6	10.1 ± 17.0	0.054
Fruits	149.2 ± 192.4	202.7 ± 258.6	<.001
Meats	80.0 ± 81.6	73.1 ± 118.9	0.062
Eggs	17.3 ± 21.3	18.0 ± 17.5	0.117
Fishes	46.8 ± 41.5	43.3 ± 58.4	0.028
Seaweeds	2.3 ± 2.4	2.3 ± 2.6	0.675
Milks	90.4 ± 137.8	104.2 ± 146.7	<.001
Fats	5.2 ± 4.9	4.7 ± 4.9	0.026
drinks	80.0 ± 127.9	87.4 ± 171.2	0.014
Spices	18.8 ± 16.7	17.5 ± 15.6	0.123

$\dagger$   $p$  values were calculated by t-test.

Table 8. Odds ratios of gastric cancer risk according to food intake

Food groups		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*
Cereals	<466.79	195	38	1.00(ref.)	1.00(ref.)
	466.79-<592.21	195	57	1.87(1.17-2.99)	1.78(1.10-2.88)
	592.21-<716.57	195	95	2.34(1.51-3.64)	2.20(1.40-3.44)
	716.57-<	195	197	5.69(3.75-8.62)	5.00(3.23-7.60)
	P for trend <sup>†</sup>			<.001	<.001
Potatoes	<14.66	195	84	1.00(ref.)	1.00(ref.)
	14.66-<29.46	195	112	1.46(1.02-2.10)	1.52(1.04-2.22)
	29.46-<54.0	195	108	1.33(0.93-1.92)	1.41(0.97-2.06)
	54.0-<	195	83	0.85(0.59-1.25)	1.00(0.67-1.47)
	P for trend			0.086	0.344
Sugars	1.32	195	88	1.00(ref.)	1.00(ref.)
	1.32-<3.6	195	64	0.80(0.54-1.19)	0.81(0.54-1.22)
	3.6-<7.8	195	95	1.11(0.77-1.60)	1.06(0.73-1.55)
	7.8-<	195	140	1.60(1.13-2.27)	1.39(0.97-2.00)
	P for trend			0.003	0.010
Legumes	<23.38	195	98	1.00(ref.)	1.00(ref.)
	23.38-<42.0	195	77	0.76(0.52-1.10)	0.79(0.54-1.16)
	42.0-<74.3	195	113	1.03(0.73-1.46)	1.04(0.72-1.50)
	74.3-<	195	99	0.93(0.65-1.33)	1.01(0.70-1.47)
	P for trend			0.861	0.635
Seeds	<0.52	195	119	1.00(ref.)	1.00(ref.)
	0.52-<2.39	195	105	0.83(0.59-1.18)	0.82(0.57-1.17)
	2.39-<6.8	195	80	0.63(0.44-0.91)	0.65(0.45-0.94)
	6.8-<	195	83	0.59(0.41-0.85)	0.68(0.47-0.99)
	P for trend			0.007	0.071
Vegetables	<182.6	195	77	1.00(ref.)	1.00(ref.)
	182.6-<275.8	195	79	1.05(0.71-1.54)	1.07(0.71-1.59)
	275.8-<401.4	195	100	1.24(0.86-1.80)	1.34(0.91-1.98)
	401.4-<	195	131	1.49(1.04-2.13)	1.64(0.13-2.38)
	P for trend			0.016	0.005
Mushrooms	<2.68	195	119	1.00(ref.)	1.00(ref.)
	2.68-<5.44	195	80	0.81(0.57-1.17)	0.81(0.55-1.17)
	5.44-<10.92	195	94	0.97(0.68-1.38)	0.97(0.67-1.40)
	10.92-<	195	94	0.95(0.67-1.35)	1.06(0.74-1.53)
	P for trend			0.910	0.475
Fruits	<54.99	195	146	1.00(ref.)	1.00(ref.)
	54.99-123.0	195	95	0.72(0.51-1.01)	0.82(0.57-1.16)
	123.0-<263.9	195	78	0.58(0.41-0.82)	0.71(0.49-1.03)
	263.9-<	195	68	0.50(0.35-0.72)	0.67(0.46-0.97)
	P for trend			<.001	0.028
Meats	<30.8	195	97	1.00(ref.)	1.00(ref.)
	30.8-<50.96	195	78	0.99(0.69-1.45)	0.98(0.66-1.46)
	50.96-<83.5	195	81	1.13(0.77-1.65)	1.07(0.72-1.59)
	83.5-<	195	131	1.95(1.37-2.77)	1.65(1.13-2.41)
	P for trend			<.001	0.002

continued

Nutrients		No. Control	No. Case	Age adjusted odds ratio	Multivariate odds ratio*
Eggs	<6.07	195	105	1.00(ref.)	1.00(ref.)
	6.07-<12.6	188	114	1.25(0.88-1.77)	1.09(0.76-1.56)
	12.6-<25.88	202	85	0.93(0.65-1.34)	0.80(0.55-1.16)
	25.88-<	195	83	0.89(0.62-1.28)	0.82(0.56-1.19)
	P for trend <sup>†</sup>			0.261	0.203
Fishes	<18.8	195	94	1.00(ref.)	1.00(ref.)
	18.8-<30.4	195	70	0.80(0.55-1.18)	0.76(0.51-1.13)
	30.4-<49.82	195	95	1.10(0.77-1.58)	1.01(0.69-1.47)
	49.82-<	195	128	1.39(1.00-1.97)	1.32(0.92-1.89)
	P for trend			0.010	0.278
Seaweeds	<0.78	195	100	1.00(ref.)	1.00(ref.)
	0.78-<1.54	195	91	0.96(0.67-1.38)	1.04(0.71-1.51)
	1.54-<2.83	195	102	1.01(0.71-1.44)	1.05(0.73-1.52)
	2.83-<	195	94	0.90(0.63-1.29)	1.09(0.75-1.59)
	P for trend			0.565	0.747
Milks	<15.3	195	140	1.00(ref.)	1.00(ref.)
	15.3-<56.6	194	87	0.74(0.52-1.05)	0.76(0.53-1.09)
	56.6-<160	196	87	0.72(0.51-1.02)	0.79(0.55-1.13)
	160-<	195	73	0.57(0.40-0.81)	0.62(0.53-0.90)
	P for trend			0.009	0.025
Fats	<1.28	195	88	1.00(ref.)	1.00(ref.)
	1.28-<2.87	195	75	1.00(0.68-1.46)	0.97(0.65-1.44)
	2.87-<6.29	195	92	1.23(0.85-1.78)	1.14(0.77-1.67)
	6.29-<	195	132	1.83(1.29-2.61)	1.44(0.99-2.10)
	P for trend			<.001	0.023
Beverage & drinks	<13.8	195	120	1.00(ref.)	1.00(ref.)
	13.8-<38.7	194	93	0.97(0.68-1.38)	0.93(0.65-1.35)
	38.7-<109.4	196	87	0.95(0.66-1.36)	0.93(0.64-1.34)
	109.4-<	195	87	0.92(0.64-1.31)	0.95(0.66-1.38)
	P for trend			0.645	0.870
Spices	<8.0	195	91	1.00(ref.)	1.00(ref.)
	8.0-<13.45	195	88	0.97(0.67-1.41)	1.01(0.69-1.49)
	13.45-<22	195	103	1.10(0.77-1.57)	1.07(0.74-1.56)
	22-<	195	105	1.06(0.74-1.52)	1.11(0.77-1.61)
	P for trend			0.649	0.623

\* Adjusted for age, bmi, supplement use, smoking, alcohol.

† Test for trend calculated with median intake of each category of intake as a continuous variable.

1) 데이터의 품질 평가 (Quality Controls, QC)

▷ 분석대상 SNP의 개수

- 본 연구에서는 성염색체에서 6,761개 (2.12%)와 상염색체 311,697개(97.72%)를 포함하여 총 318,983개의 SNP를 분석하였다. 염색체(chromosome)의 종류에 따른 분석대상 SNP의 분포는 다음과 같다.

Chromosome	Count	Percent	분석대상
Autosome	311,697	97.72%	Total
Pseudo-autosomal region of X	318	1.10%	Total
Mitochondrial	207	0.06%	Total
소계	312,222	97.88%	
X chromosome	6,600	2.07%	Female
Y chromosome	161	0.05%	Male
소 계	6,761	2.12%	
총 계	318,983	100%	

▷ 데이터의 품질 평가: Quality Controls (QC)

- 본 연구에서는 Market QC의 기준을 정하기 위한 방법으로 QQ plot을 사용하였다.
- QC를 위한 기준은 Hardy-Weinberg Equilibrium (HWE) test 결과와 MAF (Minor Allele Frequency)를 고정한 후, call Rate을 변화시키면서 적절한 기준을 결정하였다. 통계적 분포함수를 근거로 하며, 예측값을 기준으로해서 call rate를 변화시키면서 관찰값이 예측값에 근사할 때를 QC 기준으로 결정하였다.
- 본 연구에서 사용한 QC의 기준은 다음과 같다.
  - HWE: control 대상 (Chromosome X는 female control 대상),  $p\text{-value} \geq 1E-07$
  - Call Rate: case  $> 0.95$  and control  $> 0.95$
  - MAF: Case  $> 0$  or control  $> 0$
  - Cluster QC:  $P\text{-value} < 0.001$ 을 만족하는 SNP을 대상으로 QC를 실시하였다.

▷ 최종분석 SNP의 개수

- 총 318,983개의 SNP 중에서 QC를 거쳐 총 84,950개 (26.63%)의 SNP를 최종 분석에 사용하였다. QC 전후의 SNP 개수의 변화는 다음과 같다.

	Before QC	After QC	Percent
Chromosome X	6,600	1,450	21.97%
Chromosome Y	161	12	7.45%
Other	312,222	83,488	26.74%
Total	318,983	84,950	26.63%

2) 위암과 분석한 SNP와의 연관성

- 위암과 발견된 SNP 사이의 연관성을 여러 가지 통계분석 방법을 이용하여 분석하였다.



- 분석결과 P-value가 <1E-07인 SNP가 1개, <1E-06인 SNP가 2개, <1E-05인 SNP가 6개, <1E-04인 SNP가 30개, 이를 포함한 P<1E-03인 SNP가 138개로 나타나서 이 138개의 SNP를 중심으로 gene-review를 하였다. P-value가 0.05 이하인 SNP의 개수는 총 4,839개였다. P-value에 따른 SNP의 개수는 Table 9에 나타내었다.

Table 9. The number of SNPs which are associated with gastric cancer

P-value	Total		Other		Chromosome X		Chromosome Y	
	Count	Cumulative	Count	Cumulative	Count	Cumulative	Count	Cumulative
<1E-07	1	1	1	1				
<1E-06	1	2	1	2				
<1E-05	4	6	4	6				
<1E-04	24	30	24	30				
<1E-03	108	138	108	138				
<0.01	1,106	1,244	1,083	1,221	23	23		
<0.05	4,839	6,083	4,718	5,939	121	144		
NS	78,867	84,950	77,549	83,488	1,306	1,450	12	12

- 엑솜 어레이(Exome array)로부터의 검정결과의 P-값은 Q-Q plot(quantile-quantile plot)과 Manhattan plot을 이용하여 먼저 시각적으로 분석 결과를 확인하고 관련성이 있다고 판단된 SNP의 정보를 확인하였다.
- 위암과 SNP들의 연관분석에서 예상되는 이론적인 분포 (균일분포)에서의 P-value와 실제 계산된 P-value를 이용하여 Q-Q plot을 작성하여 Figure 2에 나타내었다. P-value가 높은 몇 개의 SNP들이 라인을 벗어나서 분포하는 것을 확인할 수 있는데 이로써 이들 SNP들은 위암과 관련성이 있을 가능성이 있음을 예측할 수 있다.
- 위암과 SNP들과 연관분석 결과를 Manhattan plot으로 유전체 전반에 걸친 정보를 시각화하여 분석결과를 확인하였다 (Figure 3). Manhattan plot에서 연관분석결과 P-value는 염색체 번호, 물리적 거리순으로 나타나 있는데 위암과 관련성이 있는 유전자 영역이 있는 SNP들의 P값들이 고층 빌딩처럼 불쑥 솟아오른 모양이 되는 것을 확인할 수 있다. P-value가 0.001 이하 ( $-\log_{10}P=3.00$ )인 라인 위로 138개의 SNP들을 확인할 수 있다.
- 위암과 유의한 연관관계(P<0.001)를 나타내는 기본정보를 Table 10에 나타내었다. 기본정보로는 rs number, 염색체 번호, 염색체 내에서의 위치, genic region, 관련된 유전자, major/minor allele, minor allele frequency (MAF), Hardy-Weinberg Equilibrium (HWE)을 나타내었다. 또한 위암과 SNP 간의 연관 분석 결과를 요약하여 여러 genetic model과 통계분석을 사용한 여러 가지 검정 중 가장 적절하게 작은 P-value값을 대표값으로 결정하였으며 그 결과와 그 결과를 도출한 genetic model을 나타내었다. Gene과 region정보는 Affymetrix사의 NetAffx에서 제공하는

annotation 정보를 이용하였으며 여기에서 gene은 SNP와 가장 가까이에 있는 gene을 표기하였다. 이들 SNP와 가까이 위치한 유전자로 이들을 포함할 것으로 예측되는 유전자는 KIF1B (kinesin family member 1B), PGD (phosphogluconate dehydrogenase), EPHA2 (EPH receptor A2), CDA (cytidine deaminase), PHC2 (polyhomeotic homolog 2), YBX1 (Y box binding protein 1), TTC22 (tetratricopeptide repeat domain 22), IL23R (interleukin 23 receptor), CELSR2 (cadherin, EGF LAG seven-pass G-type receptor 2), SPAG17 (sperm associated antigen 17), CERS2 (ceramide synthase 2), SETDB1 (SET domain, bifurcated 1), IGSF9 (immunoglobulin superfamily, member 9), FAM179A (family with sequence similarity 179, member A), SULT1C2 (sulfotransferase family, cytosolic, 1C, member 2), PSMD14 (proteasome (prosome, macropain) 26S subunit, non-ATPase, 14), TTN (titin), CPS1 (carbamoyl-phosphate synthase 1, mitochondrial), TM4SF20 (transmembrane 4 L six family member 20), HEATR7B1 (maestro heat-like repeat family member 2A), HJURP (Holliday junction recognition protein), UGT1A6 (UDP glucuronosyltransferase 1 family, polypeptide A6), FBLN2 (fibulin 2), CHRDL1 (chordin), EIF2B5 (eukaryotic translation initiation factor 2B, subunit 5 epsilon, 82kDa), GPR78 (G protein-coupled receptor 78), PROM1 (prominin 1), BMPRI1 (bone morphogenetic protein receptor, type IB), PRSS48 (protease, serine, 48), C1QTNF3 (C1q and tumor necrosis factor related protein 3), C1QTNF3-AMACR (C1q and tumor necrosis factor related protein 3-alpha-methylacyl-CoA racemase readthrough (NMD candidate)), ADAMTS6 (ADAM metalloproteinase with thrombospondin type 1 motif, 6), HAPLN1 (hyaluronan and proteoglycan link protein 1), GLRX (glutaredoxin (thioltransferase)), RHOBTB3 (Rho-related BTB domain containing 3), LIX1 (Lix1 homolog), RIOK2 (RIO kinase 2), GABBR1 (gamma-aminobutyric acid (GABA) B receptor, 1), SNORD32B (small nucleolar RNA, C/D box 32B), UBD (ubiquitin D), OR2H2 (olfactory receptor, family 2, subfamily H, member 2), TRIM31 (tripartite motif containing 31), TRIM40 (tripartite motif containing 40), TRIM10 (tripartite motif containing 10), TRIM15 (tripartite motif containing 15), TRIM26 (tripartite motif containing 26), HCG17 (HLA complex group 17 (non-protein coding)), HCG18 (HLA complex group 18 (non-protein coding)), C7orf69 (chromosome 7 open reading frame 69), HUS1 (HUS1 checkpoint homolog), PKD1L1 (polycystic kidney disease 1 like 1), PPP1R3B (protein phosphatase 1, regulatory subunit 3B), EPHX2 (epoxide hydrolase 2, cytoplasmic), JRK (jerky homolog), PSCA (prostate stem cell antigen), PLEC (plectin), TEK (TEK tyrosine kinase, endothelial), FXN (frataxin), ROR2 (receptor tyrosine kinase-like orphan receptor 2), MIR548Q (microRNA 548q), ZNF462 (zinc finger protein 462), AKAP2 (A kinase (PRKA) anchor protein 2), PALM2-AKAP2 (paralemmin 2-A kinase anchor protein 2), ABO (ABO blood group (transferase A, alpha 1-3-N-acetylgalactosaminyltransferase; transferase B, alpha 1-3-galactosyltransferase)), DHTKD1 (dehydrogenase E1 and transketolase domain containing 1), ITGA8 (integrin, alpha 8), ANKRD22 (ankyrin repeat domain 22), LIPM (lipase, family member M), MKI67 (marker of proliferation Ki-67), CALCA (calcitonin-related polypeptide alpha), CALCB (calcitonin-related polypeptide beta), CYP2R1 (cytochrome P450, family 2, subfamily R, polypeptide 1), AMOTL1 (angiomin like 1), RBP5 (retinol binding protein 5, cellular), KLRC4 (killer cell lectin-like receptor subfamily C, member 4), KLRC4-KLRK1 (killer cell lectin-like receptor subfamily C, member 4-killer cell

lectin-like receptor subfamily K, member 1 readthrough), KLRK1 (killer cell lectin-like receptor subfamily K, member 1), IFLTD1 (intermediate filament tail domain containing 1), SP7 (Sp7 transcription factor), SFSWAP (splicing factor, suppressor of white-apricot homolog), ABCC4 (ATP-binding cassette, sub-family C (CFTR/MRP), member 4), DPF3 (D4, zinc and double PHD fingers, family 3), CYP19A1 (cytochrome P450, family 19, subfamily A, polypeptide 1), CNTNAP4 (contactin associated protein-like 4), PLD2 (phospholipase D2), KRBA2 (KRAB-A domain containing 2), GALK1 (galactokinase 1), LAMA1 (laminin, alpha 1), PIEZO2 (piezo-type mechanosensitive ion channel component 2), TUBB6 (tubulin, beta 6 class V), LOXHD1 (lipoxygenase homology domains 1), TNFRSF11A (tumor necrosis factor receptor superfamily, member 11a, NFkB activator), GP6 (glycoprotein VI (platelet)), COL6A2 (collagen, type VI, alpha 2), APOL5 (apolipoprotein L, 5) 등이었다.

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- 위암과 유의한 연관관계를 나타낸 SNP들의 genotype과 allele frequency를 환자군과 대조군으로 나누어 Table 11에 나타내었다. 환자군에서는 MAF가 0.01-0.60으로 나타났고, 대조군에서는 MAF가 0.00-0.47로 나타났다.
- 위암과 SNP들의 연관관계를 분석하여 그 결과를 Table 12에 나타내었다. 조사한 SNP들 중 62개는 위암을 증가시키는 것으로 63개는 위암의 위험을 줄여주는 것으로 나타났다. 위암의 위험을 증가시키는 SNP는 rs10492972 (OR [95% CI]=1.76[1.33, 2.34], dominant model), rs17401966, rs1049887, rs3754334 (6.49[2.34, 18.01], recessive model), rs2072671 (1.61[1.22, 2.12], dominant model), rs11554674 (1.51[1.19, 1.92], allele-based model), rs12026290 (1.51[1.19, 1.92], allele-based model), rs138700771 (2.61[1.55, 4.40], recessive model), rs671108 (1.66[1.28, 2.17], dominant model), rs200084754 (10.56[2.31, 48.32], allele-based model), rs17185492, rs75743857, rs2494250 (1.59[1.21, 2.09], dominant model), rs3747617 (1.61[1.23, 2.12], allele-based model), rs1479640 (1.71[1.25, 2.33], recessive model), rs72786179 (1.47[1.19, 1.83], allele-based model), rs6734275 (1.75[1.30, 2.35], recessive model), rs17036104 (7.87[2.18, 28.39], recessive model), rs6432679 (1.85[1.29, 2.67], recessive model), rs201192415 (7.40[2.43, 22.58], allele-based model), rs12629412 (1.62[1.23, 2.14], dominant model), rs16858778, rs1859156 (1.77[1.28, 2.45], allele-based model), rs840398 (1.69[1.26, 2.28], recessive model), rs34899 (1.47[1.19, 1.81], allele-based model), rs1233391 (1.37[1.14, 1.65], allele-based model), rs1233388 (1.40[1.16, 1.69], allele-based model), rs2290386 (1.47[1.17, 1.84], allele-based model), rs61756425 (1.98[1.36, 2.88], dominant model), rs10112232 (1.70[1.30, 2.22], dominant model), rs2294008 (2.53[1.77, 3.61], dominant model), rs1045531 (2.60[1.82, 3.70], dominant model), rs200893203 (12.65[2.82, 56.69], allele-based model), rs55979986 (2.27[1.41, 3.66], allele-based model), rs3935601 (1.61[1.21, 2.13], dominant model), rs3814538 (1.65[1.23, 2.20], recessive model), rs1053878, rs651007, rs579459, rs495828, rs635634, rs7027926 (6.07[2.17, 16.99], dominant model), rs1451668 (1.88[1.34, 2.64], recessive model), rs10788615, rs2303960 (1.67[1.25, 2.24], recessive model), rs2617170 (1.39[1.15, 1.67], allele-based model), rs1479500, rs199673881, rs138640311 (1.38[1.15, 1.67], allele-based model), rs9537824 (1.38[1.14, 1.67], allele-based model), rs4148549 (1.43[1.18, 1.72], allele-based model), rs4148546

(1.41[1.17, 1.69], allele-based model), rs3742836 (1.60[1.22, 2.10], dominant model), rs2305707 (0.38[0.21, 0.68], recessive model), rs11546303 (2.10[0.78, 5.65], recessive model), rs3764897, rs55715426 (4.63[1.74, 12.29], recessive model), rs79992793 1.73[1.25, 2.40], allele-based model), rs4796901 1.77[1.34, 2.35], dominant model), rs11267036 (2.45[1.42, 4.23], recessive model), rs12606417 (2.02[1.32, 3.06], allele-based model), rs884205 (2.95[1.55, 5.61], recessive model), rs1157329 (1.72[1.29, 2.29], recessive model), rs6048138(1.25[1.03, 1.51], allele-based model)이었다. 위암의 위험감소와 연관된 SNP는 rs1884444 (0.63[0.48, 0.83], dominant model), rs305163 (0.59[0.43, 0.80], dominant model), rs60719900 (0.59[0.45, 0.77], dominant model), rs2244492 (0.57[0.40, 0.79], dominant model), rs3835047 (0.48[0.31, 0.75], recessive model), rs7574414, rs11563246 (0.28[0.15, 0.54], recessive model), rs2286455 (0.63[0.48, 0.82], dominant model), rs1436512, rs1946267 (0.62[0.47, 0.82], dominant model), rs3830368 (0.60[0.46, 0.79], dominant model), rs39597 (0.71[0.58, 0.87], allele-based model), rs1119080 (0.65[0.54, 0.79], allele-based model), rs362522 (0.66[0.53, 0.83], allele-based model), rs2240070 (0.53[0.40, 0.71], dominant model), rs3132680 (0.51[0.39, 0.68], dominant model), rs2844795, rs2523990 (0.54[0.41, 0.70], dominant model), rs2239529, rs2517598, rs2844793, rs9261438 (0.61[0.49, 0.77], allele-based model), rs9261440 (0.63[0.50, 0.80], allele-based model), rs1419673 (0.61[0.48, 0.77], allele-based model), rs1419671 (0.61[0.48, 0.77], allele-based model), rs1541267 (0.64[0.51, 0.80], allele-based model), rs9261468 (0.59[0.46, 0.76], allele-based model), rs9261485 (0.59[0.46, 0.75], allele-based model), rs9261492 (0.63[0.50, 0.80], allele-based model), rs9261508 (0.64[0.50, 0.80], allele-based model), rs757262 (0.52[0.46, 0.76], allele-based model), rs757259 (0.59[0.46, 0.75], allele-based model), rs1557611 (0.59[0.46, 0.76], allele-based model), rs1557608 (0.64[0.51, 0.81], allele-based model), rs2517653 (0.59[0.46, 0.74], allele-based model), rs2022065, rs9261535 (0.59[0.46, 0.75], allele-based model), rs929156 (0.63[0.49, 0.80], allele-based model), rs2844782 (0.71[0.58, 0.87], allele-based model), rs2239530 (0.60[0.47, 0.77], allele-based model), rs4711211, rs3132672 (0.49[0.31, 0.75], recessive model), rs3132671 (0.46[0.29, 0.73], recessive model), rs2844775 (0.61[0.48, 0.78], allele-based model), rs3130391 (0.45[0.28, 0.72], recessive model), rs3132667 (0.47[0.30, 0.74], recessive model), rs885915 (0.46[0.29, 0.73], recessive model), rs2844780 (0.45[0.28, 0.72], recessive model), rs2844779 (0.45[0.28, 0.73], recessive model), rs1264585, rs6910017 (0.62[0.47, 0.82], dominant model), rs7759938, rs751141, rs10739288 (0.68[0.56, 0.83], allele-based model), rs2062988, rs2071498 (0.63[0.49, 0.83], dominant model), rs903809 (0.63[0.48, 0.82], dominant model), rs878874 (0.63[0.48, 0.82], dominant model), rs7969705, rs1959258 (0.51[0.34, 0.76], recessive model), rs12914996 (0.53[0.37, 0.77], recessive model), rs28584228 (0.62[0.47, 0.82], dominant model), rs671871, rs2304167 (0.33[0.13, 0.84], recessive model), rs34515071, rs117931394 (0.13[0.03, 0.54], recessive model), rs2076672로 나타났다. 전체 SNP 중 9개의 SNP (rs7574414, rs189070828, rs2239529, rs2517598, rs2844793, rs141858334, rs7969705, rs3764897, rs141572082)는 case나 control에서 genotype 중 major homo, hetero 혹은 minor homo가 나타나지 않거나 minor 혹은 major allele이 나타나지 않았으므로 각각이 존재할 경우 위암의 위험성이 있을 것이라고 예측할 수 있을 것으로 보이나 추가적인 연구가 필요하다. 나머지 4개의 SNP는 rs number에 대한 정보를 얻을 수 없었다.

