Genome-wide association study of coronary artery disease in Korean population

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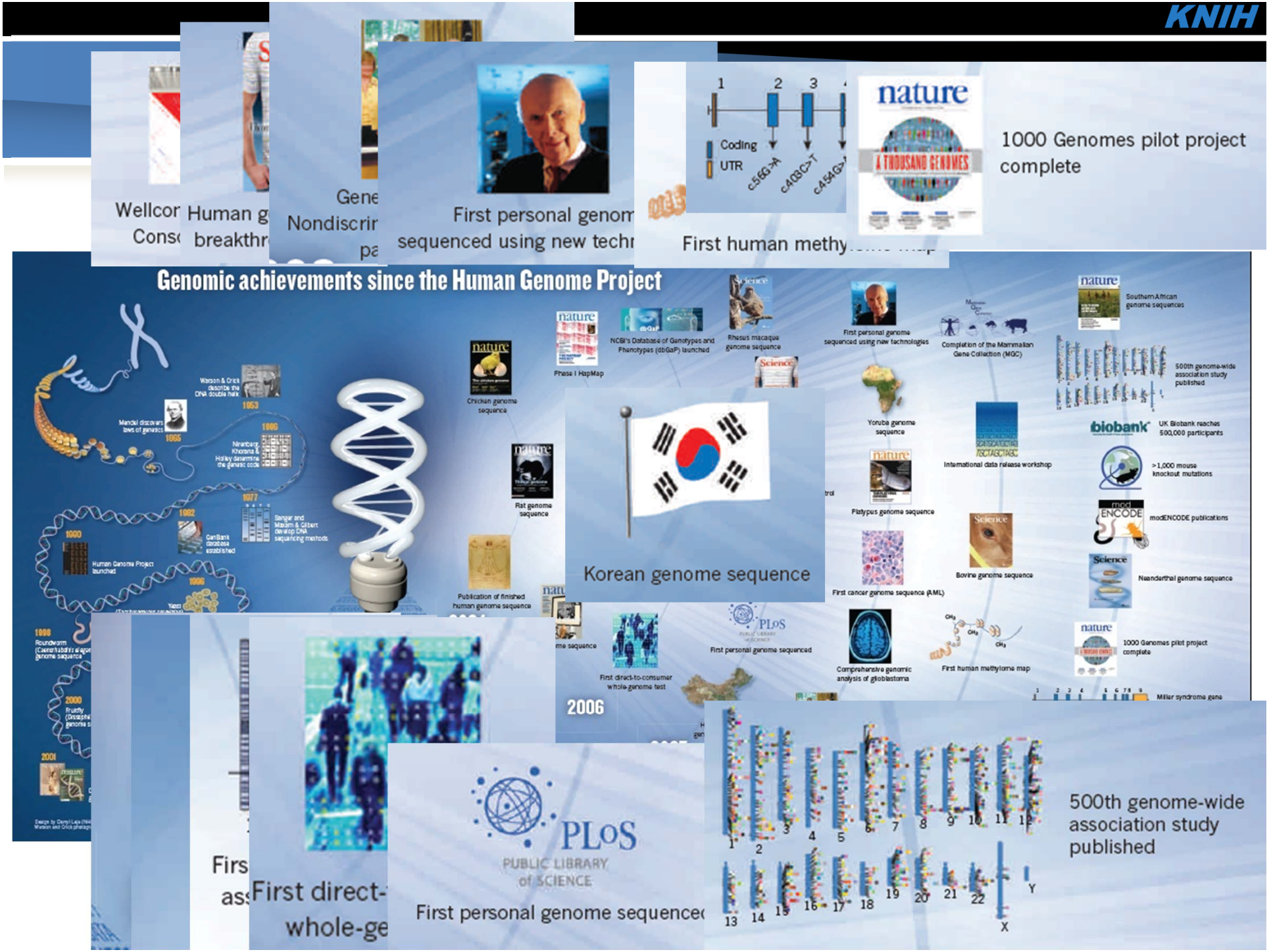
What is the Human Genome ?