- P-value<0.001을 만족하는 SNP 중 가까운 거리(100 Kb)에서 2개 이상의 SNP를 갖는 구간 선정하여 이들 유전체 변이의 chromosome내에서의 위치, 위암과의 연관관계, 그리고 그들의 연관불균형 (LD, Linkage Disequilibrium)을 나타내었다. Chromosome 1번에 위암과 유의한 연관관계를 나타내는 3개의 SNP들 (rs10492972, rs1049887, rs17401966)은 KIF1B, PGD 유전자에 포함되는 것으로 추정되며 이들은 강한 연관불균형을 나타내는 것으로 보인다 (Figure 4). Chromosome 1번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs11554674, rs12026290)은 PHC2 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 5). Chromosome 5번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs1946267, rs840398)은 C1QTNF3, C1QTNF3-AMACR, AMACR 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 6). Chromosome 6번에서 위암과 유의한 연관관계를 나타내는 4개의 SNP들 (rs1119080, rs1233388, rs1233391, rs362522)은 OR2H2, SNORD32B 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 7). Chromosome 6번에서 위암과 유의한 연관관계를 나타내는 36개의 SNP들 (rs1264585, rs1419671, rs1419673, rs1541267, rs1557608, rs1557611, rs2022065, rs2239529, rs2239530, rs2240070, rs2517598, rs2517653, rs2523990, rs2844775, rs2844779, rs2844780, rs2844782, rs2844793, rs2844795, rs3130391, rs3132667, rs3132671, rs3132672, rs3132680, rs4711211, rs757259, rs757262, rs885915, rs9261438, rs9261440, rs9261468, rs9261485, rs9261492, rs9261508, rs9261535, rs929156)은 HCG17, HCG18, TRIM39, RPP21, TRIM39-RPP21, TRIM26, TRIM10, TRIM40, TRIM15, TRIM31 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 8). Chromosome 8번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs1045531, rs2294008)은 PSCA 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 9). Chromosome 9번에서 위암과 유의한 연관관계를 나타내는 5개의 SNP들 (rs1053878, rs495828, rs579459, rs635634, rs651007)은 ABO 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 10). Chromosome 11번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs2303960, rs878874)은 AMOTL1 유전자에 포함되는 것으로 추정되며 이들도 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 11). Chromosome 12번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs1479500)은 IFLTD1 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 12). Chromosome 12번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs138640311)은 SFSWAP 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 13). Chromosome 13번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs4148546, rs4148549)은 ABCC4 유전자에 포함되는 것으로 추정되며 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 14). Chromosome 18번에서 위암과 유의한 연관관계를 나타내는 2개의 SNP들 (rs4796901, rs79992793)은 PIEZO2 유전자에 포함되는 것으로 추정되며 이들도 강한 연관불균형성을 나타내는 것으로 보인다 (Figure 15).

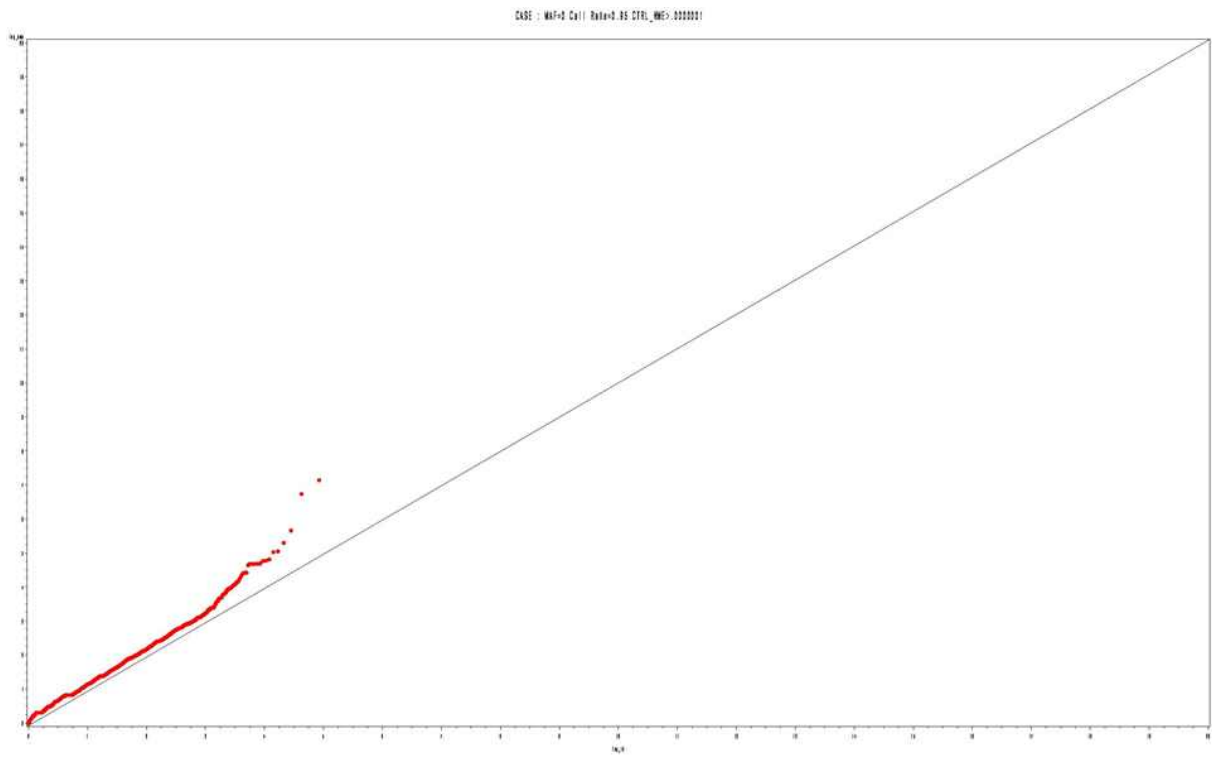


Figure 2. Quantile-Quantile plots for gastric cancer. The observed P-value (y axis) were compared with the expected P-values under the null distribution (x axis) for gastric cancer risk.



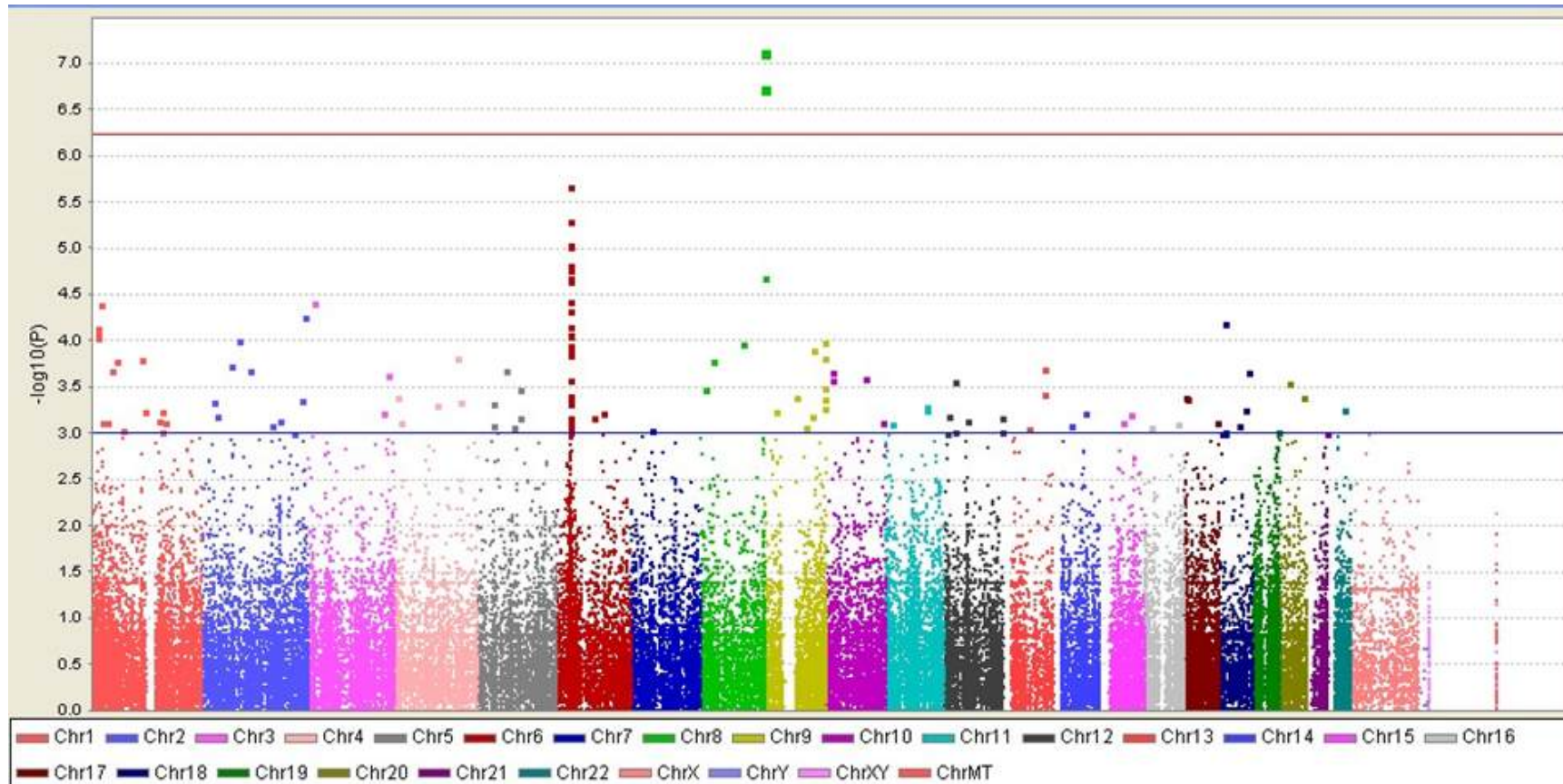


Figure 3. A visualization of exome study of SNPs using a Manhattan plot of significance against chromosomal location, shown here for a gastric cancer risk. The plot represents the significance of the association between SNPs and the gastric cancer. The Y-axis shows  $-\log_{10}$  transformed P-values, which represent the strength of association. The horizontal line indicates the exome-wide significance level ( $P < 0.0001$ ) for the most significant gene.

Table 10. Basic information of SNPs associated with the risk of gastric cancer

rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs10492972	1	10353112	intron	KIF1B	T<C	0.44	0.36	0.68	8.20E-05	Dominant
rs17401966	1	10385471	intron	KIF1B	A<G	0.35	0.27	0.56	9.16E-05	Codominant
rs1049887	1	10460485	exon, intron, missense, synon	PGD	T<C	0.34	0.26	0.55	7.13E-05	Codominant
rs3754334	1	16451767	synon	EPHA2	A<G	0.14	0.13	0.03	4.10E-05	Recessive
rs2072671	1	20915701	exon, missense	CDA	A<C	0.22	0.16	0.38	7.70E-04	Dominant
rs11554674	1	33790496	cds, exon, intron, synon	PHC2	A<G	0.21	0.15	0.88	7.57E-04	Allele
rs12026290	1	33820134	UTR-5, exon, intron, missense	PHC2	T<C	0.21	0.15	0.88	7.57E-04	Allele
rs138700771	1	43166410	intron	YBX1	-<AGA	0.25	0.23	0.13	2.05E-04	Recessive
rs671108	1	55266797	missense	TTC22	C<G	0.33	0.27	0.12	1.64E-04	Dominant
rs1884444	1	67633812	UTR-5, missense	IL23R	T<G	0.35	0.41	0.13	9.13E-04	Dominant
rs200084754	1	109812674	exon, intron, missense	CELSR2	A<C	0.02	0.00	0.00	1.59E-04	Allele
rs17185492	1	118644524	missense	SPAG17	A<T	0.15	0.10	0.19	5.68E-04	Codominant
rs75743857	1	150935173	exon, intron, missense	CERS2, SETDB1	T<C	0.02	0.00	1.00	7.20E-04	Dominant, Codominant
rs2494250	1	159278251			C<G	0.22	0.17	0.09	9.77E-04	Dominant
rs3747617	1	159912899	exon, missense	IGSF9	T<C	0.16	0.10	0.03	5.79E-04	Allele
rs1479640	1	163948373			A<C	0.50	0.45	0.02	7.50E-04	Recessive
rs72786179	2	29225504	intron, missense	FAM179A	T<C	0.27	0.20	0.40	4.58E-04	Allele
rs305163	2	36309662			A<G	0.12	0.18	0.60	6.47E-04	Dominant
rs6734275	2	67241174			G<A	0.55	0.48	0.11	1.83E-04	Recessive
rs60719900	2	85299783			A<C	0.34	0.39	0.13	9.93E-05	Dominant
rs17036104	2	108922036	UTR-3, exon, intron, missense	SULT1C2	T<G	0.11	0.08	0.79	2.07E-04	Recessive
rs6432679	2	162208258	intron	PSMD14	T<C	0.41	0.36	0.04	8.32E-04	Recessive
rs2244492	2	179554305	cds, intron, missense	TTN	T<C	0.09	0.14	0.76	7.19E-04	Dominant
rs3835047	2	211421452	UTR-5, aa-indel	CPS1	-<TCT	0.33	0.38	0.26	9.83E-04	Recessive
rs7574414	2	228243905	missense	TM4SF20	A<G	0.15	0.18	0.36	4.42E-04	Recessive



rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs11563246	2	234708868	downstream, exon, missense	HEATR7B1, HJURP, UGT1A6	C<G	0.25	0.31	0.07	5.58E-05	Recessive
rs201192415	3	13672855	cds, missense	FBLN2	A<G	0.02	0.00	0.00	3.81E-05	Allele
rs12629412	3	174127605			T<C	0.42	0.35	0.80	6.09E-04	Dominant
rs16858778	3	184102396	UTR-3, cds,exon, intron, synon	CHRD, EIF2B5	T<C	0.25	0.18	0.44	2.30E-04	Codominant
rs189070828	4	8584332	exon, missense	GPR78	T<C	0.01	0.00	1.00	4.10E-04	Allele
rs2286455	4	16020162	UTR-3, exon, splice-site, synon	PROM1	T<C	0.21	0.26	0.84	7.63E-04	Dominant
rs1859156	4	95834034	intron	BMPR1B	T<G	0.11	0.07	0.76	4.84E-04	Allele
rs1436512	4	142334360			T<C	0.20	0.28	0.85	1.50E-04	Codominant
	4	152201018	cds, intron, missense	PRSS48	T<G	0.17	0.24	0.29	4.57E-04	Dominant
rs1946267	5	33921810			A<G	0.40	0.45	0.14	8.24E-04	Dominant
rs840398	5	34016023	intron	C1QTNF3, C1QTNF3-AMACR	T<C	0.55	0.47	0.22	4.81E-04	Recessive
rs3830368	5	64747918	intron	ADAMTS6	—<G	0.23	0.30	0.52	2.12E-04	Dominant
	5	82940271	frameshift	HAPLN1	—<G	0.31	0.37	0.32	8.61E-04	Dominant
rs34899	5	95091201	UTR-3, exon, intron, missense	GLRX, RHOBTB3	A<G	0.30	0.22	0.05	3.30E-04	Allele
rs39597	5	96484131	downstream, intron, upstream	LIX1, RIOK2	T<G	0.31	0.39	0.30	6.74E-04	Allele
rs1119080	6	29536685	intron, upstream	GABBR1, SNORD32B, UBD	A<G	0.33	0.44	0.16	1.54E-05	Allele
rs362522	6	29545208	intron, upstream	GABBR1, SNORD32B, UBD	T<C	0.21	0.29	1.00	2.61E-04	Allele
rs1233391	6	29550618	downstream, exon, intron, upstream	GABBR1, OR2H2, SNORD32B	T<C	0.54	0.46	0.94	9.68E-04	Allele
rs1233388	6	29553727	downstream, intron, upstream	GABBR1, OR2H2, SNORD32B	A<G	0.54	0.46	0.94	4.72E-04	Allele
rs2240070	6	30071110	UTR-3, exon, intron	TRIM31	T<C	0.17	0.25	0.36	8.95E-06	Dominant
rs3132680	6	30073195	exon, intron	TRIM31	A<C	0.17	0.26	0.84	2.17E-06	Dominant
rs2844795	6	30073847	intron	TRIM31	T<C	0.29	0.36	0.62	4.76E-04	Codominant
rs2523990	6	30077229	intron	TRIM31	A<G	0.30	0.39	0.17	5.02E-06	Dominant
rs2239529	6	30078330	exon, intron, synon	TRIM31	T<C	0.08	0.08	0.01	3.95E-04	Recessive
rs2517598	6	30080274	exon, intron, synon	TRIM31	A<G	0.08	0.08	0.01	4.03E-04	Recessive

rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs2844793	6	30080496	exon, intron, synon	TRIM31	A<G	0.08	0.08	0.01	4.11E-04	Recessive
rs9261438	6	30089280			T<C	0.19	0.28	0.70	2.06E-05	Allele
rs9261440	6	30090820			T<C	0.18	0.26	0.77	8.81E-05	Allele
rs1419673	6	30096717			A<G	0.17	0.25	0.76	3.77E-05	Allele
rs1419671	6	30097170			A<T	0.17	0.25	0.76	3.77E-05	Allele
rs1541267	6	30103571			A<G	0.18	0.26	0.84	1.24E-04	Allele
rs9261468	6	30104480	intron, upstream	TRIM31, TRIM40	A<G	0.16	0.24	0.75	2.09E-05	Allele
rs9261485	6	30108751	intron	TRIM40	A<G	0.16	0.24	0.83	2.06E-05	Allele
rs9261492	6	30110058	intron	TRIM40	A<G	0.18	0.26	0.92	1.11E-04	Allele
rs9261508	6	30112704	intron	TRIM40	T<C	0.18	0.26	0.84	1.10E-04	Allele
rs757262	6	30114955	missense	TRIM40	T<C	0.16	0.24	0.75	2.09E-05	Allele
rs757259	6	30115542	missense	TRIM40	A<G	0.16	0.24	0.75	1.66E-05	Allele
rs1557611	6	30118360			T<C	0.16	0.24	0.75	2.09E-05	Allele
rs1557608	6	30118582			T<G	0.18	0.26	0.84	1.42E-04	Allele
rs2517653	6	30121185	UTR-3	TRIM10	A<G	0.17	0.26	0.84	9.36E-06	Allele
rs2022065	6	30121460	UTR-3	TRIM10	T<C	0.25	0.34	0.44	1.71E-05	Codominant
rs9261535	6	30127323	intron	TRIM10	A<G	0.15	0.23	0.52	2.28E-05	Allele
rs929156	6	30139699	cds, intron, missense	TRIM15	A<G	0.17	0.24	0.76	1.16E-04	Allele
rs2844782	6	30150043			T<G	0.29	0.37	0.10	7.95E-04	Allele
rs2239530	6	30152115			C<G	0.15	0.23	0.51	4.74E-05	Allele
rs4711211	6	30162809	intron	TRIM26	A<G	0.15	0.23	0.75	8.35E-05	Codominant
rs3132672	6	30175847	intron	TRIM26	A<C	0.32	0.39	0.30	9.75E-04	Recessive
rs3132671	6	30178287	intron	TRIM26	T<C	0.30	0.37	0.22	7.96E-04	Recessive
rs2844775	6	30179422	intron	TRIM26	A<G	0.16	0.23	0.67	7.04E-05	Allele
rs3130391	6	30190640			T<C	0.30	0.37	0.16	6.72E-04	Recessive
rs3132667	6	30191587			A<G	0.30	0.37	0.06	7.95E-04	Recessive
rs885915	6	30202715	intron	HCG17	T<C	0.30	0.37	0.19	8.20E-04	Recessive

rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs2844780	6	30204526	intron	HCG17	T<G	0.30	0.36	0.21	7.08E-04	Recessive
rs2844779	6	30205407	intron	HCG17	T<G	0.30	0.36	0.25	8.88E-04	Recessive
rs1264585	6	30285650	intron	HCG17, HCG18	A<T	0.19	0.25	0.54	7.89E-04	Codominant
rs6910017	6	84971363			A<G	0.42	0.47	0.28	6.76E-04	Dominant
rs7759938	6	105378954			T<C	0.19	0.26	0.37	6.11E-04	Codominant
rs2290386	7	47852837	exon, intron, missense	C7orf69, HUS1, PKD1L1	T<C	0.24	0.18	0.35	9.35E-04	Allele
rs61756425	8	8999039	exon, missense	PPP1R3B	T<G	0.09	0.05	0.70	3.33E-04	Dominant
rs751141	8	27373865	cds, exon, missense	EPHX2	A<G	0.18	0.26	1.00	1.65E-04	Codominant
rs10112232	8	95825034			A<G	0.37	0.29	0.40	1.08E-04	Dominant
rs2294008	8	143761931	UTR-5, intron	JRK, PSCA	C<T	0.60	0.47	0.40	1.83E-07	Dominant
rs1045531	8	143763547	exon, synon	PSCA	C<A	0.60	0.47	0.28	7.24E-08	Dominant
rs200893203	8	145007500	missense	PLEC	A<G	0.02	0.00	0.00	2.04E-05	Allele
rs55979986	9	27197557	synon	TEK	A<G	0.05	0.02	0.34	5.83E-04	Allele
rs141858334	9	71661314	UTR-5, missense	FXN	A<G	0.01	0.00	1.00	4.13E-04	Allele
rs3935601	9	94508700	intron	ROR2	T<C	0.43	0.37	0.14	8.67E-04	Dominant
rs3814538	9	109691676	cds, intron, missense	MIR548Q, ZNF462	G<A	0.56	0.50	0.40	6.52E-04	Recessive
rs10739288	9	112775268	intron	AKAP2, PALM2-AKAP2	A<G	0.31	0.40	0.75	1.25E-04	Allele
rs1053878	9	136131651	exon, missense	ABO	A<G	0.31	0.24	0.21	3.15E-04	Codominant
rs651007	9	136153875			T<C	0.33	0.25	0.42	4.24E-04	Codominant
rs579459	9	136154168			T<C	0.33	0.25	0.36	5.24E-04	Codominant
rs495828	9	136154867			T<G	0.33	0.25	0.42	4.24E-04	Codominant
rs635634	9	136155000			T<C	0.33	0.25	0.18	1.52E-04	Codominant
rs7027926	9	137925543			A<G	0.02	0.01	0.00	1.02E-04	Dominant
rs2062988	10	12143105	cds, missense	DHTKD1	C<G	0.27	0.35	0.08	2.63E-04	Codominant
rs1451668	10	15626513	intron	ITGA8	T<C	0.44	0.39	0.13	2.17E-04	Recessive
rs10788615	10	90580144	UTR-3, synon	ANKRD22, LIPM	T<C	0.43	0.35	0.67	2.58E-04	Codominant
rs2071498	10	129917560	exon, intron, missense	MKI67	T<C	0.31	0.37	1.00	7.62E-04	Dominant

rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs903809	11	14974477	downstream, intron, upstream	CALCA, CALCB, CYP2R1	T<C	0.19	0.25	0.22	7.76E-04	Dominant
rs2303960	11	94533373	cds, synon	AMOTL1	C<T	0.57	0.50	0.06	5.12E-04	Recessive
rs878874	11	94588465	intron	AMOTL1	A<G	0.31	0.37	0.10	5.62E-04	Dominant
rs7969705	12	7280880	UTR-3, exon, missense	RBP5	C<G	0.13	0.15	0.03	9.88E-04	Recessive
rs2617170	12	10560957	UTR-5, exon, missense	KLRC4, KLRC4-KLRK1, KLRK1	T<C	0.47	0.39	0.87	6.41E-04	Allele
	12	25666033	intron	IFLTD1	A<G	0.40	0.33	0.86	9.74E-04	Allele
rs1479500	12	25671759	cds, missense	IFLTD1	A<T	0.14	0.09	0.81	2.72E-04	Codominant
rs199673881	12	53722361	missense	SP7	A<G	0.02	0.00	1.00	7.24E-04	Dominant, Codominant
rs138640311	12	132209933	intron	SFSWAP	—<TG	0.52	0.44	0.35	6.66E-04	Allele
	12	132209938	intron	SFSWAP	—<G	0.52	0.44	0.31	9.54E-04	Allele
rs9537824	13	58408486			T<C	0.42	0.34	0.80	8.96E-04	Allele
rs4148549	13	95674164	intron	ABCC4	C<T	0.57	0.48	0.19	2.02E-04	Allele
rs4148546	13	95680285	intron	ABCC4	G<A	0.56	0.48	0.40	3.71E-04	Allele
rs1959258	14	41113268			A<G	0.36	0.42	0.08	8.24E-04	Recessive
rs3742836	14	73220020	cds, synon	DPF3	A<G	0.24	0.18	0.12	5.98E-04	Dominant
rs2305707	15	51569410	exon, intron	CYP19A1	A<G	0.25	0.31	0.15	7.65E-04	Recessive
rs12914996	15	68734797			A<G	0.39	0.46	0.59	6.23E-04	Recessive
rs11546303	16	14742400			A<G	0.39	0.46	0.59	6.23E-04	Recessive
rs28584228	16	76486581	exon, missense, synon	CNTNAP4	A<G	0.17	0.23	0.33	7.87E-04	Dominant
rs3764897	17	4722876	intron, missense, splice-site	PLD2	A<G	0.11	0.09	0.00	3.99E-04	Recessive
rs141572082	17	8273305	missense	KRBA2	T<C	0.01	0.00	1.00	4.14E-04	Allele
rs55715426	17	73760820	intron, missense	GALK1	A<G	0.15	0.11	0.44	7.63E-04	Recessive
rs671871	18	6977844	missense	LAMA1	A<G	0.08	0.13	0.12	9.93E-04	Codominant
rs79992793	18	10699087	UTR-5, missense	PIEZO2	C<G	0.11	0.06	0.10	9.80E-04	Allele
rs4796901	18	10704619	missense	PIEZO2	C<G	0.21	0.14	0.52	6.35E-05	Dominant
rs11267036	18	12308793	UTR-5, splice-site, synon	TUBB6	C<G	0.24	0.21	0.49	9.72E-04	Recessive

rs number	Chr	Position†	Region	Gene‡	Allele	MAF		HWE	Association	
						CASE	CTRL		P-value	Model*
rs12606417	18	44104437	missense	LOXHD1	T<C	0.07	0.04	1.00	8.18E-04	Allele
rs884205	18	60054857	UTR-3	TNFRSF11A	A<C	0.23	0.21	0.00	5.60E-04	Recessive
rs1157329	18	64645270			C<A	0.56	0.48	0.94	2.19E-04	Recessive
rs2304167	19	55527081			C<A	0.56	0.48	0.94	2.19E-04	Recessive
rs6048138	20	22484805	exon, missense	GP6	T<C	0.14	0.20	0.55	9.66E-04	Allele
rs34515071	20	56034988			A<G	0.35	0.43	0.58	4.07E-04	Codominant
rs117931394	21	47552386	missense	COL6A2	A<G	0.14	0.17	0.00	9.97E-04	Recessive
rs2076672	22	36123083	missense	APOL5	T<C	0.06	0.11	0.84	5.63E-04	Codominant

\*Genetic model used for the best P-value

† Position within chromosome. Nearby genes are defined as the closes genes to the SNP.

‡ The information of gene and region was from NetAffx of Affymetrix.

KIF1B (kinesin family member 1B), PGD (phosphogluconate dehydrogenase), EPHA2 (EPH receptor A2), CDA (cytidine deaminase), PHC2 (polyhomeotic homolog 2), YBX1 (Y box binding protein 1), TTC22 (tetratricopeptide repeat domain 22), IL23R (interleukin 23 receptor), CELSR2 (cadherin, EGF LAG seven-pass G-type receptor 2), SPAG17 (sperm associated antigen 17), CERS2 (ceramide synthase 2), SETDB1 (SET domain, bifurcated 1), IGSF9 (immunoglobulin superfamily, member 9), FAM179A (family with sequence similarity 179, member A), SULT1C2 (sulfotransferase family, cytosolic, 1C, member 2), PSMD14 (proteasome (prosome, macropain) 26S subunit, non-ATPase, 14), TTN (titin), CPS1 (carbamoyl-phosphate synthase 1, mitochondrial), TM4SF20 (transmembrane 4 L six family member 20), HEATR7B1 (maestro heat-like repeat family member 2A), HJURP (Holliday junction recognition protein), UGT1A6 (UDP glucuronosyltransferase 1 family, polypeptide A6), FBLN2 (fibulin 2), CHRDL1 (chordin), EIF2B5 (eukaryotic translation initiation factor 2B, subunit 5 epsilon, 82kDa), GPR78 (G protein-coupled receptor 78), PROM1 (prominin 1), BMPRI1 (bone morphogenetic protein receptor, type I), PRSS48 (protease, serine, 48), C1QTNF3 (C1q and tumor necrosis factor related protein 3), C1QTNF3-AMACR (C1q and tumor necrosis factor related protein 3-alpha-methylacyl-CoA racemase readthrough (NMD candidate)), ADAMTS6 (ADAM metalloproteinase with thrombospondin type 1 motif, 6), HAPLN1 (hyaluronan and proteoglycan link protein 1), GLRX (glutaredoxin (thioltransferase)), RHOBTB3 (Rho-related BTB domain containing 3), LIX1 (Lix1 homolog), RIOK2 (RIO kinase 2), GABBR1 (gamma-aminobutyric acid (GABA) B receptor, 1), SNORD32B (small nucleolar RNA, C/D box 32B), UBD (ubiquitin D), OR2H2 (olfactory receptor, family 2, subfamily H, member 2), TRIM31 (tripartite motif containing 31), TRIM40 (tripartite motif containing 40), TRIM10 (tripartite motif containing 10), TRIM15 (tripartite motif containing 15), TRIM26 (tripartite motif containing 26), HCG17 (HLA complex group 17 (non-protein coding)), HCG18 (HLA complex group 18 (non-protein coding)), C7orf69 (chromosome 7 open reading frame 69), HUS1 (HUS1 checkpoint homolog), PKD1L1 (polycystic kidney disease 1 like 1), PPP1R3B (protein phosphatase 1, regulatory subunit 3B), EPHX2 (epoxide hydrolase 2, cytoplasmic), JRK (jerky homolog), PSCA (prostate stem cell antigen), PLEC (plectin), TEK (TEK tyrosine kinase, endothelial), FXN (frataxin), ROR2 (receptor tyrosine kinase-like orphan receptor 2), MIR548Q (microRNA 548q), ZNF462 (zinc finger protein 462), AKAP2 (A kinase (PKA) anchor protein 2), PALM2-AKAP2 (paralemmn 2-A kinase anchor protein 2), ABO (ABO blood group (transferase A, alpha 1-3-N-acetylgalactosaminyltransferase; transferase B, alpha 1-3-galactosyltransferase)), DHTKD1 (dehydrogenase E1 and transketolase domain containing 1), ITGA8 (integrin, alpha 8), ANKRD22 (ankyrin repeat domain 22),

LIPM (lipase, family member M), MKI67 (marker of proliferation Ki-67), CALCA (calcitonin-related polypeptide alpha), CALCB (calcitonin-related polypeptide beta), CYP2R1 (cytochrome P450, family 2, subfamily R, polypeptide 1), AMOTL1 (angiomin like 1), RBP5 (retinol binding protein 5, cellular), KLRC4 (killer cell lectin-like receptor subfamily C, member 4), KLRC4-KLRK1 (killer cell lectin-like receptor subfamily C, member 4-killer cell lectin-like receptor subfamily K, member 1 readthrough), KLRK1 (killer cell lectin-like receptor subfamily K, member 1), IFLTD1 (intermediate filament tail domain containing 1), SP7 (Sp7 transcription factor), SFSWAP (splicing factor, suppressor of white-apricot homolog), ABCC4 (ATP-binding cassette, sub-family C (CFTR/MRP), member 4), DPF3 (D4, zinc and double PHD fingers, family 3), CYP19A1 (cytochrome P450, family 19, subfamily A, polypeptide 1), CNTNAP4 (contactin associated protein-like 4), PLD2 (phospholipase D2), KRBA2 (KRAB-A domain containing 2), GALK1 (galactokinase 1), LAMA1 (laminin, alpha 1), PIEZO2 (piezo-type mechanosensitive ion channel component 2), TUBB6 (tubulin, beta 6 class V), LOXHD1 (lipoxygenase homology domains 1), TNFRSF11A (tumor necrosis factor receptor superfamily, member 11a, NFkB activator), GP6 (glycoprotein VI (platelet)), COL6A2 (collagen, type VI, alpha 2), APOL5 (apolipoprotein L, 5)

Table 11. Distributions of genotype and allele of discovered SNPs in this study, according to gastric cancer status

rs_number	N (%)									
	Case					Control				
	Genotype			Allele		Genotype			Allele	
	Major homo	Hetero	Minor homo	Minor	Major	Major homo	Hetero	Minor homo	Minor	Major
rs10492972	94(0.29)	182(0.55)	53(0.16)	288(0.44)	370(0.56)	282(0.41)	309(0.45)	91(0.13)	491(0.36)	873(0.64)
rs17401966	134(0.41)	160(0.49)	35(0.11)	230(0.35)	428(0.65)	364(0.53)	274(0.40)	45(0.07)	364(0.27)	1002(0.73)
rs1049887	136(0.42)	159(0.48)	33(0.10)	225(0.34)	431(0.66)	369(0.54)	268(0.39)	42(0.06)	352(0.26)	1006(0.74)
rs3754334	253(0.77)	60(0.18)	15(0.05)	90(0.14)	566(0.86)	508(0.74)	169(0.25)	5(0.01)	179(0.13)	1185(0.87)
rs2072671	200(0.61)	114(0.35)	14(0.04)	142(0.22)	514(0.78)	487(0.72)	174(0.26)	20(0.03)	214(0.16)	1148(0.84)
rs11554674	209(0.64)	104(0.32)	16(0.05)	136(0.21)	522(0.79)	497(0.73)	171(0.25)	15(0.02)	201(0.15)	1165(0.85)
rs12026290	209(0.64)	104(0.32)	16(0.05)	136(0.21)	522(0.79)	497(0.73)	171(0.25)	15(0.02)	201(0.15)	1165(0.85)
rs138700771	197(0.60)	99(0.30)	33(0.10)	165(0.25)	493(0.75)	400(0.59)	255(0.37)	28(0.04)	311(0.23)	1055(0.77)
rs671108	140(0.43)	159(0.48)	30(0.09)	219(0.33)	439(0.67)	377(0.55)	250(0.37)	56(0.08)	362(0.27)	1004(0.74)
rs1884444	145(0.44)	139(0.42)	45(0.14)	229(0.35)	429(0.65)	227(0.33)	349(0.51)	105(0.15)	559(0.41)	803(0.59)
rs200084754	323(0.98)	0(0)	5(0.02)	10(0.02)	646(0.98)	682(1.00)	0(0)	1(0.00)	2(0.00)	1364(1.00)
rs17185492	238(0.72)	85(0.26)	6(0.02)	97(0.15)	561(0.85)	554(0.81)	126(0.18)	3(0.00)	132(0.10)	1234(0.90)
rs75743857	315(0.96)	13(0.04)	0(0)	13(0.02)	643(0.98)	677(0.99)	6(0.01)	0(0)	6(0.00)	1360(1.00)
rs2494250	198(0.60)	116(0.35)	15(0.05)	146(0.22)	512(0.78)	482(0.71)	176(0.26)	25(0.04)	226(0.17)	1140(0.83)
rs3747617	232(0.71)	92(0.28)	5(0.02)	102(0.16)	556(0.85)	544(0.80)	135(0.20)	2(0.00)	139(0.10)	1223(0.90)
rs1479640	90(0.27)	150(0.46)	89(0.27)	328(0.50)	330(0.50)	191(0.28)	370(0.54)	122(0.18)	614(0.45)	752(0.55)
rs72786179	175(0.53)	131(0.40)	23(0.07)	177(0.27)	481(0.73)	441(0.65)	211(0.31)	31(0.05)	273(0.20)	1093(0.80)
rs305163	255(0.78)	67(0.20)	6(0.02)	79(0.12)	577(0.88)	457(0.67)	203(0.30)	19(0.03)	241(0.18)	1117(0.82)
rs6734275	71(0.22)	151(0.46)	107(0.33)	365(0.55)	293(0.45)	172(0.25)	361(0.53)	147(0.22)	655(0.48)	705(0.52)
rs60719900	160(0.49)	112(0.34)	57(0.17)	226(0.34)	432(0.66)	244(0.36)	344(0.51)	93(0.14)	530(0.39)	832(0.61)
rs17036104	269(0.82)	48(0.15)	11(0.03)	70(0.11)	586(0.89)	581(0.85)	99(0.14)	3(0.00)	105(0.08)	1261(0.92)
rs6432679	119(0.36)	148(0.45)	62(0.19)	272(0.41)	386(0.59)	266(0.39)	340(0.50)	76(0.11)	492(0.36)	872(0.64)
rs2244492	273(0.83)	51(0.16)	5(0.02)	61(0.09)	597(0.91)	501(0.73)	167(0.24)	15(0.02)	197(0.14)	1169(0.86)
rs3835047	140(0.43)	162(0.49)	27(0.08)	216(0.33)	442(0.67)	266(0.39)	308(0.45)	107(0.16)	522(0.38)	840(0.62)

rs_number	N (%)									
	Case					Control				
	Genotype		Minor homo	Allele		Genotype		Allele		
Major homo	Hetero	Minor		Major	Major homo	Hetero	Minor homo	Minor	Major	
rs7574414	230(0.70)	99(0.30)	0(0)	99(0.15)	559(0.85)	467(0.68)	191(0.28)	25(0.04)	241(0.18)	1125(0.82)
rs11563246	173(0.53)	145(0.44)	11(0.03)	167(0.25)	491(0.75)	338(0.50)	270(0.40)	74(0.11)	418(0.31)	946(0.69)
rs201192415	322(0.98)	0(0)	7(0.02)	14(0.02)	644(0.98)	681(1.00)	0(0)	2(0.00)	4(0.00)	1362(1.00)
rs12629412	103(0.31)	175(0.53)	51(0.16)	277(0.42)	381(0.58)	290(0.43)	307(0.45)	85(0.12)	477(0.35)	887(0.65)
rs16858778	186(0.57)	120(0.36)	23(0.07)	166(0.25)	492(0.75)	453(0.66)	210(0.31)	19(0.03)	248(0.18)	1116(0.82)
rs189070828	326(0.99)	0(0)	3(0.01)	6(0.01)	652(0.99)	683(1.00)	0(0)	0(0)	0(0)	1366(1.00)
rs2286455	214(0.65)	95(0.29)	20(0.06)	135(0.21)	523(0.79)	368(0.54)	269(0.39)	46(0.07)	361(0.26)	1005(0.74)
rs1859156	259(0.79)	67(0.20)	3(0.01)	73(0.11)	585(0.89)	595(0.87)	86(0.13)	2(0.00)	90(0.07)	1276(0.93)
rs1436512	209(0.64)	107(0.33)	13(0.04)	133(0.20)	525(0.80)	352(0.52)	279(0.41)	52(0.08)	383(0.28)	983(0.72)
	232(0.71)	83(0.25)	14(0.04)	111(0.17)	547(0.83)	404(0.59)	236(0.35)	43(0.06)	322(0.24)	1044(0.76)
rs1946267	128(0.39)	136(0.41)	65(0.20)	266(0.40)	392(0.60)	194(0.28)	358(0.52)	130(0.19)	618(0.45)	746(0.55)
rs840398	68(0.21)	158(0.48)	103(0.31)	364(0.55)	294(0.45)	181(0.27)	357(0.52)	145(0.21)	647(0.47)	719(0.53)
rs3830368	201(0.61)	106(0.32)	22(0.07)	150(0.23)	508(0.77)	332(0.49)	293(0.43)	57(0.08)	407(0.30)	957(0.70)
	166(0.50)	123(0.37)	40(0.12)	203(0.31)	455(0.69)	269(0.39)	329(0.48)	85(0.12)	499(0.37)	867(0.63)
rs34899	169(0.51)	125(0.38)	35(0.11)	195(0.30)	463(0.70)	421(0.62)	218(0.32)	43(0.06)	304(0.22)	1060(0.78)
rs39597	158(0.48)	132(0.40)	37(0.11)	206(0.32)	448(0.69)	258(0.38)	312(0.46)	112(0.16)	536(0.39)	828(0.61)
rs1119080	153(0.47)	127(0.39)	45(0.14)	217(0.33)	433(0.67)	225(0.33)	315(0.47)	137(0.20)	589(0.44)	765(0.57)
rs362522	204(0.62)	110(0.33)	15(0.05)	140(0.21)	518(0.79)	345(0.51)	281(0.41)	57(0.08)	395(0.29)	971(0.71)
rs1233391	71(0.22)	162(0.49)	96(0.29)	354(0.54)	304(0.46)	200(0.29)	338(0.49)	145(0.21)	628(0.46)	738(0.54)
rs1233388	67(0.21)	159(0.50)	95(0.30)	349(0.54)	293(0.46)	195(0.29)	335(0.50)	141(0.21)	617(0.46)	725(0.54)
rs2240070	229(0.70)	85(0.26)	15(0.05)	115(0.17)	543(0.83)	375(0.55)	268(0.39)	39(0.06)	346(0.25)	1018(0.75)
rs3132680	228(0.70)	84(0.26)	14(0.04)	112(0.17)	540(0.83)	369(0.54)	266(0.39)	45(0.07)	356(0.26)	1004(0.74)
rs2844795	168(0.51)	134(0.41)	27(0.08)	188(0.29)	470(0.71)	273(0.40)	323(0.47)	87(0.13)	497(0.36)	869(0.64)
rs2523990	166(0.50)	128(0.39)	35(0.11)	198(0.30)	460(0.70)	242(0.35)	344(0.50)	97(0.14)	538(0.39)	828(0.61)
rs2239529	283(0.86)	39(0.12)	6(0.02)	51(0.08)	605(0.92)	570(0.83)	113(0.17)	0(0)	113(0.08)	1253(0.92)