- The entire genetic make up of the human cell nucleus.
- Genes carry the information for making all of the proteins required by the body for growth and maintenance.
- Made up of ~20,000-25,000 genes and a much smaller mitochondrial genome with 37 genes
- Includes non-coding sequences located between genes, which makes up the vast majority of the DNA in the genome (~95%)
- The particular order of nucleotide bases (As, Gs, Cs, and Ts) determines the amino acid composition of proteins


Genomic achievements since the Human Genome Project
Korean genome sequence
2006
First personal genome sequenced
PLoS
PUBLIC LIBRARY of SCIENCE
500th genome-wide association study published
1000 Genomes pilot project complete
First human methylome map
First direct-to-consumer whole-genome test
Comprehensive genomic analysis of glioblastoma
Neanderthal genome sequence
modENCODE publications
>1,000 mouse knockout mutations
UK Biobank reaches 500,000 participants
Southern African genome sequences
Platypus genome sequence
Bovine genome sequence
Rhesus macaque genome sequence
Chicken genome sequence
Rat genome sequence
Phase I HapMap
NCBI's Database of Genotypes and Phenotypes (dbGaP) launched
Yoruba genome sequence
International data release workshop
First cancer genome sequence (AML)
Publication of finished human genome sequence
Human Genome Project launched
GenBank database established
Sanger and Maxam & Gilbert develop DNA sequencing methods
Watson & Crick describe the DNA double helix
Mendel discovers laws of genetics
Nirenberg, Khorana & Holley determine the genetic code
Miller syndrome gene
First personal genome sequenced using new technologies
Completion of the Mammalian Gene Collection (MGC)

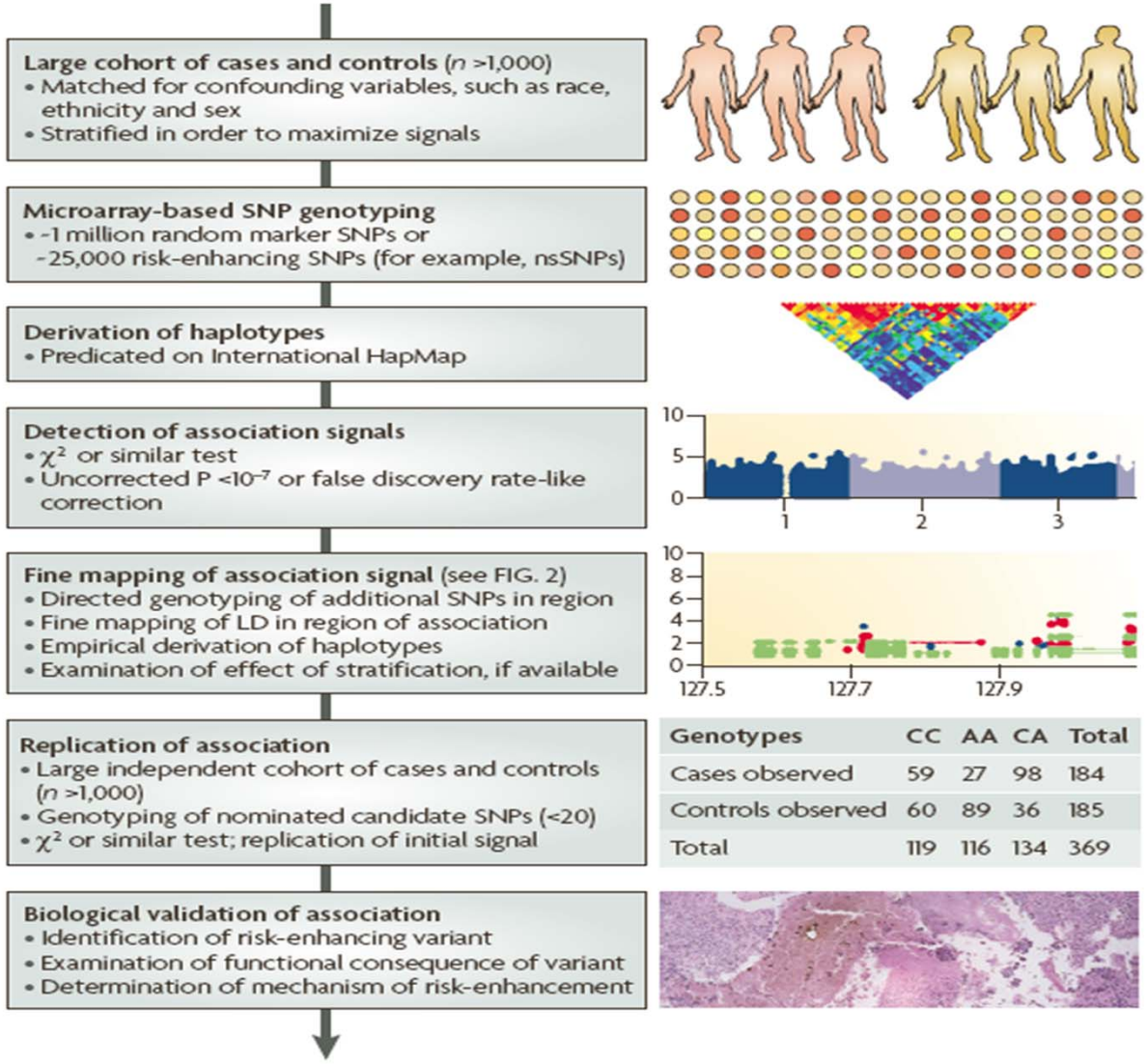
전장유전체연관분석 연구란 ?