rs_number	N (%)									
	Case					Control				
	Genotype		Minor homo	Allele		Genotype		Allele		
Major homo	Hetero	Minor		Major	Major homo	Hetero	Minor homo	Minor	Major	
rs2517598	283(0.86)	40(0.12)	6(0.02)	52(0.08)	606(0.92)	569(0.83)	114(0.17)	0(0)	114(0.08)	1252(0.92)
rs2844793	284(0.86)	39(0.12)	6(0.02)	51(0.08)	607(0.92)	569(0.84)	112(0.16)	0(0)	112(0.08)	1250(0.92)
rs9261438	214(0.65)	103(0.31)	12(0.04)	127(0.19)	531(0.81)	355(0.52)	271(0.40)	56(0.08)	383(0.28)	981(0.72)
rs9261440	221(0.67)	96(0.29)	12(0.04)	120(0.18)	538(0.82)	373(0.55)	260(0.39)	48(0.07)	356(0.26)	1006(0.74)
rs1419673	230(0.70)	89(0.27)	10(0.03)	109(0.17)	549(0.83)	389(0.57)	251(0.37)	43(0.06)	337(0.25)	1029(0.75)
rs1419671	230(0.70)	89(0.27)	10(0.03)	109(0.17)	549(0.83)	389(0.57)	251(0.37)	43(0.06)	337(0.25)	1029(0.75)
rs1541267	220(0.67)	98(0.30)	11(0.03)	120(0.18)	538(0.82)	375(0.55)	260(0.38)	47(0.069)	354(0.26)	1010(0.74)
rs9261468	234(0.71)	86(0.26)	9(0.03)	104(0.16)	554(0.84)	395(0.58)	247(0.36)	41(0.06)	329(0.24)	1037(0.76)
rs9261485	233(0.71)	86(0.26)	9(0.03)	104(0.16)	552(0.84)	394(0.58)	248(0.36)	41(0.06)	330(0.24)	1036(0.76)
rs9261492	221(0.67)	97(0.29)	11(0.03)	119(0.18)	539(0.82)	375(0.55)	260(0.38)	46(0.07)	352(0.26)	1010(0.74)
rs9261508	220(0.67)	97(0.30)	11(0.03)	119(0.18)	537(0.82)	376(0.55)	260(0.38)	47(0.07)	354(0.26)	1012(0.74)
rs757262	234(0.71)	86(0.26)	9(0.03)	104(0.16)	554(0.84)	395(0.58)	247(0.36)	41(0.06)	329(0.24)	1037(0.76)
rs757259	234(0.71)	85(0.26)	9(0.03)	103(0.17)	553(0.84)	395(0.58)	247(0.36)	41(0.06)	329(0.24)	1037(0.76)
rs1557611	234(0.71)	86(0.26)	9(0.03)	104(0.16)	554(0.84)	395(0.58)	247(0.36)	41(0.06)	329(0.24)	1037(0.76)
rs1557608	219(0.67)	98(0.30)	11(0.03)	120(0.18)	536(0.82)	375(0.55)	260(0.38)	47(0.07)	354(0.26)	1010(0.74)
rs2517653	227(0.69)	93(0.28)	9(0.03)	111(0.17)	547(0.83)	378(0.55)	259(0.38)	46(0.07)	351(0.26)	1015(0.74)
rs2022065	186(0.57)	124(0.38)	19(0.06)	162(0.25)	496(0.75)	293(0.43)	316(0.46)	74(0.11)	464(0.34)	902(0.66)
rs9261535	236(0.72)	88(0.27)	5(0.02)	98(0.15)	560(0.85)	408(0.60)	236(0.35)	39(0.06)	314(0.23)	1052(0.77)
rs929156	225(0.68)	97(0.29)	7(0.02)	111(0.17)	547(0.83)	390(0.57)	249(0.37)	42(0.06)	333(0.24)	1029(0.76)
rs2844782	162(0.49)	141(0.43)	25(0.08)	191(0.29)	465(0.71)	284(0.42)	297(0.43)	102(0.15)	501(0.37)	865(0.63)
rs2239530	235(0.72)	88(0.27)	5(0.02)	98(0.15)	558(0.85)	411(0.60)	234(0.34)	38(0.06)	310(0.23)	1056(0.77)
rs4711211	233(0.71)	91(0.28)	5(0.02)	101(0.15)	557(0.85)	407(0.60)	238(0.35)	37(0.05)	312(0.23)	1052(0.77)
rs3132672	149(0.45)	152(0.46)	28(0.09)	208(0.32)	450(0.68)	262(0.38)	311(0.46)	110(0.16)	531(0.39)	835(0.61)
rs3132671	157(0.48)	147(0.45)	25(0.08)	197(0.30)	461(0.70)	275(0.40)	305(0.45)	103(0.15)	511(0.37)	855(0.63)
rs2844775	231(0.70)	93(0.28)	5(0.02)	103(0.16)	555(0.84)	403(0.59)	240(0.35)	39(0.06)	318(0.23)	1046(0.77)

rs_number	N (%)									
	Case					Control				
	Genotype		Allele			Genotype		Allele		
	Major homo	Hetero	Minor homo	Minor	Major	Major homo	Hetero	Minor homo	Minor	Major
rs3130391	156(0.47)	149(0.45)	24(0.07)	197(0.30)	461(0.70)	281(0.41)	300(0.44)	101(0.15)	502(0.37)	862(0.63)
rs3132667	156(0.48)	146(0.45)	26(0.08)	198(0.30)	458(0.70)	281(0.41)	296(0.43)	106(0.16)	508(0.37)	858(0.63)
rs885915	157(0.48)	148(0.45)	24(0.07)	196(0.30)	462(0.70)	281(0.41)	301(0.44)	100(0.15)	501(0.37)	863(0.63)
rs2844780	157(0.48)	149(0.45)	23(0.07)	195(0.30)	463(0.70)	284(0.42)	300(0.44)	98(0.14)	496(0.36)	868(0.64)
rs2844779	157(0.48)	149(0.45)	23(0.07)	195(0.30)	463(0.70)	284(0.42)	302(0.44)	97(0.14)	496(0.36)	870(0.64)
rs1264585	212(0.65)	104(0.32)	9(0.03)	122(0.19)	528(0.81)	371(0.55)	263(0.39)	40(0.06)	343(0.25)	1005(0.75)
rs6910017	122(0.37)	139(0.42)	68(0.21)	275(0.42)	383(0.58)	181(0.27)	354(0.52)	145(0.21)	644(0.47)	716(0.53)
rs7759938	212(0.65)	106(0.32)	10(0.03)	126(0.19)	530(0.81)	366(0.54)	271(0.40)	41(0.06)	353(0.26)	1003(0.74)
rs2290386	194(0.59)	111(0.34)	23(0.07)	157(0.24)	499(0.76)	464(0.68)	190(0.28)	25(0.04)	240(0.18)	1118(0.82)
rs61756425	270(0.82)	59(0.18)	0(0)	59(0.09)	599(0.91)	615(0.90)	66(0.10)	2(0.00)	70(0.05)	1296(0.95)
rs751141	219(0.67)	101(0.31)	9(0.03)	119(0.18)	539(0.82)	378(0.55)	260(0.38)	45(0.07)	350(0.26)	1016(0.74)
rs10112232	124(0.38)	169(0.51)	36(0.11)	241(0.37)	417(0.63)	344(0.51)	272(0.40)	63(0.09)	398(0.29)	960(0.71)
rs2294008	45(0.14)	175(0.53)	109(0.33)	393(0.60)	265(0.40)	193(0.29)	325(0.48)	157(0.23)	639(0.47)	711(0.53)
rs1045531	45(0.14)	175(0.53)	109(0.33)	393(0.60)	265(0.40)	199(0.29)	326(0.48)	158(0.23)	642(0.47)	724(0.53)
rs200893203	323(0.98)	0(0)	6(0.018)	12(0.02)	646(0.98)	681(1.00)	0(0)	1(0.00)	2(0.00)	1362(1.00)
rs55979986	295(0.90)	32(0.40)	2(0.00)	36(0.05)	622(0.95)	650(0.95)	32(0.05)	1(0.00)	34(0.02)	1332(0.98)
rs141858334	324(0.99)	0(0)	3(0.01)	6(0.01)	648(0.99)	678(1.00)	0(0)	0(0)	0(0)	1356(1.00)
rs3935601	100(0.30)	178(0.54)	51(0.16)	280(0.43)	378(0.57)	280(0.41)	298(0.44)	101(0.15)	500(0.37)	858(0.63)
rs3814538	72(0.22)	145(0.44)	112(0.34)	369(0.56)	289(0.44)	167(0.24)	353(0.52)	163(0.24)	679(0.50)	687(0.50)
rs10739288	159(0.49)	134(0.41)	34(0.10)	202(0.31)	452(0.69)	243(0.36)	328(0.49)	104(0.15)	536(0.40)	814(0.60)
rs1053878	155(0.47)	141(0.43)	33(0.10)	207(0.31)	451(0.69)	388(0.57)	262(0.38)	33(0.05)	328(0.24)	1038(0.76)
rs651007	149(0.45)	145(0.44)	35(0.11)	215(0.33)	443(0.67)	377(0.55)	267(0.39)	39(0.06)	345(0.25)	1021(0.75)
rs579459	149(0.45)	145(0.44)	35(0.11)	215(0.33)	443(0.67)	374(0.55)	267(0.39)	39(0.06)	345(0.25)	1015(0.75)
rs495828	149(0.45)	145(0.44)	35(0.11)	215(0.33)	443(0.67)	377(0.55)	267(0.39)	39(0.06)	345(0.25)	1021(0.75)
rs635634	148(0.45)	145(0.44)	35(0.11)	215(0.33)	441(0.67)	376(0.55)	267(0.39)	35(0.05)	337(0.25)	1019(0.75)

rs_number	N (%)									
	Case					Control				
	Genotype		Allele	Genotype		Allele				
Major homo	Hetero	Minor homo		Minor	Major		Major homo	Hetero	Minor homo	Minor
rs7027926	313(0.96)	14(0.04)	0(0)	14(0.02)	640(0.98)	678(0.99)	3(0.00)	2(0.00)	7(0.01)	1359(0.99)
rs2062988	167(0.51)	146(0.44)	16(0.05)	178(0.27)	480(0.73)	279(0.41)	331(0.49)	72(0.11)	475(0.35)	889(0.65)
rs1451668	112(0.34)	141(0.43)	75(0.23)	291(0.44)	365(0.56)	246(0.36)	344(0.50)	93(0.14)	530(0.39)	836(0.61)
rs10788615	105(0.32)	165(0.50)	59(0.18)	283(0.43)	375(0.57)	288(0.42)	315(0.46)	79(0.12)	473(0.35)	891(0.65)
rs2071498	165(0.51)	119(0.37)	42(0.13)	203(0.31)	449(0.69)	267(0.39)	317(0.47)	94(0.14)	505(0.37)	851(0.63)
rs903809	217(0.66)	101(0.31)	11(0.03)	123(0.19)	535(0.81)	374(0.55)	271(0.40)	37(0.05)	345(0.25)	1019(0.75)
rs2303960	65(0.20)	155(0.47)	109(0.33)	373(0.57)	285(0.43)	159(0.23)	367(0.54)	156(0.23)	679(0.50)	685(0.50)
rs878874	163(0.4954)	131(0.40)	35(0.11)	201(0.31)	457(0.69)	260(0.38)	339(0.50)	83(0.12)	505(0.37)	859(0.63)
rs7969705	244(0.74)	85(0.26)	0(0)	85(0.13)	573(0.87)	506(0.74)	154(0.23)	22(0.03)	198(0.15)	1166(0.85)
rs2617170	94(0.29)	158(0.48)	76(0.23)	310(0.47)	346(0.53)	249(0.37)	327(0.48)	103(0.15)	533(0.39)	825(0.61)
	118(0.36)	156(0.47)	55(0.17)	266(0.40)	392(0.60)	308(0.45)	300(0.44)	75(0.11)	450(0.33)	916(0.67)
rs1479500	242(0.74)	81(0.25)	6(0.02)	93(0.14)	565(0.86)	566(0.83)	113(0.17)	4(0.01)	121(0.09)	1245(0.91)
rs199673881	317(0.96)	12(0.04)	0(0)	12(0.02)	646(0.98)	678(0.99)	5(0.01)	0(0)	5(0.00)	1361(1.00)
rs138640311	76(0.23)	165(0.50)	88(0.27)	341(0.52)	317(0.48)	222(0.33)	323(0.47)	137(0.20)	597(0.44)	767(0.56)
	76(0.23)	165(0.50)	87(0.27)	339(0.52)	317(0.48)	222(0.33)	323(0.47)	138(0.20)	599(0.434)	767(0.56)
rs9537824	109(0.33)	163(0.50)	56(0.17)	275(0.42)	381(0.58)	296(0.43)	304(0.45)	82(0.12)	468(0.34)	896(0.66)
rs4148549	62(0.19)	160(0.49)	107(0.33)	374(0.57)	284(0.43)	193(0.28)	323(0.47)	166(0.24)	655(0.48)	709(0.52)
rs4148546	63(0.19)	160(0.49)	105(0.32)	370(0.56)	286(0.44)	190(0.28)	329(0.48)	162(0.24)	653(0.48)	709(0.52)
rs1959258	130(0.40)	164(0.50)	35(0.11)	234(0.36)	424(0.64)	244(0.36)	309(0.45)	129(0.19)	567(0.42)	797(0.58)
rs3742836	186(0.57)	130(0.40)	13(0.04)	156(0.24)	502(0.76)	461(0.68)	192(0.28)	29(0.04)	250(0.18)	1114(0.82)
rs2305707	177(0.54)	138(0.42)	14(0.04)	166(0.25)	492(0.75)	337(0.49)	273(0.40)	72(0.11)	417(0.31)	947(0.69)
rs12914996	114(0.36)	172(0.52)	43(0.13)	258(0.39)	400(0.61)	199(0.29)	333(0.49)	151(0.22)	635(0.4649)	731(0.54)
rs11546303	223(0.68)	98(0.30)	8(0.02)	114(0.17)	544(0.83)	527(0.77)	147(0.22)	8(0.01)	163(0.1195)	1201(0.88)
rs28584228	228(0.69)	87(0.26)	14(0.04)	115(0.17)	543(0.83)	395(0.58)	251(0.37)	31(0.05)	313(0.2312)	1041(0.77)
rs3764897	262(0.80)	60(0.18)	6(0.02)	72(0.11)	584(0.89)	554(0.81)	128(0.19)	0(0)	128(0.09)	1236(0.91)

rs_number	N (%)									
	Case					Control				
	Genotype		Allele			Genotype		Allele		
	Major homo	Hetero	Minor homo	Minor	Major	Major homo	Hetero	Minor homo	Minor	Major
rs141572082	326(0.99)	0(0)	3(0.01)	6(0.01)	652(0.99)	682(1.00)	0(0)	0(0)	0(0)	1364(1.00)
rs55715426	243(0.74)	73(0.22)	13(0.04)	99(0.15)	559(0.85)	534(0.78)	141(0.21)	6(0.01)	153(0.11)	1209(0.89)
rs671871	279(0.85)	49(0.15)	1(0.00)	51(0.08)	607(0.92)	517(0.76)	159(0.23)	6(0.01)	171(0.13)	1193(0.87)
rs79992793	264(0.80)	60(0.18)	5(0.02)	70(0.11)	588(0.89)	595(0.87)	88(0.13)	0(0)	88(0.06)	1278(0.94)
rs4796901	204(0.62)	111(0.34)	12(0.04)	135(0.21)	519(0.79)	509(0.75)	158(0.23)	15(0.02)	188(0.14)	1176(0.86)
rs11267036	201(0.61)	98(0.30)	29(0.09)	156(0.24)	500(0.76)	424(0.62)	232(0.34)	26(0.04)	284(0.21)	1080(0.79)
rs12606417	286(0.87)	41(0.12)	2(0.01)	45(0.07)	613(0.93)	635(0.93)	48(0.07)	0(0)	48(0.04)	1318(0.96)
rs884205	198(0.61)	105(0.32)	23(0.07)	151(0.23)	501(0.77)	404(0.60)	257(0.38)	17(0.03)	291(0.21)	1065(0.79)
rs1157329	74(0.23)	141(0.43)	113(0.34)	367(0.56)	289(0.44)	183(0.27)	340(0.50)	160(0.23)	660(0.48)	706(0.52)
rs2304167	240(0.73)	84(0.26)	5(0.02)	94(0.14)	564(0.86)	436(0.64)	216(0.32)	31(0.05)	278(0.20)	1088(0.80)
rs6048138	112(0.34)	146(0.44)	71(0.22)	288(0.44)	370(0.56)	245(0.36)	351(0.51)	87(0.13)	525(0.38)	841(0.62)
rs34515071	138(0.42)	153(0.47)	38(0.12)	229(0.35)	429(0.65)	218(0.32)	342(0.50)	122(0.18)	586(0.43)	778(0.57)
rs117931394	235(0.72)	91(0.28)	2(0.01)	95(0.14)	561(0.86)	481(0.70)	171(0.25)	31(0.05)	233(0.17)	1133(0.83)
rs2076672	289(0.88)	38(0.12)	1(0.00)	40(0.06)	616(0.94)	542(0.79)	134(0.20)	7(0.01)	148(0.11)	1218(0.89)

Table 12. Association between gastric cancer risk and discovered SNPs in this study

rs number	OR (95% CI)			P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere-Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive	Allele	Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs10492972	1.76(1.33, 2.34)*	1.25(0.86, 1.80)	1.38(1.15, 1.67)	8.20E-05*	2.38E-01	4.27E-04	7.67E-04	6.54E-04	8.27E-05	2.39E-01	3.29E-04	7.69E-04
rs17401966	1.66(1.27, 2.17)	1.69(1.06, 2.68)	1.48(1.21, 1.81)	1.80E-04	2.53E-02	4.34E-04*	1.21E-04	9.16E-05	1.82E-04	2.54E-02	8.60E-05	1.21E-04
rs1049887	1.68(1.29, 2.19)	1.70(1.05, 2.73)	1.49(1.22, 1.83)	1.27E-04	2.82E-02	3.34E-04*	9.72E-05	7.13E-05	1.28E-04	2.82E-02	6.48E-05	9.76E-05
rs3754334	0.87(0.64, 1.18)	6.49(2.34, 18.01)*	1.05(0.80, 1.38)	3.61E-01	4.10E-05*	3.03E-05	7.12E-01	7.14E-01	3.61E-01	4.13E-05	5.71E-01	7.12E-01
rs2072671	1.61(1.22, 2.12)*	1.47(0.74, 2.96)	1.48(1.17, 1.88)	7.70E-04*	2.72E-01	3.44E-03	1.05E-03	1.17E-03	7.75E-04	2.73E-01	7.79E-04	1.06E-03
rs11554674	1.53(1.16, 2.03)	2.28(1.11, 4.66)	1.51(1.19, 1.92)*	2.72E-03	2.11E-02	3.34E-03	7.57E-04*	8.58E-04	2.73E-03	2.12E-02	1.65E-03	7.59E-04
rs12026290	1.53(1.16, 2.03)	2.28(1.11, 4.66)	1.51(1.19, 1.92)*	2.72E-03	2.11E-02	3.34E-03	7.57E-04*	8.58E-04	2.73E-03	2.12E-02	1.65E-03	7.59E-04
rs138700771	0.95(0.72, 1.24)	2.61(1.55, 4.40)*	1.14(0.91, 1.41)	6.91E-01	2.05E-04*	2.81E-04	2.51E-01	2.58E-01	6.91E-01	2.06E-04	7.21E-01	2.51E-01
rs671108	1.66(1.28, 2.17)*	1.12(0.71, 1.79)	1.38(1.13, 1.69)	1.64E-04*	6.23E-01	6.35E-04	1.58E-03	1.69E-03	1.65E-04	6.23E-01	5.27E-04	1.59E-03
rs1884444	0.63(0.48, 0.83)*	0.87(0.60, 1.27)	0.77(0.63, 0.93)	9.13E-04*	4.66E-01	3.85E-03	7.05E-03	6.61E-03	9.18E-04	4.66E-01	3.82E-03	7.06E-03
rs200084754	10.56(1.23, 90.73)	10.56(1.23, 90.73)	10.56(2.31, 48.32)*						7.60E-03	7.60E-03	7.60E-03	1.59E-04*
rs17185492	1.64(1.21, 2.24)	4.21(1.05, 16.94)	1.62(1.22, 2.14)	1.53E-03		1.68E-03*	7.29E-04	5.68E-04	1.54E-03	2.81E-02	1.18E-03	7.31E-04
rs75743857	4.66(1.75, 12.36)		4.58(1.73, 12.11)	7.20E-04*		7.20E-04*	7.64E-04	7.20E-04	7.25E-04		7.25E-04	7.66E-04
rs2494250	1.59(1.21, 2.09)*	1.26(0.65, 2.42)	1.44(1.14, 1.82)	9.77E-04*	4.92E-01	4.19E-03	2.14E-03	2.58E-03	9.83E-04	4.92E-01	1.23E-03	2.14E-03
rs3747617	1.66(1.23, 2.25)	5.24(1.01, 27.15)	1.61(1.23, 2.12)*	9.45E-04			5.79E-04*		9.51E-04	2.78E-02	7.29E-04	5.81E-04
rs1479640	1.03(0.77, 1.38)	1.71(1.25, 2.33)*	1.22(1.01, 1.47)	8.39E-01	7.50E-04*	2.24E-03	3.85E-02	3.53E-02	8.39E-01	7.54E-04	4.43E-02	3.85E-02
rs72786179	1.60(1.23, 2.10)	1.58(0.91, 2.76)	1.47(1.19, 1.83)*	5.14E-04	1.04E-01	1.97E-03	4.58E-04*	5.30E-04	5.17E-04	1.04E-01	4.19E-04	4.60E-04
rs305163	0.59(0.43, 0.80)*	0.65(0.26, 1.64)	0.64(0.48, 0.83)	6.47E-04*	3.54E-01	2.96E-03	1.03E-03	1.01E-03	6.51E-04	3.55E-01	6.70E-04	1.04E-03
rs6734275	1.23(0.90, 1.69)	1.75(1.30, 2.35)*	1.34(1.11, 1.62)	1.96E-01	1.83E-04*	9.10E-04	2.08E-03	1.92E-03	1.96E-01	1.84E-04	1.86E-03	2.08E-03
rs60719900	0.59(0.45, 0.77)*	1.33(0.93, 1.90)	0.82(0.68, 1.00)	9.93E-05*	1.24E-01	4.95E-06	4.68E-02	5.08E-02	1.00E-04	1.25E-01	1.44E-02	4.69E-02
rs17036104	1.25(0.88, 1.78)	7.87(2.18, 28.39)*	1.44(1.04, 1.97)	2.14E-01		9.88E-04	2.55E-02	3.16E-02	2.14E-01	2.07E-04*	1.58E-01	2.55E-02
rs6432679	1.13(0.86, 1.48)	1.85(1.29, 2.67)*	1.25(1.03, 1.51)	3.85E-01	8.32E-04*	3.70E-03	2.21E-02	2.04E-02	3.85E-01	8.37E-04	4.11E-02	2.21E-02
rs2244492	0.57(0.40, 0.79)*	0.69(0.25, 1.91)	0.61(0.45, 0.82)	7.19E-04*	4.69E-01	3.25E-03	1.13E-03	1.35E-03	7.24E-04	4.69E-01	7.79E-04	1.14E-03
rs3835047	0.87(0.66, 1.13)	0.48(0.31, 0.75)*	0.79(0.65, 0.96)	2.89E-01	9.83E-04*	4.38E-03	1.61E-02	1.60E-02	2.89E-01	9.89E-04	3.36E-02	1.62E-02
rs7574414	0.93(0.70, 1.24)		0.83(0.64, 1.07)	6.22E-01	4.42E-04*	1.96E-03	1.43E-01	1.38E-01	6.22E-01	4.44E-04	3.99E-01	1.43E-01
rs11563246	0.89(0.68, 1.15)	0.28(0.15, 0.54)*	0.77(0.624,0.95)	3.68E-01	5.58E-05*	2.80E-04	1.44E-02	1.45E-02	3.68E-01	5.62E-05	6.18E-02	1.45E-02

rs number	OR (95% CI)			P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere–Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive	Allele	Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs201192415	7.40(1.53, 35.83)	7.40(1.53, 35.83)	7.40(2.43, 22.58)*				3.81E-05*		3.61E-03	3.61E-03	3.61E-03	3.83E-05
rs12629412	1.62(1.23, 2.14)*	1.29(0.89, 1.88)	1.35(1.12, 1.67)	6.09E-04*	1.85E-01	2.72E-03	1.90E-03	1.72E-03	6.13E-04	1.85E-01	1.07E-03	1.91E-03
rs16858778	1.52(1.16, 1.99)	2.62(1.41, 4.89)	1.52(1.21, 1.90)	2.26E-03	1.69E-03	5.33E-04*	2.34E-04	2.30E-04	2.27E-03	1.70E-03	7.58E-04	2.35E-04
rs189070828									1.25E-02	1.25E-02	1.25E-02	4.10E-04*
rs2286455	0.63(0.48, 0.82)*	0.90(0.52, 1.54)	0.72(0.57, 0.90)	7.63E-04*	6.92E-01	2.77E-03	3.78E-03	4.29E-03	7.68E-04	6.92E-01	1.55E-03	3.79E-03
rs1859156	1.83(1.29, 2.58)	3.13(0.52, 18.84)	1.77(1.28, 2.45)*	5.71E-04			4.84E-04*		5.74E-04	1.89E-01	5.31E-04	4.86E-04
rs1436512	0.61(0.47, 0.80)	0.50(0.27, 0.93)	0.65(0.52, 0.81)	3.25E-04	2.60E-02	7.36E-04*	1.55E-04	1.50E-04	3.28E-04	2.61E-02	1.64E-04	1.55E-04
	0.61(0.46, 0.80)*	0.66(0.36, 1.23)	0.66(0.52, 0.84)	4.57E-04*	1.87E-01	2.10E-03	5.72E-04	8.34E-04	4.60E-04	1.87E-01	4.82E-04	5.74E-04
rs1946267	0.62(0.47, 0.82)*	1.05(0.75, 1.46)	0.82(0.68, 0.99)	8.24E-04*	7.93E-01	1.27E-03	3.81E-02	3.88E-02	8.29E-04	7.93E-01	2.53E-02	3.82E-02
rs840398	1.38(1.01, 1.90)	1.69(1.26, 2.28)*	1.38(1.14, 1.66)	4.36E-02	4.81E-04*	1.46E-03	8.01E-04	7.17E-04	4.37E-02	4.84E-04	7.23E-04	8.03E-04
rs3830368	0.60(0.46, 0.79)*	0.79(0.47, 1.31)	0.69(0.56, 0.86)	2.12E-04*	3.54E-01	1.02E-03	8.97E-04	9.58E-04	2.14E-04	3.54E-01	3.90E-04	8.99E-04
	0.64(0.49, 0.83)*	0.97(0.65, 1.45)	0.78(0.64, 0.95)	8.61E-04*	8.97E-01	2.33E-03	1.19E-02	1.25E-02	8.66E-04	8.97E-01	5.20E-03	1.19E-02
rs34899	1.53(1.17, 1.99)	1.77(1.11, 2.82)	1.47(1.19, 1.81)*	1.74E-03	1.55E-02	2.65E-03	3.30E-04*	5.75E-04	1.75E-03	1.56E-02	7.82E-04	3.31E-04
rs39597	0.65(0.50, 0.85)	0.65(0.44, 0.97)	0.71(0.58, 0.87)*	1.54E-03	3.23E-02	3.60E-03	6.74E-04*	9.25E-04	1.55E-03	3.24E-02	8.07E-04	6.76E-04
rs1119080	0.56(0.43, 0.73)	0.63(0.44, 0.91)	0.65(0.54, 0.79)*	2.32E-05	1.40E-02	8.05E-05	1.54E-05*	3.25E-05	2.34E-05	1.41E-02	2.16E-05	1.54E-05
rs362522	0.63(0.48, 0.82)	0.53(0.29, 0.94)	0.66(0.53, 0.83)*	5.86E-04	2.82E-02	1.30E-03	2.61E-04*	2.74E-04	5.90E-04	2.83E-02	2.96E-04	2.62E-04
rs1233391	1.51(1.10, 2.05)	1.53(1.13, 2.06)	1.37(1.14, 1.65)*	9.55E-03	5.42E-03	4.49E-03	9.68E-04*	1.03E-03	9.58E-03	5.44E-03	1.05E-03	9.71E-04
rs1233388	1.55(1.13, 2.13)	1.58(1.17, 2.14)	1.40(1.16, 1.69)*	6.20E-03	2.98E-03	2.20E-03	4.72E-04*	4.83E-04	6.23E-03	2.99E-03	4.92E-04	4.74E-04
rs2240070	0.53(0.40, 0.71)*	0.79(0.43, 1.45)	0.62(0.49, 0.79)	8.95E-06*	4.42E-01	4.51E-05	7.44E-05	7.95E-05	9.04E-06	4.43E-01	1.89E-05	7.47E-05
rs3132680	0.51(0.39, 0.68)*	0.63(0.34, 1.17)	0.59(0.46, 0.74)	2.17E-06*	1.42E-01	1.34E-05	7.77E-06	1.01E-05	2.20E-06	1.42E-01	3.12E-06	7.82E-06
rs2844795	0.64(0.49, 0.83)	0.61(0.39, 0.96)	0.70(0.57, 0.86)	8.57E-04	3.27E-02	1.99E-03*	5.03E-04	4.76E-04	8.62E-04	3.28E-02	4.24E-04	5.05E-04
rs2523990	0.54(0.41, 0.70)*	0.72(0.48, 1.09)	0.66(0.54, 0.81)	5.02E-06*	1.15E-01	2.97E-05	4.67E-05	4.36E-05	5.08E-06	1.15E-01	1.71E-05	4.69E-05
rs2239529	0.80(0.55, 1.17)		0.94(0.66, 1.32)	2.47E-01			7.01E-01		2.47E-01	3.95E-04*	3.02E-01	7.01E-01
rs2517598	0.81(0.56, 1.18)		0.94(0.67, 1.33)	2.68E-01			7.34E-01		2.69E-01	4.03E-04*	3.26E-01	7.34E-01
rs2844793	0.81(0.55, 1.17)		0.94(0.66, 1.32)	2.55E-01			7.15E-01		2.55E-01	4.11E-04*	3.11E-01	7.15E-01
rs9261438	0.58(0.45, 0.77)	0.42(0.22, 0.80)	0.61(0.49, 0.77)*	9.54E-05	6.64E-03	1.37E-04	2.06E-05*	2.46E-05	9.61E-05	6.67E-03	3.38E-05	2.07E-05
rs9261440	0.59(0.45, 0.78)	0.50(0.26, 0.95)	0.63(0.50, 0.80)*	1.75E-04	3.21E-02	4.96E-04	8.81E-05*	1.05E-04	1.76E-04	3.22E-02	1.03E-04	8.84E-05

rs number	OR (95% CI)			P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere–Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive	Allele	Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs1419673	0.57(0.43, 0.75)	0.47(0.23, 0.94)	0.61(0.48, 0.77)*	7.47E-05	2.94E-02	2.25E-04	3.77E-05*	4.58E-05	7.54E-05	2.95E-02	4.51E-05	3.79E-05
rs1419671	0.57(0.43, 0.75)	0.477(0.23, 0.94)	0.61(0.48, 0.77)*	7.47E-05	2.94E-02	2.25E-04	3.77E-05*	4.58E-05	7.54E-05	2.95E-02	4.51E-05	3.79E-05
rs1541267	0.61(0.46, 0.80)	0.477(0.24, 0.91)	0.64(0.51, 0.80)*	3.21E-04	2.30E-02	6.92E-04	1.24E-04*	1.38E-04	3.23E-04	2.31E-02	1.65E-04	1.25E-04
rs9261468	0.56(0.42, 0.74)	0.44(0.21, 0.92)	0.59(0.46, 0.76)*	4.43E-05	2.47E-02	1.30E-04	2.09E-05*	2.56E-05	4.47E-05	2.47E-02	2.61E-05	2.10E-05
rs9261485	0.56(0.42, 0.74)	0.44(0.21, 0.92)	0.59(0.46, 0.75)*	4.23E-05	2.53E-02	1.26E-04	2.06E-05*	2.49E-05	4.27E-05	2.53E-02	2.50E-05	2.07E-05
rs9261492	0.60(0.46, 0.79)	0.48(0.24, 0.94)	0.63(0.50, 0.80)*	2.46E-04	2.77E-02	6.02E-04	1.11E-04*	1.22E-04	2.48E-04	2.78E-02	1.35E-04	1.11E-04
rs9261508	0.60(0.46, 0.79)	0.47(0.24, 0.92)	0.64(0.50, 0.80)*	2.75E-04	2.39E-02	6.21E-04	1.10E-04*	1.24E-04	2.77E-04	2.40E-02	1.44E-04	1.11E-04
rs757262	0.56(0.42, 0.74)	0.44(0.21, 0.92)	0.52(0.46, 0.76)*	4.43E-05	2.47E-02	1.30E-04	2.09E-05*	2.56E-05	4.47E-05	2.47E-02	2.61E-05	2.10E-05
rs757259	0.55(0.42, 0.73)	0.44(0.21, 0.92)	0.59(0.46, 0.75)*	3.36E-05	2.53E-02	1.04E-04	1.66E-05*	2.06E-05	3.39E-05	2.53E-02	2.02E-05	1.67E-05
rs1557611	0.56(0.42, 0.74)	0.44(0.21, 0.92)	0.59(0.46, 0.76)*	4.43E-05	2.47E-02	1.30E-04	2.09E-05*	2.56E-05	4.47E-05	2.47E-02	2.61E-05	2.10E-05
rs1557608	0.61(0.46, 0.80)	0.47(0.24,0.916)	0.64(0.51, 0.81)*	3.67E-04	2.36E-02	7.83E-04	1.42E-04*	1.57E-04	3.69E-04	2.37E-02	1.89E-04	1.43E-04
rs2517653	0.56(0.42, 0.74)	0.39(0.19, 0.81)	0.59(0.46, 0.74)*	3.34E-05	8.57E-03	6.11E-05	9.36E-06*	1.06E-05	3.37E-05	8.60E-03	1.41E-05	9.40E-06
rs2022065	0.58(0.44, 0.75)	0.50(0.30, 0.85)	0.64(0.52, 0.78)	4.71E-05	9.06E-03	8.85E-05*	2.03E-05	1.71E-05	4.75E-05	9.09E-03	1.63E-05	2.04E-05
rs9261535	0.59(0.44, 0.78)	0.26(0.10, 0.65)	0.59(0.46, 0.75)*	2.02E-04	2.20E-03	1.11E-04	2.28E-05*	2.56E-05	2.04E-04	2.21E-03	6.86E-05	2.29E-05
rs929156	0.62(0.47, 0.82)	0.33(0.15, 0.74)	0.63(0.49, 0.80)*	6.89E-04	5.10E-03	4.97E-04	1.16E-04*	1.17E-04	6.93E-04	5.13E-03	2.52E-04	1.16E-04
rs2844782	0.73(0.56, 0.95)	0.47(0.30, 0.74)	0.71(0.58, 0.87)*	1.92E-02	1.02E-03	1.92E-03	7.95E-04*	9.91E-04	1.93E-02	1.03E-03	2.03E-03	7.97E-04
rs2239530	0.60(0.45, 0.80)	0.26(0.10, 0.67)	0.60(0.47, 0.77)*	3.78E-04	2.89E-03	2.13E-04	4.74E-05*	5.23E-05	3.80E-04	2.90E-03	1.37E-04	4.77E-05
rs4711211	0.61(0.46, 0.81)	0.27(0.11, 0.69)	0.61(0.48, 0.78)	5.73E-04	3.55E-03	3.23E-04*	8.42E-05	8.35E-05	5.76E-04	3.56E-03	2.13E-04	8.45E-05
rs3132672	0.75(0.58, 0.98)	0.49(0.31, 0.75)*	0.73(0.60, 0.89)	3.55E-02	9.75E-04*	2.43E-03	1.48E-03	1.59E-03	3.56E-02	9.80E-04	3.05E-03	1.48E-03
rs3132671	0.74(0.57, 0.96)	0.46(0.29, 0.73)*	0.72(0.59, 0.87)	2.47E-02	7.96E-04*	1.73E-03	9.65E-04	1.07E-03	2.47E-02	8.01E-04	2.24E-03	9.68E-04
rs2844775	0.61(0.46, 0.81)	0.25(0.10, 0.65)	0.61(0.48, 0.78)*	6.12E-04	2.17E-03	2.49E-04	7.04E-05*	7.10E-05	6.16E-04	2.18E-03	2.03E-04	7.07E-05
rs3130391	0.78(0.60, 1.01)	0.45(0.28, 0.72)*	0.73(0.60, 0.90)	6.17E-02	6.72E-04*	2.24E-03	2.36E-03	2.58E-03	6.18E-02	6.76E-04	5.96E-03	2.37E-03
rs3132667	0.77(0.59, 1.00)	0.47(0.30, 0.74)*	0.73(0.60, 0.89)	5.38E-02	7.95E-04*	2.52E-03	1.98E-03	2.39E-03	5.39E-02	7.99E-04	5.23E-03	1.98E-03
rs885915	0.77(0.59, 1.00)	0.46(0.29, 0.73)*	0.73(0.60, 0.89)	5.00E-02	8.20E-04*	2.44E-03	2.09E-03	2.27E-03	5.02E-02	8.24E-04	5.07E-03	2.09E-03
rs2844780	0.78(0.60, 1.02)	0.45(0.28, 0.72)*	0.74(0.60, 0.90)	6.79E-02	7.08E-04*	2.41E-03	2.80E-03	2.98E-03	6.80E-02	7.12E-04	7.02E-03	2.81E-03
rs2844779	0.78(0.60, 1.02)	0.45(0.28, 0.73)*	0.74(0.61, 0.90)	6.51E-02	8.88E-04*	2.86E-03	3.01E-03	3.14E-03	6.52E-02	8.93E-04	7.17E-03	3.02E-03
rs1264585	0.65(0.50, 0.86)	0.45(0.22, 0.94)	0.68(0.54, 0.85)	2.22E-03	3.00E-02	3.48E-03*	9.39E-04	7.89E-04	2.23E-03	3.01E-02	1.14E-03	9.41E-04



rs number	OR (95% CI)			P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere–Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive	Allele	Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs6910017	0.62(0.47, 0.82)*	0.96(0.70, 1.33)	0.80(0.66, 0.96)	6.76E-04*	8.11E-01	1.93E-03	1.87E-02	1.96E-02	6.80E-04	8.11E-01	1.47E-02	1.88E-02
rs7759938	0.64(0.49, 0.84)	0.49(0.24, 0.99)	0.68(0.54, 0.85)	1.36E-03	4.21E-02	2.82E-03*	7.53E-04	6.11E-04	1.37E-03	4.22E-02	7.58E-04	7.55E-04
rs2290386	1.49(1.13, 1.96)	2.00(1.10, 3.53)	1.47(1.17, 1.84)*	4.08E-03	2.01E-02	5.13E-03	9.35E-04*	1.28E-03	4.10E-03	2.02E-02	2.21E-03	9.38E-04
rs61756425	1.98(1.36, 2.88)*		1.82(1.27, 2.61)	3.33E-04*			9.18E-04		3.35E-04	3.26E-01	3.68E-04	9.21E-04
rs751141	0.62(0.47, 0.82)	0.40(0.19, 0.83)	0.64(0.51, 0.81)	6.75E-04	1.06E-02	7.86E-04*	1.67E-04	1.65E-04	6.79E-04	1.07E-02	2.76E-04	1.68E-04
rs10112232	1.70(1.30, 2.22)*	1.20(0.78, 1.85)	1.39(1.15, 1.70)	1.08E-04*	4.05E-01	5.17E-04	9.29E-04	8.73E-04	1.09E-04	4.05E-01	3.26E-04	9.31E-04
rs2294008	2.53(1.77, 3.61)*	1.64(1.22, 2.19)	1.65(1.37, 1.99)	1.83E-07*	8.78E-04	3.03E-07	1.84E-07	1.92E-07	1.85E-07	8.84E-04	2.20E-07	1.85E-07
rs1045531	2.60(1.82, 3.70)*	1.65(1.23, 2.20)	1.67(1.39, 2.02)	7.24E-08*	7.24E-04	1.27E-07	8.06E-08	9.25E-08	7.35E-08	7.28E-04	1.05E-07	8.12E-08
rs200893203	12.65(1.52, 105.51)	12.65(1.52, 105.51)	12.65(2.82, 56.69)*						2.60E-03	2.60E-03	2.60E-03	2.04E-05*
rs55979986	2.27(1.38, 3.74)	4.17(0.38, 46.17)	2.27(1.41, 3.66)*	9.74E-04			5.83E-04*		9.80E-04	2.06E-01	9.52E-04	5.85E-04
rs141858334									1.25E-02	1.25E-02	1.25E-02	4.13E-04*
rs3935601	1.61(1.21, 2.13)*	1.05(0.73, 1.51)	1.27(1.05, 1.54)	8.67E-04*	7.94E-01	2.65E-03	1.32E-02	1.34E-02	8.72E-04	7.94E-01	6.88E-03	1.32E-02
rs3814538	1.16(0.84, 1.58)	1.65(1.23, 2.20)*	1.29(1.07, 1.56)	3.68E-01	6.52E-04*	2.89E-03	7.20E-03	7.63E-03	3.68E-01	6.56E-04	6.89E-03	7.22E-03
rs10739288	0.59(0.46, 0.78)	0.64(0.42, 0.96)	0.68(0.56, 0.83)*	1.32E-04	3.10E-02	4.23E-04	1.25E-04*	1.34E-04	1.33E-04	3.10E-02	9.43E-05	1.25E-04
rs1053878	1.48(1.13, 1.92)	2.20(1.33, 3.63)	1.453(1.18, 1.79)	3.76E-03	1.70E-03	8.17E-04*	3.72E-04	3.15E-04	3.78E-03	1.71E-03	8.18E-04	3.74E-04
rs651007	1.49(1.14, 1.94)	1.97(1.22, 3.17)	1.44(1.17, 1.76)	3.12E-03	4.79E-03	1.56E-03*	4.75E-04	4.24E-04	3.14E-03	4.81E-03	8.11E-04	4.76E-04
rs579459	1.48(1.13, 1.92)	1.96(1.22, 3.15)	1.43(1.17, 1.75)	3.80E-03	5.10E-03	1.88E-03*	5.89E-04	5.24E-04	3.82E-03	5.12E-03	1.00E-03	5.91E-04
rs495828	1.49(1.14, 1.94)	1.97(1.22, 3.17)	1.44(1.17, 1.76)	3.12E-03	4.79E-03	1.56E-03*	4.75E-04	4.24E-04	3.14E-03	4.81E-03	8.11E-04	4.76E-04
rs635634	1.51(1.16, 1.97)	2.20(1.35, 3.58)	1.47(1.20, 1.81)	2.10E-03	1.29E-03	4.46E-04*	1.89E-04	1.52E-04	2.11E-03	1.29E-03	3.86E-04	1.90E-04
rs7027926	6.07(2.17, 16.99)*		4.25(1.71, 10.57)	1.02E-04*			7.36E-04		1.03E-04	3.28E-01	1.09E-04	7.38E-04
rs2062988	0.67(0.52, 0.88)	0.43(0.25, 0.76)	0.69(0.57, 0.85)	3.12E-03	2.62E-03	9.30E-04*	4.62E-04	2.63E-04	3.14E-03	2.63E-03	4.79E-04	4.63E-04
rs1451668	1.09(0.82, 1.43)	1.88(1.34, 2.64)*	1.26(1.04, 1.52)	5.60E-01	2.17E-04*	8.49E-04	1.71E-02	1.74E-02	5.60E-01	2.18E-04	3.42E-02	1.72E-02
rs10788615	1.56(1.18, 2.06)	1.67(1.16, 2.41)	1.42(1.18, 1.72)	1.62E-03	5.86E-03	1.25E-03*	2.86E-04	2.58E-04	1.63E-03	5.89E-03	2.99E-04	2.87E-04
rs2071498	0.63(0.49, 0.83)*	0.92(0.62, 1.36)	0.76(0.62, 0.93)	7.62E-04*	6.71E-01	2.55E-03	7.32E-03	8.82E-03	7.67E-04	6.71E-01	3.91E-03	7.33E-03
rs903809	0.63(0.48, 0.82)*	0.60(0.30, 1.20)	0.68(0.54, 0.86)	7.76E-04*	1.45E-01	2.96E-03	9.77E-04	7.94E-04	7.81E-04	1.45E-01	6.48E-04	9.80E-04
rs2303960	1.24(0.89, 1.71)	1.67(1.25, 2.24)*	1.32(1.10, 1.59)	2.02E-01	5.12E-04*	2.35E-03	3.58E-03	3.04E-03	2.02E-01	5.15E-04	2.73E-03	3.59E-03
rs878874	0.63(0.48, 0.82)*	0.86(0.57, 1.31)	0.75(0.61, 0.91)	5.62E-04*	4.77E-01	2.44E-03	4.21E-03	3.78E-03	5.66E-04	4.77E-01	1.82E-03	4.22E-03



rs number	OR (95% CI)		Allele	P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere–Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive		Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs7969705	1.00(0.74, 1.35)		0.87(0.67, 1.15)	9.92E-01	9.88E-04*	3.02E-03	3.32E-01	3.36E-01	9.92E-01	9.94E-04	7.85E-01	3.32E-01
rs2617170	1.44(1.08, 1.92)	1.69(1.21, 2.35)	1.39(1.15, 1.67)*	1.19E-02	1.86E-03	2.32E-03	6.41E-04*	6.84E-04	1.20E-02	1.86E-03	8.79E-04	6.43E-04
	1.47(1.12, 1.93)	1.63(1.12, 2.37)	1.38(1.14, 1.67)*	5.35E-03	1.06E-02	4.56E-03	9.74E-04*	1.06E-03	5.37E-03	1.07E-02	1.31E-03	9.77E-04
rs1479500	1.74(1.29, 2.39)	3.15(0.88, 11.25)	1.69(1.27, 2.26)	5.42E-04		1.22E-03*	3.00E-04	2.72E-04	5.45E-04	6.23E-02	4.45E-04	3.01E-04
rs199673881	5.13(1.79, 14.70)		5.06(1.77, 14.41)	7.24E-04*		7.24E-04*	7.63E-04	7.24E-04	7.29E-04		7.29E-04	7.65E-04
rs138640311	1.61(1.19, 2.17)	1.45(1.07, 1.98)	1.38(1.15, 1.67)*	2.01E-03	1.71E-02	3.17E-03	6.66E-04*	7.97E-04	2.02E-03	1.71E-02	7.59E-04	6.68E-04
	1.60(1.18, 2.16)	1.43(1.05, 1.94)	1.37(1.14, 1.65)*	2.31E-03	2.37E-02	4.21E-03	9.54E-04*	1.13E-03	2.32E-03	2.38E-02	1.07E-03	9.57E-04
rs9537824	1.54(1.17, 2.03)	1.51(1.04, 2.18)	1.38(1.14, 1.67)*	2.01E-03	2.87E-02	3.88E-03	8.96E-04*	9.27E-04	2.02E-03	2.87E-02	8.68E-04	8.98E-04
rs4148549	1.70(1.23, 2.35)	1.50(1.12, 2.00)	1.43(1.18, 1.72)*	1.18E-03	6.04E-03	1.20E-03	2.02E-04*	2.76E-04	1.19E-03	6.06E-03	2.82E-04	2.03E-04
rs4148546	1.63(1.18, 2.25)	1.51(1.13, 2.02)	1.41(1.17, 1.69)*	2.85E-03	5.54E-03	2.09E-03	3.71E-04*	4.54E-04	2.86E-03	5.57E-03	4.59E-04	3.72E-04
rs1959258	0.85(0.65, 1.12)	0.51(0.34, 0.76)*	0.78(0.64, 0.94)	2.49E-01	8.24E-04*	3.72E-03	9.67E-03	1.05E-02	2.49E-01	8.29E-04	1.90E-02	9.69E-03
rs3742836	1.60(1.22, 2.10)*	0.93(0.48, 1.81)	1.39(1.11, 1.74)	5.98E-04*	8.22E-01	1.30E-03	4.66E-03	4.82E-03	6.01E-04	8.22E-01	1.27E-03	4.67E-03
rs2305707	0.84(0.64, 1.09)	0.38(0.21, 0.68)*	0.77(0.62, 0.95)	1.91E-01	7.65E-04*	3.34E-03	1.29E-02	1.34E-02	1.91E-01	7.69E-04	4.04E-02	1.30E-02
rs12914996	0.78(0.59, 1.03)	0.53(0.37, 0.77)*	0.74(0.62, 0.90)	7.54E-02	6.23E-04*	2.25E-03	2.01E-03	1.89E-03	7.56E-02	6.27E-04	2.58E-03	2.02E-03
rs11546303	1.62(1.21, 2.17)	2.10(0.78, 5.65)	1.54(1.19, 2.00)	1.23E-03	1.33E-01*	3.84E-03	9.89E-04	8.52E-04	1.24E-03	1.33E-01	1.04E-03	9.92E-04
rs28584228	0.62(0.47, 0.82)*	0.93(0.49, 1.77)	0.70(0.56, 0.89)	7.87E-04*	8.16E-01	2.75E-03	3.73E-03	3.68E-03	7.92E-04	8.16E-01	1.35E-03	3.74E-03
rs3764897	1.09(0.78, 1.52)		1.19(0.88, 1.62)	6.09E-01			2.62E-01		6.09E-01	3.99E-04*	5.22E-01	2.62E-01
rs141572082									1.26E-02	1.26E-02	1.26E-02	4.14E-04*
rs55715426	1.29(0.95, 1.75)	4.63(1.74, 12.29)*	1.40(1.07, 1.84)	1.07E-01	7.63E-04*	2.55E-03	1.51E-02	1.66E-02	1.08E-01	7.68E-04	6.81E-02	1.51E-02
rs671871	0.56(0.40, 0.80)	0.34(0.04, 2.87)	0.59(0.42, 0.81)	1.06E-03			1.26E-03		1.06E-03*	3.01E-01	9.93E-04*	1.26E-03
rs79992793	1.67(1.17, 2.37)		1.73(1.25, 2.40)*	4.25E-03			9.80E-04*		4.27E-03	1.25E-03	3.31E-03	9.83E-04
rs4796901	1.77(1.34, 2.35)*	1.69(0.78, 3.66)	1.63(1.28, 2.08)	6.35E-05*	1.76E-01	3.18E-04	8.38E-05	8.98E-05	6.40E-05	1.76E-01	6.05E-05	8.42E-05
rs11267036	1.04(0.79, 1.36)	2.45(1.42, 4.23)*	1.19(0.95, 1.48)	7.85E-01	9.72E-04*	3.22E-03	1.31E-01	1.39E-01	7.85E-01	9.78E-04	4.05E-01	1.31E-01
rs12606417	1.99(1.29, 3.07)		2.02(1.32, 3.06)*	1.65E-03			8.18E-04*		1.66E-03	4.15E-02	1.54E-03	8.21E-04
rs884205	0.95(0.73, 1.25)	2.95(1.55, 5.61)*	1.10(0.88, 1.38)	7.28E-01	5.60E-04*	1.20E-03	3.89E-01	3.77E-01	7.28E-01	5.64E-04	8.30E-01	3.90E-01
rs1157329	1.26(0.92, 1.71)	1.72(1.29, 2.29)*	1.36(1.13, 1.64)	1.48E-01	2.19E-04*	1.07E-03	1.32E-03	1.70E-03	1.48E-01	2.20E-04	1.63E-03	1.32E-03
rs2304167	0.66(0.49, 0.87)	0.33(0.13, 0.84)*	0.65(0.51, 0.84)	3.94E-03	1.51E-02*	3.64E-03	9.66E-04	1.04E-03	3.95E-03	1.52E-02	2.13E-03	9.69E-04

rs number	OR (95% CI)		Allele	P-value ( $\chi^2$ test) <sup>†</sup>				Trend-P	P-value (Jonckheere-Terpstra Test) <sup>‡</sup>			
	Dominant	Recessive		Dominant	Recessive	Additive	Allele		Dominant	Recessive	Additive	Allele
rs6048138	1.08(0.82, 1.43)	1.89(1.33, 2.66)	1.25(1.03, 1.51)*	5.69E-01	2.83E-04	1.14E-03	2.18E-02*	2.04E-02	5.69E-01	2.85E-04	4.01E-02	2.18E-02
rs34515071	0.65(0.50, 0.85)	0.60(0.41, 0.89)	0.71(0.58, 0.86)	1.85E-03	9.68E-03	1.92E-03*	4.57E-04	4.07E-04	1.86E-03	9.71E-03	4.15E-04	4.59E-04
rs117931394	0.94(0.70, 1.26)	0.13(0.03, 0.54)*	0.82(0.64, 1.07)	6.89E-01	9.97E-04*	3.79E-03	1.41E-01	1.51E-01	6.89E-01	1.00E-03	4.49E-01	1.41E-01
rs2076672	0.52(0.35, 0.76)	0.30(0.04, 2.41)	0.53(0.37, 0.77)	6.58E-04		2.57E-03*	5.95E-04	5.63E-04	6.62E-04	2.27E-01	6.15E-04	5.97E-04

\*Selected P-value and genetic model

<sup>†</sup> P-values were calculated by  $\chi^2$  test

<sup>‡</sup> P-values were calculated by Jonckheere-Terpstra Test

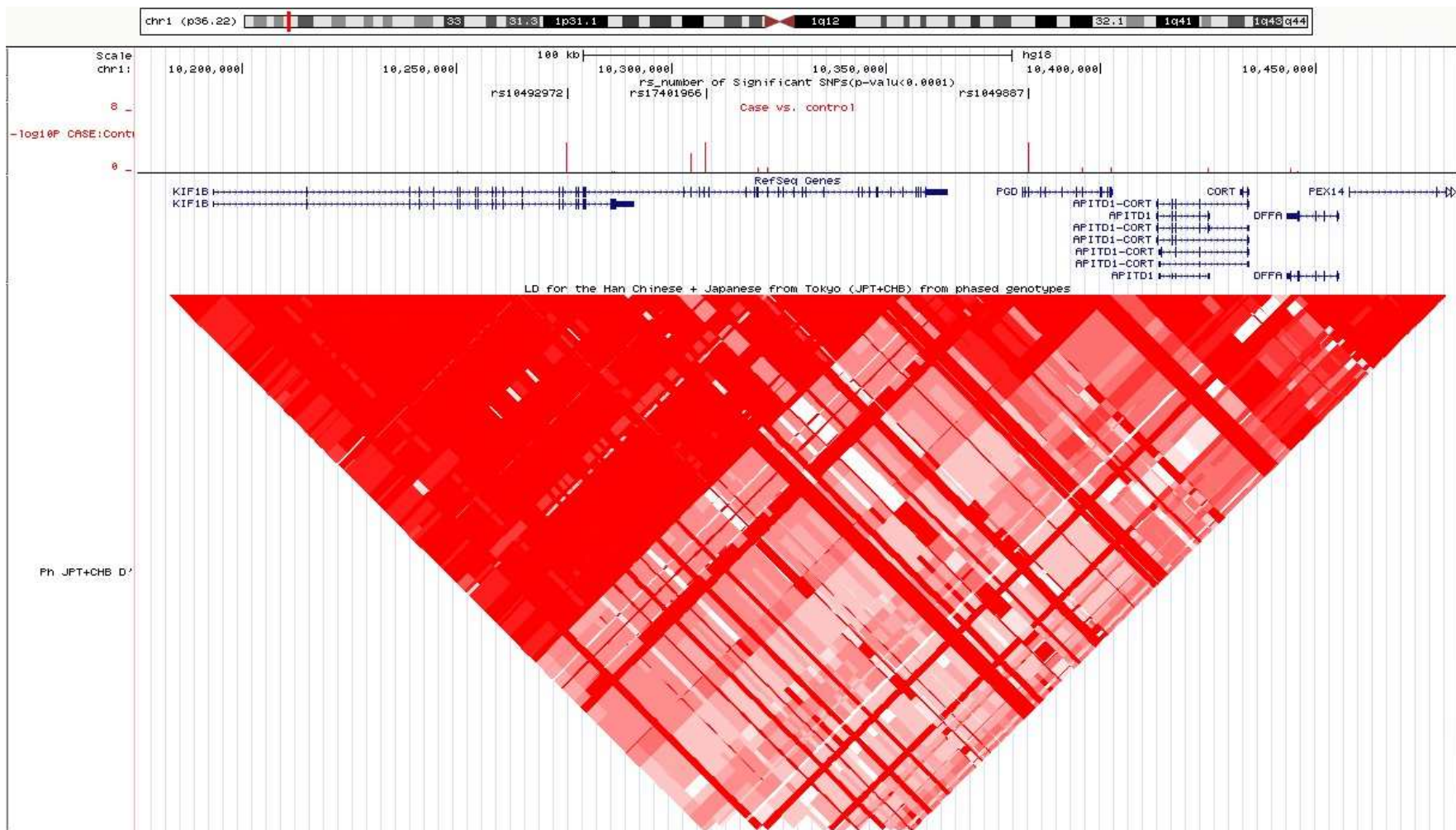


Figure 4. Locations of KIF1B, PGD mutations (rs10492972, rs1049887, rs17401966), their LD structure, and associations with gastric cancer risk

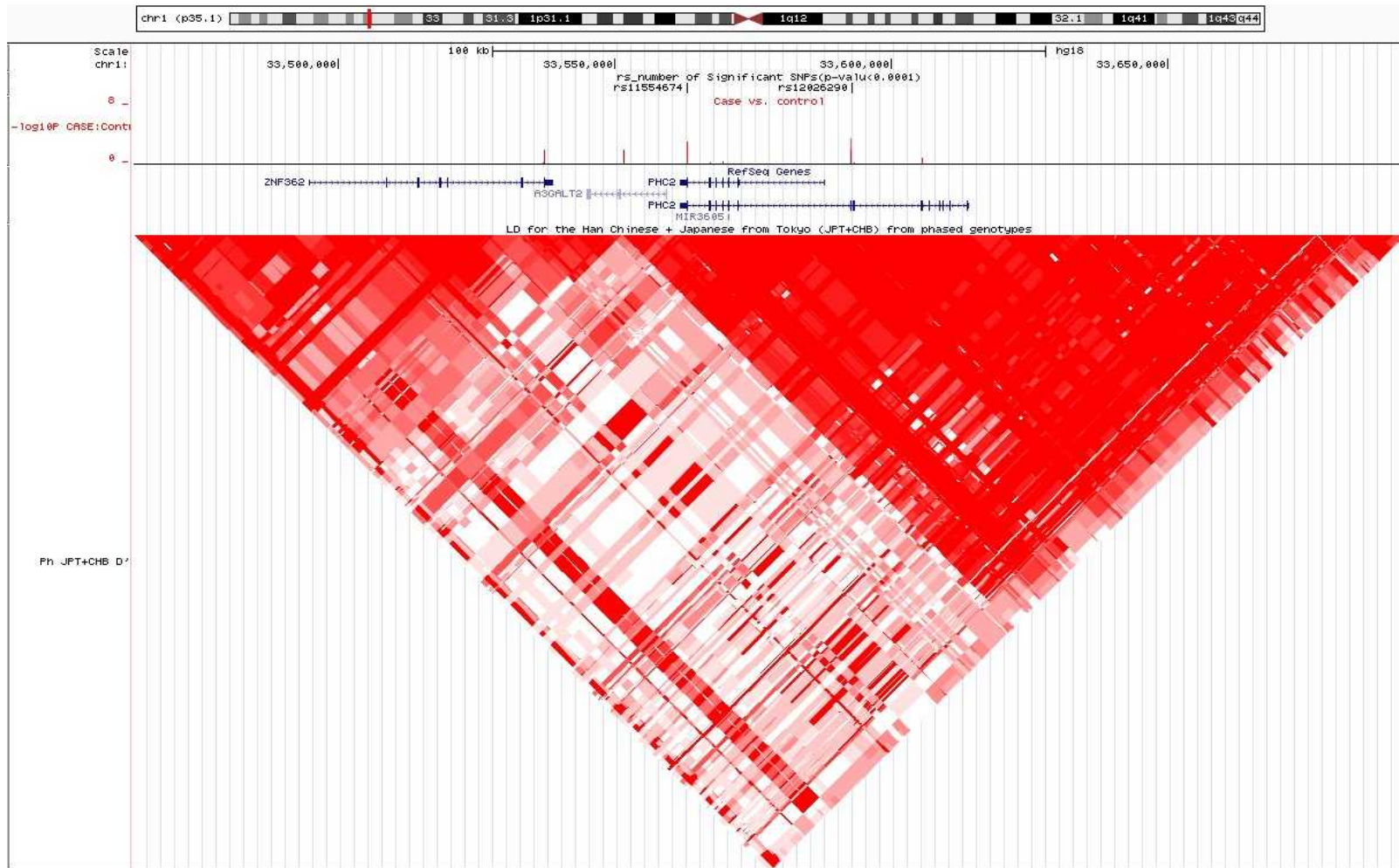


Figure 5. Locations of PHC2 mutations (rs11554674, rs12026290), their LD structure, and associations with gastric cancer risk



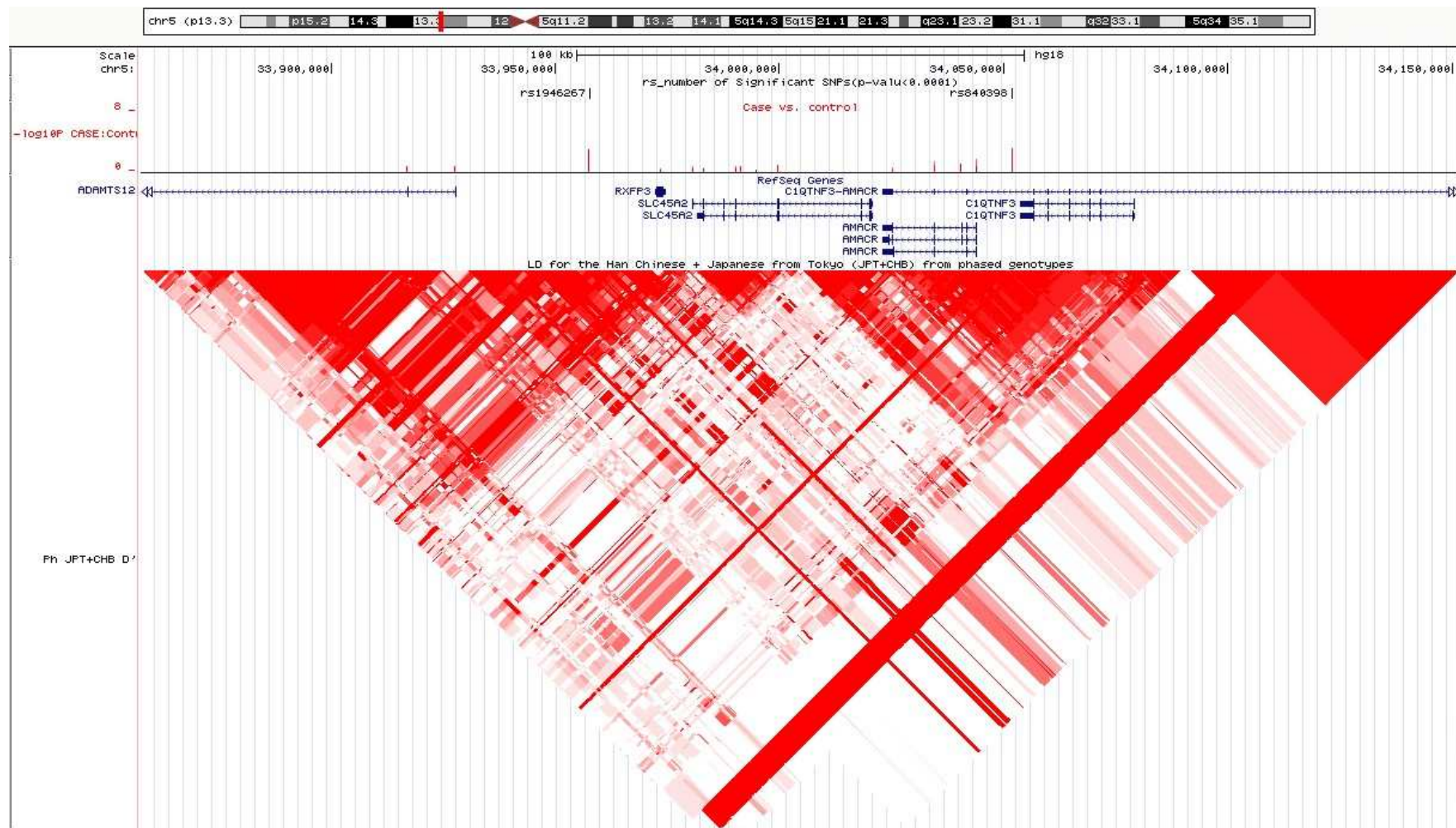


Figure 6. Locations of C1QTNF3, C1QTNF3-AMACR, AMACR mutations (rs1946267, rs840398), their LD structure, and associations with gastric cancer risk

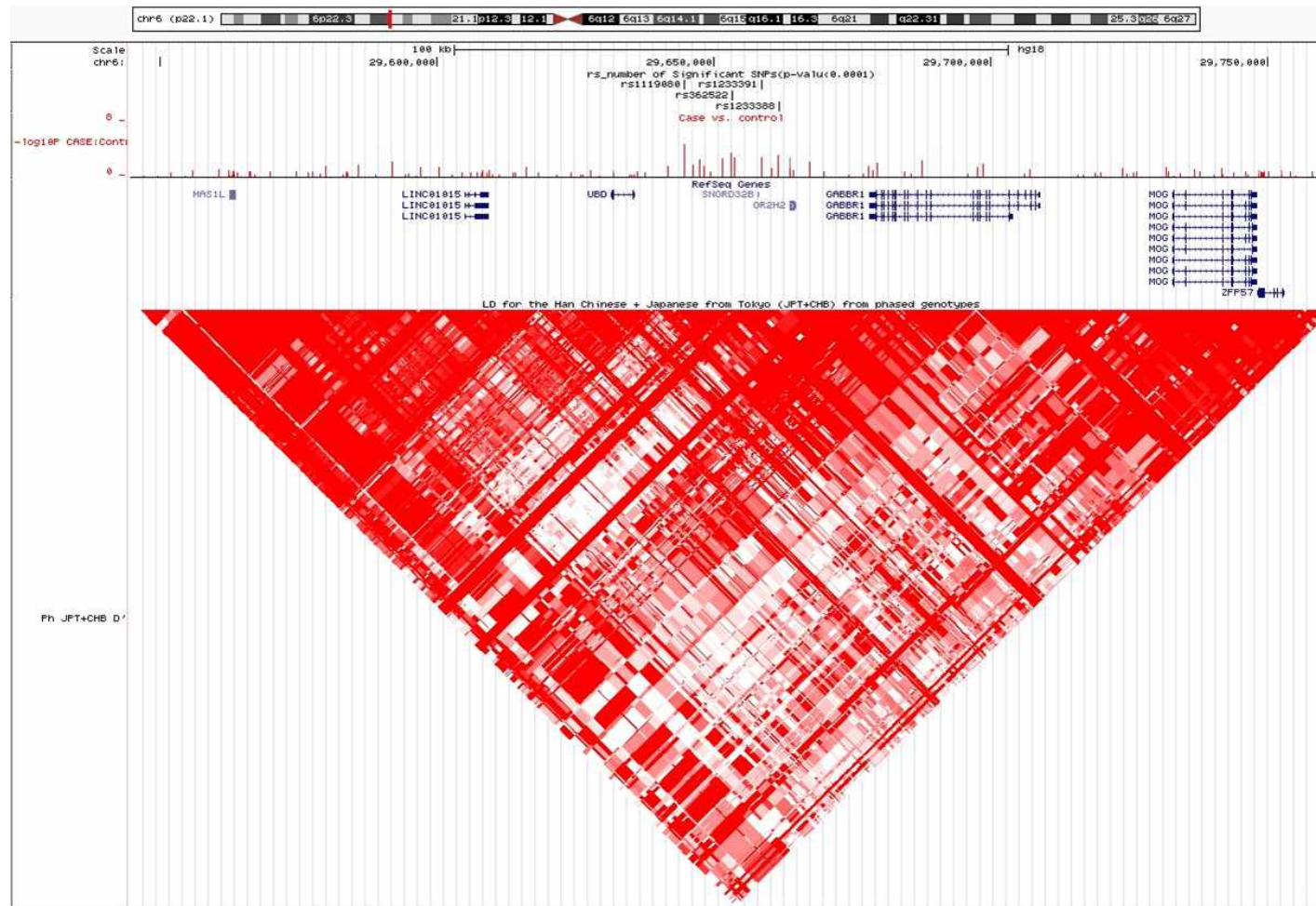


Figure 7. Locations of OR2H2, SNORD32B mutations (rs1119080, rs1233388, rs1233391, rs362522), their LD structure, and associations with gastric cancer risk



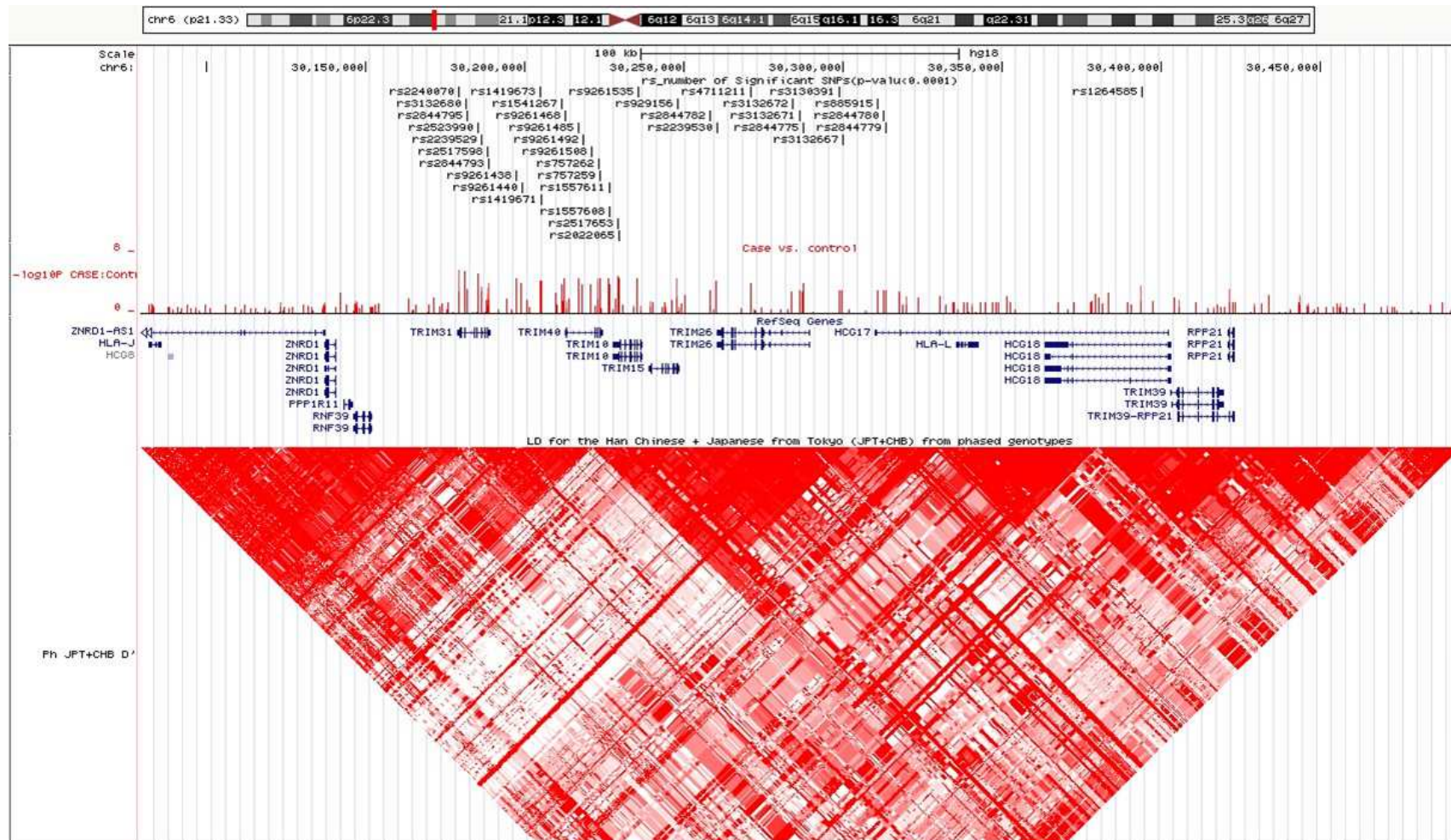


Figure 8. Locations of HCG17, HCG18, TRIM39, RPP21, TRIM39-RPP21, TRIM26, TRIM10, TRIM40, TRIM15, TRIM31 mutations (rs2517598 etc.), their LD structure, and associations with gastric cancer risk

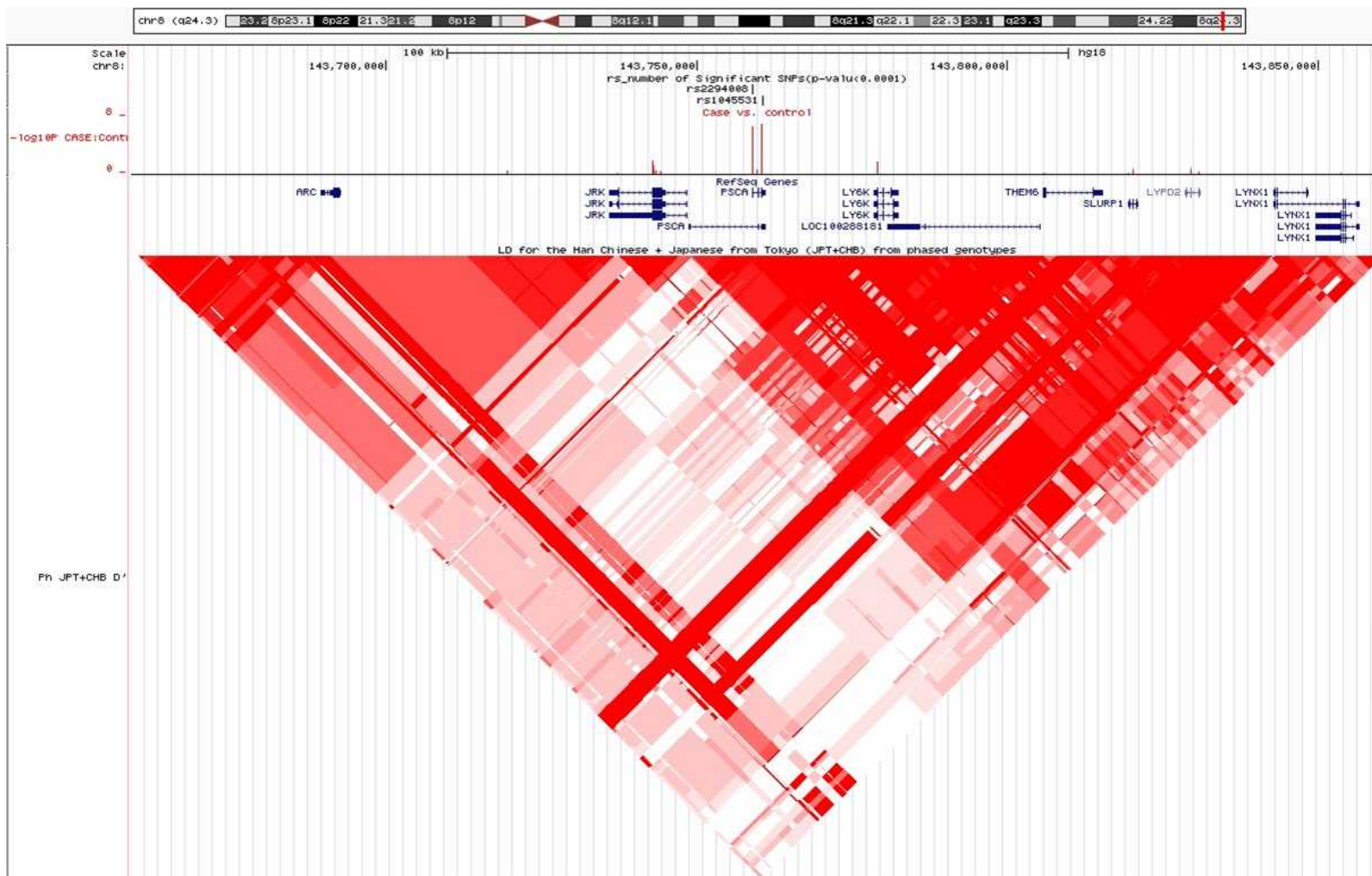


Figure 9. Locations of PSCA mutations (rs1045531, rs2294008.), their LD structure, and associations with gastric cancer risk





Figure 10. Locations of ABO mutations (rs1053878, rs495828, rs579459, rs635634, rs651007), their LD structure, and associations with gastric cancer risk

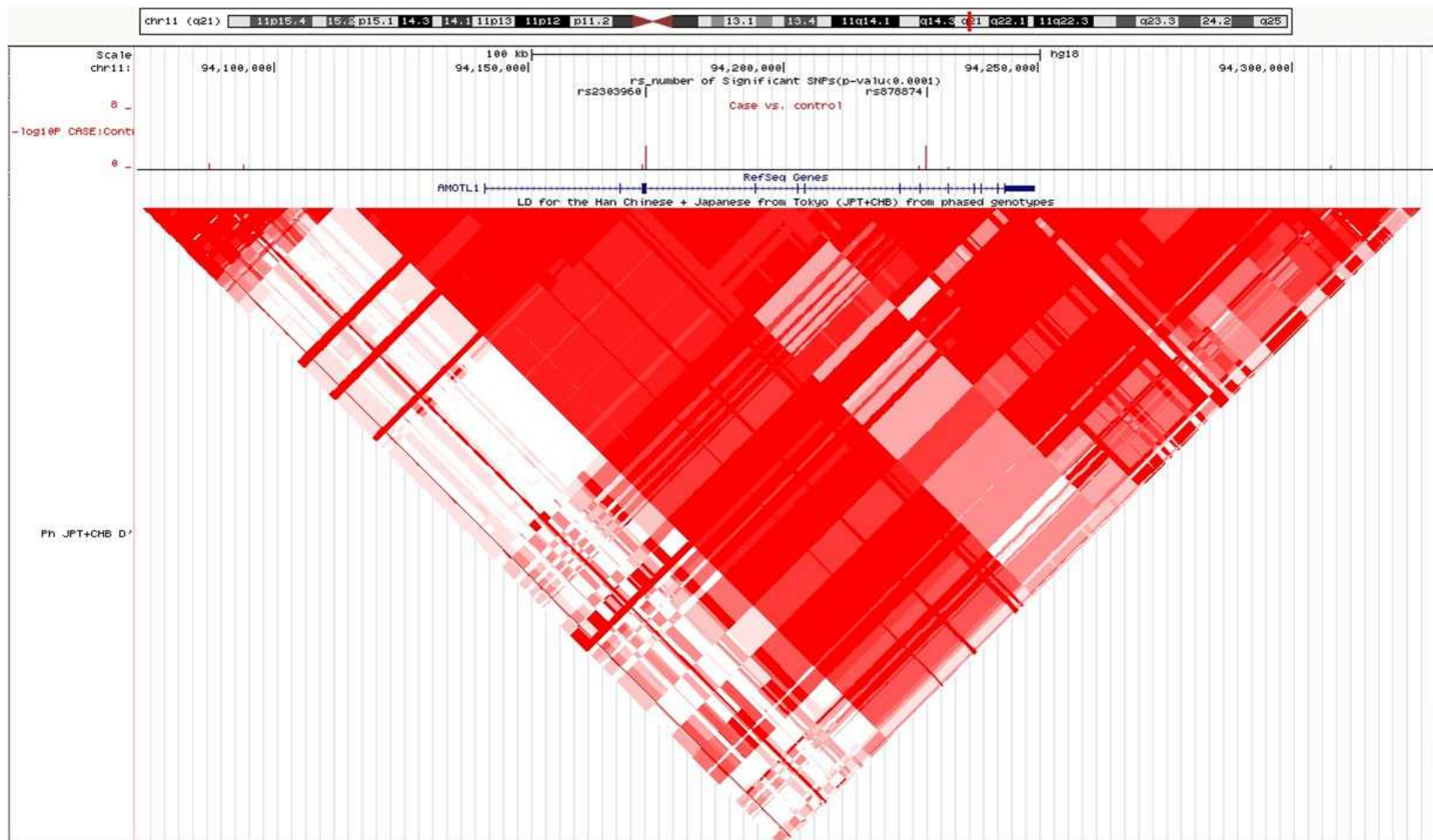


Figure 11. Locations of AMOTL1 mutations (rs2303960, rs878874), their LD structure, and associations with gastric cancer risk

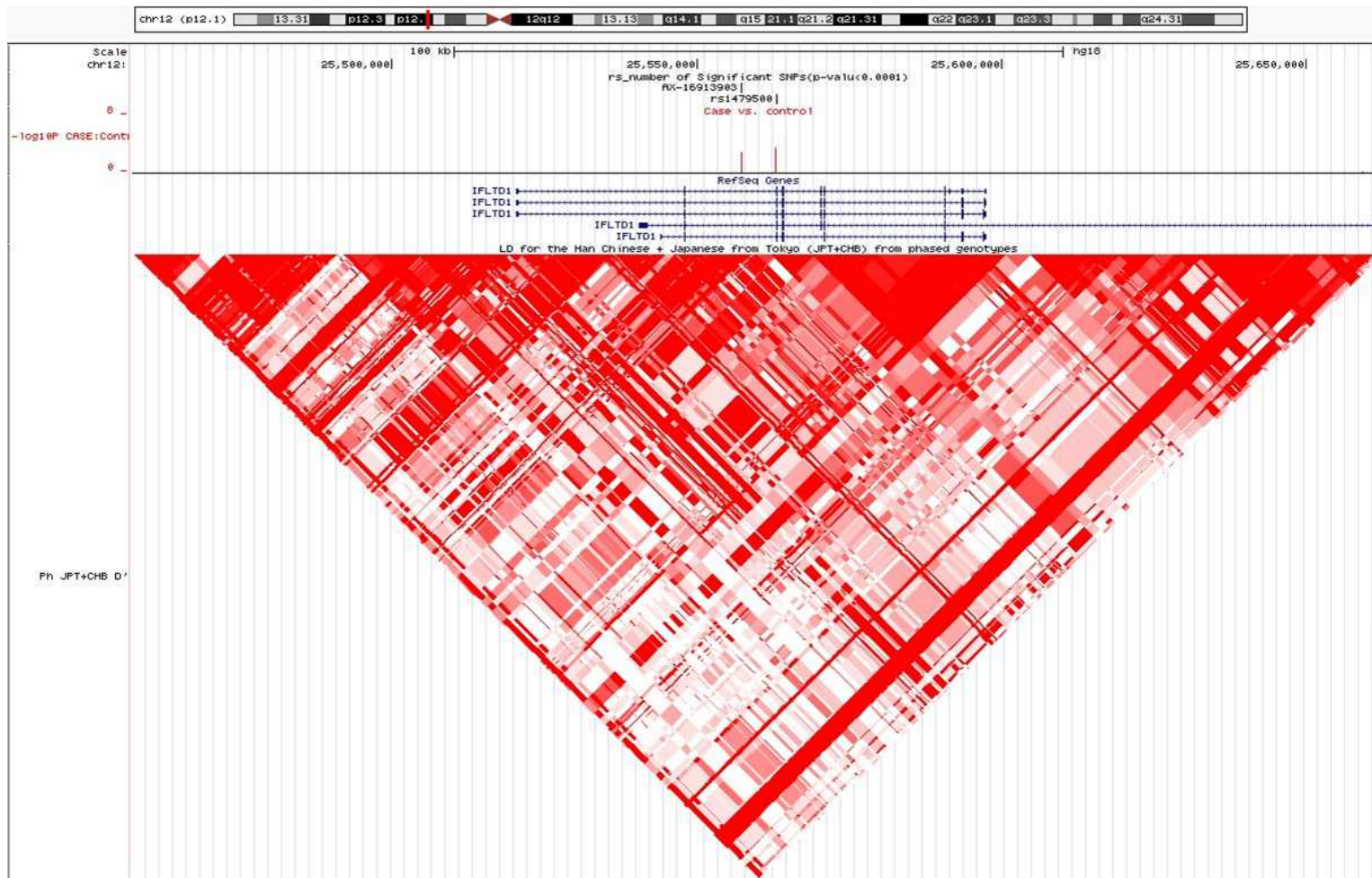


Figure 12. Locations of IFLTD1 mutations (rs1479500), their LD structure, and associations with gastric cancer risk



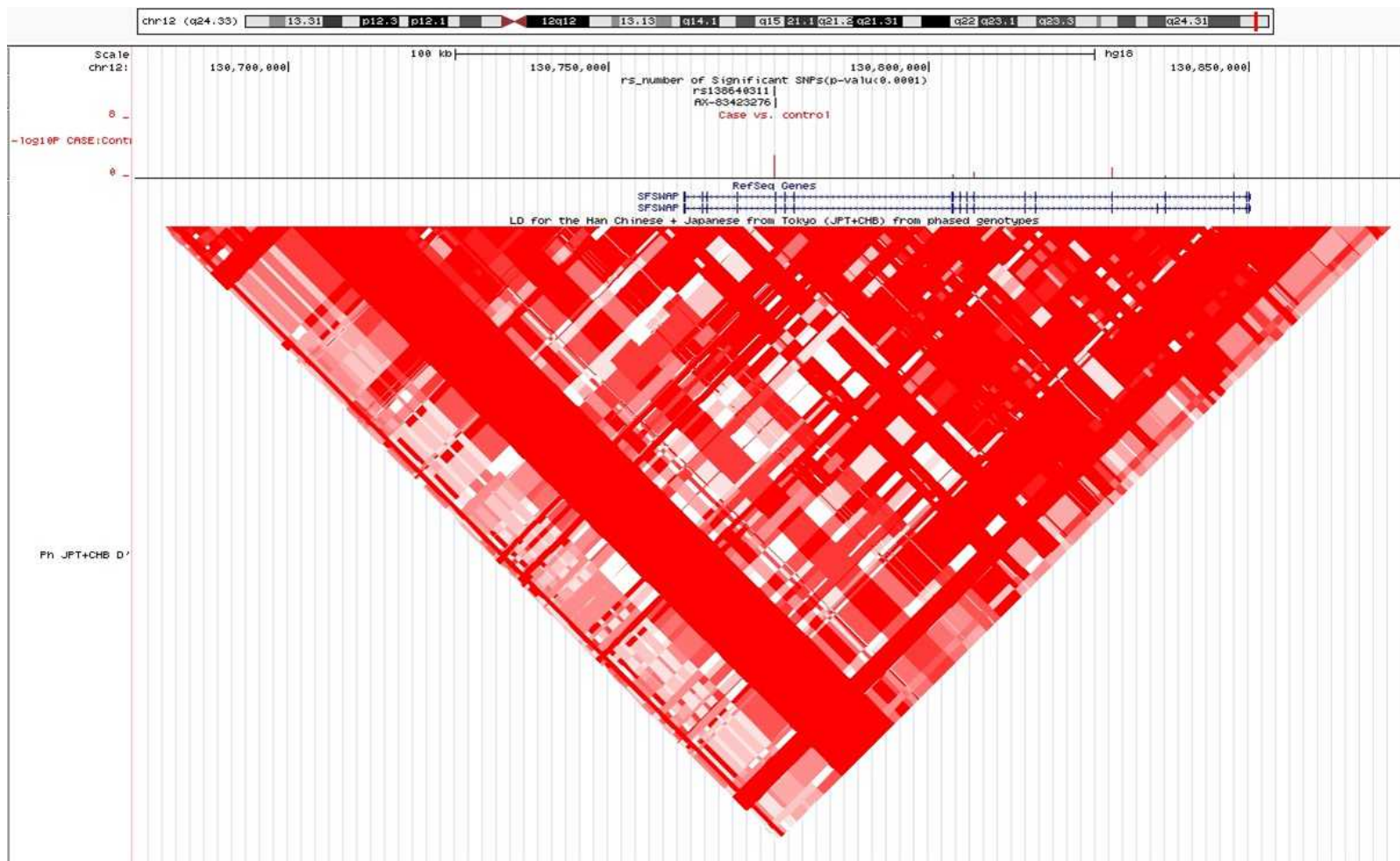


Figure 13. Locations of SFSWAP mutations (rs138640311), their LD structure, and associations with gastric cancer risk

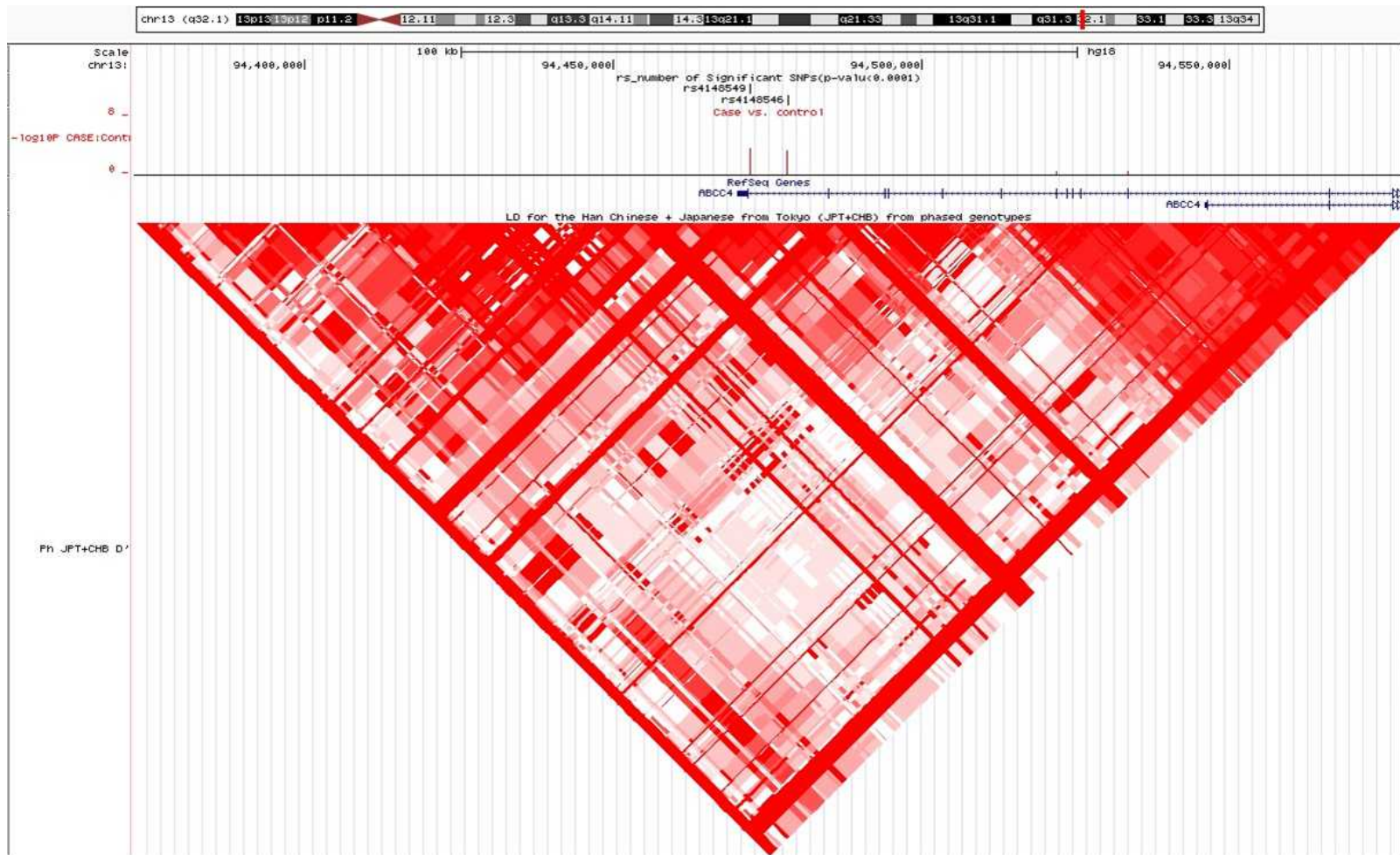


Figure 14. Locations of ABCC4 mutations (rs4148546, rs4148549), their LD structure, and associations with gastric cancer risk

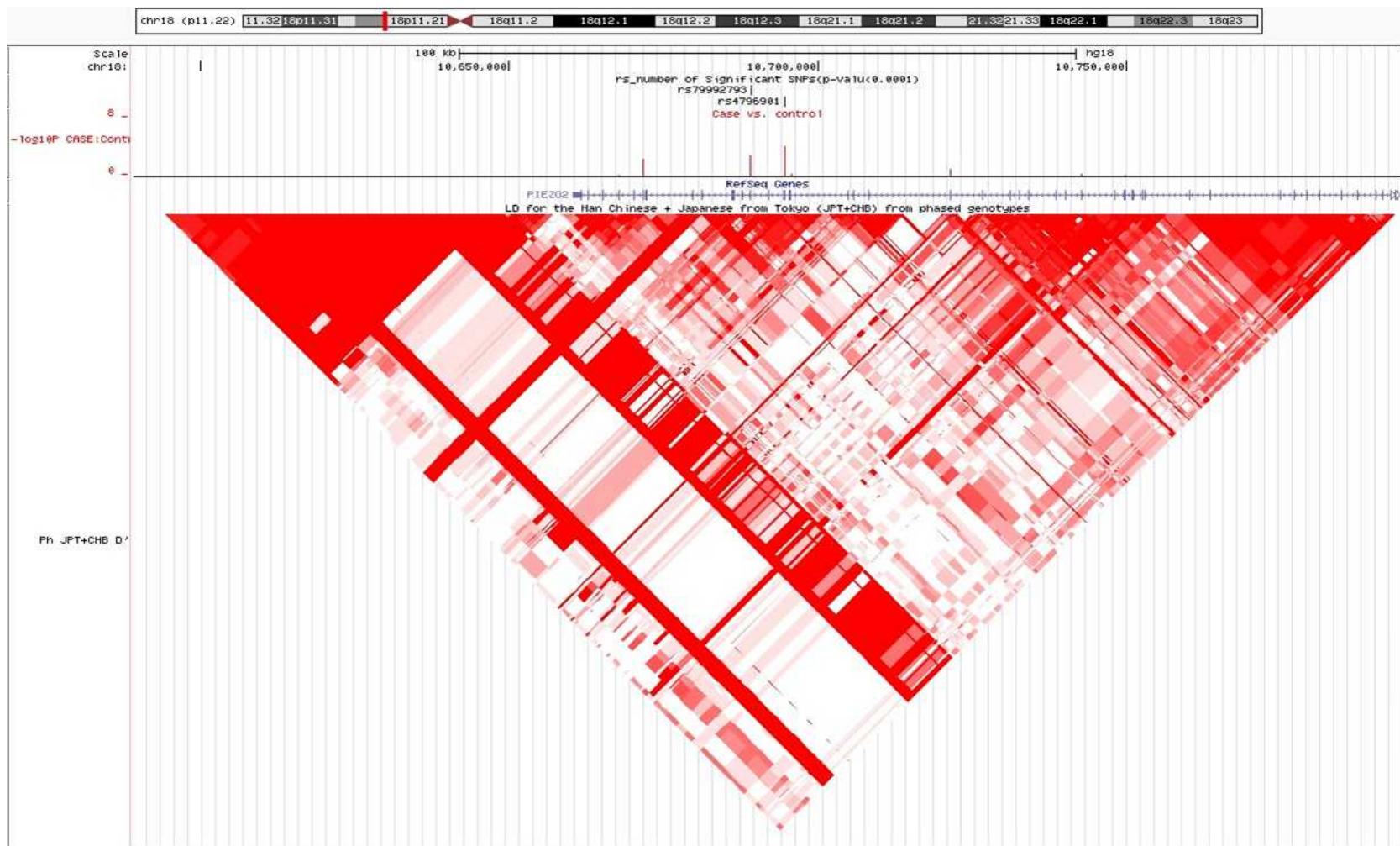


Figure 15. Locations of PIEZO2 mutations (rs4796901, rs79992793), their LD structure, and associations with gastric cancer risk

### 3. 연구결과 고찰 및 결론

- 국내·외 관련분야의 기술개발 현황과 연구결과가 국내·외 기술개발 분야에서 차지하는 위치 등을 기술
- 연구결과 해석 및 다른 결과와의 비교분석 등에 대해 고찰하고 결론을 서술함

### 4. 연구성과 및 목표달성도

#### (1) 연구성과

가. 국내 및 국제 전문학술지 논문 게재 및 신청

논문명	저자 (저자구분 <sup>1)</sup> )	저널명(I.F.)	Year; Vol(No):Page	구분 <sup>2)</sup>	지원과제번호 <sup>3)</sup>
Gastric cancer epidemiology in Korea	Shin A, Kim J, Park S (공동)	Journal of Gastric Cancer (0)	2011; 11(3):135-140	국내	1110300
Dietary flavonoid intake and smoking-related cancer risk: A meta-analysis	Woo HD, Kim J (교신)	PLoS One (3.73)	2013;8:e75604	국외 SCIE	1110300
Association of polymorphisms in the MCP-1 and CCR2 genes with the risk of cancer: A meta-analysis	Cho YA, Kim J (교신)	Cytokine (2.518)	2013;64:213-220	국외 SCI	1110300
Effects of polymorphisms of innate immunity genes and environmental factors on the risk of noncardia gastric cancer	Kim J, Cho YA, Choi IJ et al. (제1)	Cancer Research and Treatment (1.962)	2013년 12월호 게재예정	국내 SCIE	1110300
Gene-diet interactions in gastric cancer risk: A systematic review	Kim J, Cho YA et al. (제1 및 교신)	World Journal of Gastroenterol ogy (2.547)	2013년 12월호 게재예정	국외 SCIE	1110300

1) 저자구분 : 교신, 제1, 공동

2) 구분 : 국내, 국내 SCI, 국내 SCIE, 국외, 국외SCI, 국외SCIE 등

3) 지원과제번호(Acknowledgement)

- 과제번호를 연차 표시(-1, -2, -3 등)를 생략하고 7자리로 기재하고, 과제와 관련성은 있으나 불가피하게 Acknowledgement가 누락된 경우에는 '없음'으로 기재

나. 국내 및 국제 학술대회 논문 발표

논문명	저자	학술대회명	지역 <sup>1)</sup>	지원과제번호
Effects of polymorphisms of innate immunity genes and environmental factors on the risk of noncardia gastric cancer	Kim J, Cho YA, Choi IJ et al.	2011년 AACR Frontiers in Cancer Prevention Research	국외	1110300
한국인의 식이요인에 대한 암역학연구의 성과	Kim J	2011년 대한예방의학회 추계학술대회	국내	1110300
Epidemiology of gastrointestinal cancers	Kim J	2011년 연세의대 소화기병연구소 심포지엄	국내	1110300
Effects of high-fat diet on intestinal permeability and inflammation-associated tumorigenesis	Kim J, Sung MK et al.	2012년 Experimental Biology 학술대회	국외	1110300
Diet-gene interaction in cancer epidemiology	Kim J	2012년 대한소화기항암학회 춘계학술대회	국내	1110300
Global DNA hypomethylation in peripheral blood leukocytes as a biomarker for cancer risk: A meta-analysis	Woo HD, Kim J	2012년 대한암예방학회 심포지엄	국내	1110300
Association of polymorphisms in the MCP-1 and CCR2 genes with the risk of cancer: A meta-analysis	Cho YA, Kim J	2012년 AACR Post-GWAS Horizons in Molecular Epidemiology	국외	1110300
Beneficial effect of soy and isoflavone consumption on cancer prevention	Kim J	2013년 한국식품과학회 학술대회	국내	1110300
Epigenetics of isoflavones and cancer prevention	Kim J	2013년 한국유전체학회 학술대회	국내	1110300

1) 지역 : 국내, 국외

다. 산업재산권

구분 <sup>1)</sup>	특허명	출원인	출원국	출원번호

1) 구분 : 발명특허, 실용신안, 의장등록 등

라. 저서

저서명	저자	발행기관(발행국, 도시)	쪽수	Chapter 제목, 쪽수 (공저일 경우)

마. 연구성과의 정부정책 기여

보고서명	정부정책	기여내용



바. 기타연구성과

- 학술대회 발표를 통해 학술교류
- 대중매체를 통한 위암예방 교육 및 홍보

(2) 목표달성도

가. 연구목표의 달성도

최종목표	연차별목표		달성내용	달성도(%)	
				연차	최종
한국인의 호발암종인 위암의 예방을 효율적으로 관리하기 위해 유전적 요인과 식생활을 포함하는 생활습관요인의 영향, 미생물학적인 요인 및 상호작용의 규명을 통한 위암의 1차 예방 방안 제시하고자 함	1차년도	신규 위암 환자로 진단받은 사람들 150명과 검진센터 건강한 사람들 300명의 식생활(영양섭취량)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집	환자군 139명, 대조군 403명 모집하여 설문 및 임상정보를 수집하였으며 유전적 및 미생물학적 요인 등에 관한 검사를 진행하였음.	100	33
	2차년도	신규 위암 환자로 진단받은 사람들 150명과 검진센터 건강한 사람들 300명의 식생활(영양섭취량)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집	환자군 158명, 대조군 256명 모집하여 설문 및 임상정보를 수집하였으며 유전적 및 미생물학적 요인 등에 관한 검사를 진행하였음.	100	67
	3차년도	신규 위암 환자로 진단받은 사람들 100명과 검진센터 건강한 사람들 200명의 식생활(영양섭취량)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집	10월 18일까지 환자군 108명, 대조군 148명 모집하여 설문 및 임상정보를 수집하였으며 유전적 및 미생물학적 요인 등에 관한 검사를 진행하였음.	100	100

나. 평가의 착안점에 따른 목표달성도에 대한 자체평가

평가의 착안점	자 체 평 가
환자군 및 대조군 연구대상자 모집	환자군 및 대조군 연구대상자 확보
식생활(식품 또는 식품군)을 포함한 생활습관정보 및 유전적 요인과 미생물학적 위험요인 분석을 위한 생체시료 수집	설문 및 임상정보, 시료 등의 확보, 유전적 및 미생물학적 분석 진행 중

## 5. 연구결과의 활용계획

### (1) 연구종료 2년후 예상 연구성과

- 연구종료 2년후까지 연구사업 결과로 발생할 것으로 예상되는 성과, 즉 학술지 게재, 산업재산권 등을 단계별로 다음의 양식에 의거하여 작성함. 학술지 게재는 게재 예상 학술지 명과 Impact Factor 등을 기재함
- 연구사업의 내용이 논문이나 산업재산권과 연결되기 힘든 과제의 경우, 자유 형식으로 예상연구성과 및 활용정도를 기재하되 최대한 계량화할 것

예) DB 몇 건 구축완료. OOO 시스템 구축 및 OO사업 완료

구 분	건 수	비 고
학술지 논문 게재	7	Nature Genetics, International Journal of Cancer에 exome array 결과 투고예정
산업재산권 등록		
기 타		

### (2) 연구성과의 활용계획

- 연구성과물의 활용분야 및 활용방법, 활용범위 등을 구체적(특히 시간적 구체성, 예를 들어 몇 년 안에 치료기술 실용화 등)으로 기술하되, 참여기업이 포함되어 있는 과제의 경우 기업과 연계한 활용방안에 대해서도 기술함
- 추가 후속연구의 필요성에 대해서도 간략하게 기술함

## 6. 참고문헌

- 보고서 작성시 인용된 모든 참고문헌을 열거

## 7. 첨부서류



대한암학회  
KOREAN CANCER ASSOCIATION

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Homepage: www.cancer.or.kr, e-mail : cancer@kams.or.kr or cancer1@kams.or.kr

논문게재 예정 증명서

논문종류 : Original Article

논문제목 : Effects of Polymorphisms of Innate Immunity Genes and Environmental Factors on the Risk of Noncardia Gastric Cancer

저 자 : Jeongseon Kim, PhD<sup>1</sup>, Young Ae Cho, PhD, MPH<sup>1</sup>, Il Ju Choi, MD, PhD<sup>2</sup>, Yeon-Su Lee, PhD<sup>3</sup>, Sook-Young Kim, MS<sup>3</sup>, Jung-Ah Hwang, MS<sup>3</sup>, Soo-Jeong Cho, MD, PhD<sup>2</sup>, Myeong-Cherl Kook, MD, PhD<sup>2</sup>, Chan Gyo Kim, MD, PhD<sup>2</sup>, Young-Woo Kim, MD, PhD<sup>2</sup>

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2013년 10월 16일

대한암학회 편집위원장



## Gastric Cancer Epidemiology in Korea

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Gastric cancer has been the most commonly diagnosed cancer in Korea although the age-standardized mortality and incidence has decreased gradually during last two decades. *Helicobacter pylori* infection and cigarette smoking are well-established risk factors, and the role of dietary factors, such as salted foods, fresh vegetables and fruits, soy foods, and processed or grilled meats on gastric carcinogenesis has been suggested. In this review, we review national and international gastric cancer statistics, studies on environmental risk factors conducted in the Korean population, and gastric cancer screening activities.

**Key Words:** Stomach neoplasms, Epidemiology, Incidence, Mortality, Risk factors

### Introduction

Historically, gastric cancer has been one of the major cancers in East Asian countries like Korea and Japan. Although the mortality and incidence of gastric cancer has decreased in these regions, gastric cancer is still the fourth most common cancer in the world and the second most common cancer in Asia.(1) In this review, we first provide descriptive epidemiology of gastric cancer and then describe the literature on possible etiologic factors for gastric carcinogenesis. Most of gastric cancers are non-cardia cancer and only 4~5% of gastric cancers occur in the cardia.(2) The epidemiology of non-cardia and cardia gastric cancers differ. Therefore, we mainly focused on the environmental risk factors of non-cardia gastric cancer. Finally, the gastric cancer screening program is addressed.

### Gastric Cancer Incidence, Mortality, and Survival in Korea

Gastric cancer has been the most commonly diagnosed cancer in Korea since 1999 when the Korea Central Cancer Registry first reported nationwide cancer incidence data.(3) In females, gastric cancer was the most common incident cancer until 2001, and in 2008, it became the third most common incident cancer after thyroid cancer and breast cancer. However, gastric cancer has been the most common cancer in men in Korea since 1999 (3). In 2008, 28,078 new gastric cancer cases (18,898 male and 9,180 female) were diagnosed, accounting for 15.7% of all cancer occurrences. (3) Gastric cancer is relatively rare before age 30, and age-specific incidence rates increase as age advances (Table 1). Although not significant statistically, gastric cancer incidence has decreased in both males and females. The annual percentage changes in age-standardized gastric cancer incidence were -0.5% in males and -0.6% in females, respectively.(3)

Gastric cancer mortality decreased gradually between 1983 and 2009.(4) The crude mortality rates per 100,000 were 27.1 in males and 14.6 in females in 2008; these rates are expected to drop to 17.7 in males and 12.3 in females in 2011.(5) Fig. 1 showed the trend in gastric cancer incidence and mortality.

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# Dietary Flavonoid Intake and Smoking-Related Cancer Risk: A Meta-Analysis

Hae Dong Woo, Jeongseon Kim\*

Molecular Epidemiology Branch, National Cancer Centre, Goyang-si, Korea

## Abstract

**Purpose:** To systematically investigate the effects of dietary flavonoids and flavonoid subclasses on the risk of smoking-related cancer in observational studies.

**Methods:** Summary estimates and corresponding standard errors were calculated using the multivariate-adjusted odds ratio (OR) or relative risk (RR) and 95% CI of selected studies and weighted by the inverse variance.

**Results:** A total of 35 studies, including 19 case-controls (9,525 cases and 15,835 controls) and 15 cohort studies (988,082 subjects and 8,161 cases), were retrieved for the meta-analysis. Total dietary flavonoids and most of the flavonoid subclasses were inversely associated with smoking-related cancer risk (OR: 0.82, 95% CI: 0.72-0.93). In subgroup analyses by cancer site, significant associations were observed in aerodigestive tract and lung cancers. Total dietary flavonoid intake was significantly associated with aerodigestive tract cancer risk (OR: 0.67, 95% CI: 0.54-0.83) marginally associated with lung cancer risk (OR: 0.84, 95% CI: 0.71-1.00). Subgroup analyses by smoking status showed significantly different results. The intake of total flavonoids, flavonols, flavones, and flavanones, as well as the flavonols quercetin and kaempferol was significantly associated with decreased risk of smoking-related cancer in smokers, whereas no association was observed in non-smokers, except for flavanones. In meta-analysis for the effect of subclasses of dietary flavonoids by cancer type, aerodigestive tract cancer was inversely associated with most flavonoid subclasses.

**Conclusion:** The protective effects of flavonoids on smoking-related cancer risk varied across studies, but the overall results indicated that intake of dietary flavonoids, especially flavonols, was inversely associated with smoking-related cancer risk. The protective effects of flavonoids on smoking-related cancer risk were more prominent in smokers.

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**Competing Interests:** The authors have declared that no competing interests exist.

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## Introduction

Flavonoids are polyphenolic compounds that are abundant in fruits and vegetables. High intake of fruits and vegetables is associated with beneficial health effects, and these effects have been attributed in part to their high content of flavonoids. The World Cancer Research Fund (WCRF) and the American Institute of Cancer Research (AICR) reported summary estimates of the effects of fruit and vegetable consumption on cancer risk [1]. The consumption of fruits and vegetables most likely protects against cancers of the mouth, pharynx, larynx, esophagus, and stomach; the risk of lung cancer was only associated with fruit consumption. These cancers are smoking-related cancers according to the International Agency for Research on Cancer (IARC) Monograph on tobacco smoking.

Smoking is classified as the cause of cancers of the lung, oral cavity, nasal and paranasal sinuses, pharynx, larynx, esophagus, kidney, liver, uterine cervix, stomach, bladder, pancreas, as well as myeloid leukemia [2]. Adverse effects of flavonoids in human health are rare, but the potential for detrimental health effects is based on in vitro studies in which pro-oxidant activities have been observed [3,4]. However, flavonoids are known to have powerful antioxidant, anti-inflammatory, and anti-tumor activities against carcinogens [5,6,7]. Tobacco contains various carcinogens that can induce free radicals and cause gene mutations and the formation of DNA [8]. Thus, dietary flavonoids may play a role in protecting against smoking-related cancers.

The effects of dietary flavonoids on stomach and colorectal cancer were investigated using published studies [9] because



## Association of polymorphisms in the *MCP-1* and *CCR2* genes with the risk of cancer: A meta-analysis



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CCR2

### ABSTRACT

Studies investigating the impact of polymorphisms on monocyte chemoattractant protein-1 (*MCP-1*) and CC chemokine receptor 2 (*CCR2*) on the risk of cancer have reported inconsistent results. We performed a meta-analysis of 23 eligible studies to summarize the data describing the association between cancer risk and polymorphisms in *MCP-1* A2518G and *CCR2* V64I. *Q*-statistics and *I*<sup>2</sup> statistics were calculated to examine heterogeneity and summary odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated using a random effects model. Potential sources of heterogeneity were investigated via subgroup and sensitivity analyses, and publication biases were estimated. Overall, *MCP-1* and *CCR2* polymorphisms showed no significant associations with cancer risk (*MCP-1*-2518A/G, GG + GA vs. AA: OR = 0.94, 95% CI = 0.76–1.17; *CCR2* V64I, AA + AG vs. GG: OR = 1.27, 95% CI = 0.87–1.86). However, strong evidence of heterogeneity was found among the investigated studies, and subgroup analyses were therefore conducted according to study location, cancer type, source of controls, and presence of deviation from the Hardy-Weinberg equilibrium (HWE). When the data were stratified by study location, the increased risk of cancer among A allele carriers of *CCR2* V64I was observed only in studies conducted in Asian countries (AA + AG vs. GG: OR = 1.65; 95% CI = 1.25–2.18). This meta-analysis suggests that genetic polymorphisms of *CCR2* V64I may influence the susceptibility of cancer in Asian countries. Further well-designed studies with larger sample sizes should be conducted.

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### 1. Introduction

Evidence has indicated that chronic inflammation is associated with the development and progression of different types of cancer [1]. Chemokines are small proinflammatory chemotactic cytokines that regulate the migration of immune cells by binding to G-protein coupled cell-surface receptors [2]. Studies have shown that chemokines and their receptors play diverse roles in cancer initiation and progression via regulation of tumor-associated angiogenesis, activation of a tumor-specific immune response, and stimulation of tumor cell proliferation [3–5].

Monocyte chemoattractant protein-1 (*MCP-1*), which belongs to the CC chemokine family, regulates the infiltration of monocytes/macrophages and other inflammatory cells by binding to the membrane CC chemokine receptor 2 (*CCR2*) [6]. *MCP-1* is biosynthesized by

both tumor cells and stromal cells, including tumor-associated macrophages (TAMs), endothelial cells, and fibroblasts. *MCP-1* expression has been observed in a large number of tissues during inflammation-dependent disease progression, including cancer [7]. A polymorphic G allele at the -2518A/G position at the promoter region of *MCP-1* has been shown to increase the gene expression of *MCP-1* [8]. *CCR2* is a major receptor for *MCP-1* and is expressed in both immune cells and tumor cells [9,10]. The *CCR2* gene has two isoforms, *CCR2A* and *CCR2B*, which are products of the alternative splicing of the *CCR2* gene. A single nucleotide polymorphism (SNP) of G to A at position 19 of the *CCR2* gene changes the amino acid valine (GTC) to isoleucine (ATC) at codon 64 (*CCR2* V64I), introducing a conservative amino acid change into the first transmembrane domain of *CCR2A* and *CCR2B* [11]. This change makes *CCR2A* more stable and increases its half-life, although it does not affect the stability of the *CCR2B* isoform [11].

Many studies have investigated the role of *MCP-1*-2518A/G and *CCR2* V64I in the risk of various types of cancer, including cervical cancer [12–15], bladder cancer [16–19], and gastric cancer [20–22]. However, results remain inconclusive because of the difficulty associated with obtaining robust, replicable results in genetic association studies, whereby the genetic effects are small and require large sample sizes to be detected. A meta-analysis may address this

Abbreviation: *MCP-1*, monocyte chemoattractant protein-1; *CCR2*, CC chemokine receptor 2; ORs, odds ratios; 95% CI, 95% confidence intervals; HWE, Hardy-Weinberg equilibrium; TAMs, tumor-associated macrophages; SNP, single nucleotide polymorphism.

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