Genome-Wide Association Study (GWAS)

대규모 연구대상자(정상-환자)들의 유전체시료(DNA)를 이용하여 유전체 전장을 대표할 수 있도록 선택된 대량의 마커 (SNPs)들을 타이핑하고, 이 정보를 역학·임상정보와 연계하여 특정 질환이나 형질과 연관된 유전변이(유전적요인)들을 발굴하는 연구

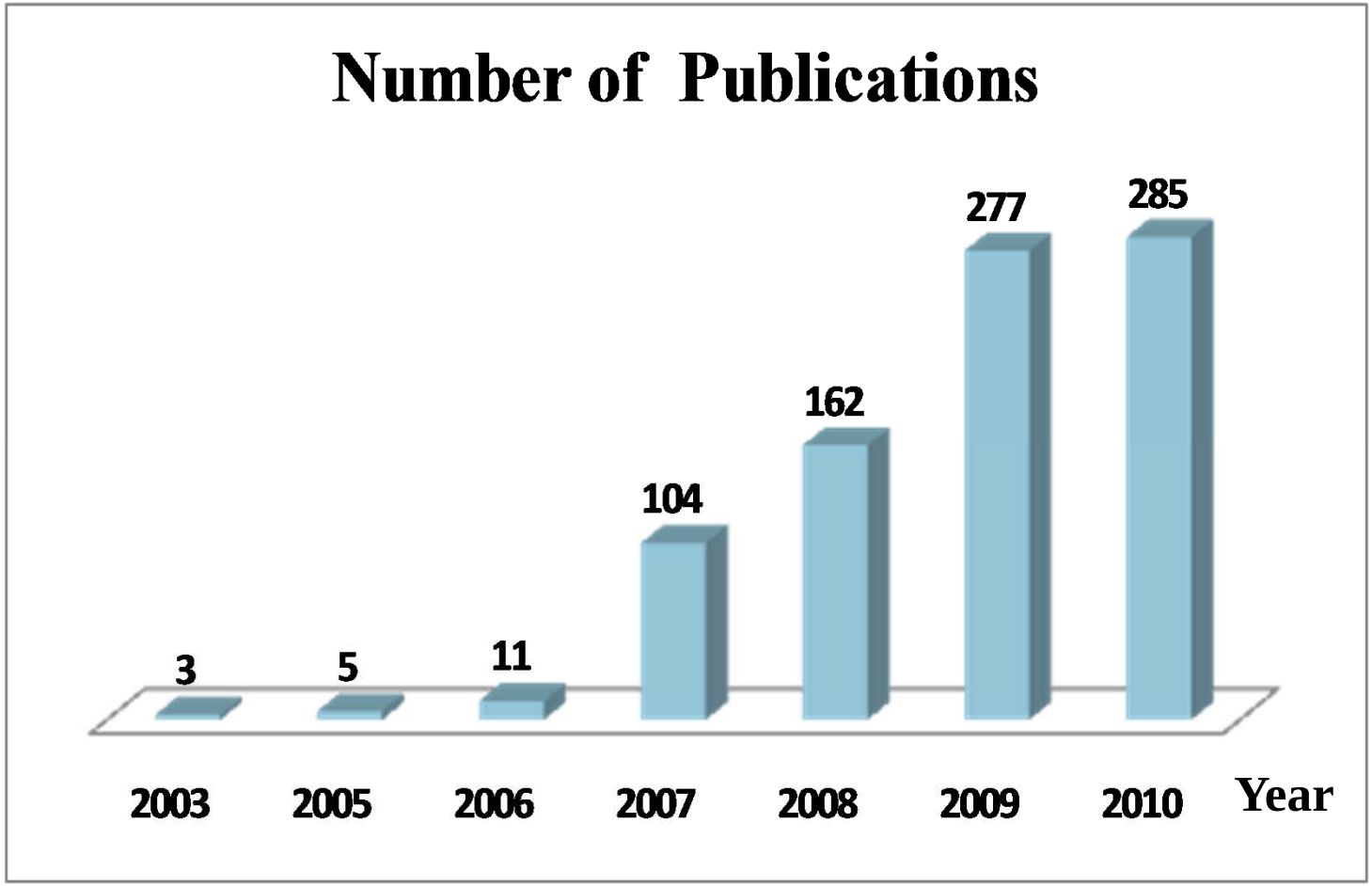
(Pearson & Manolio, JAMA. 2008)

Overview of the general design and workflow GWAS



(Kingsmore et al., Nature Reviews Drug Discovery. 2008)

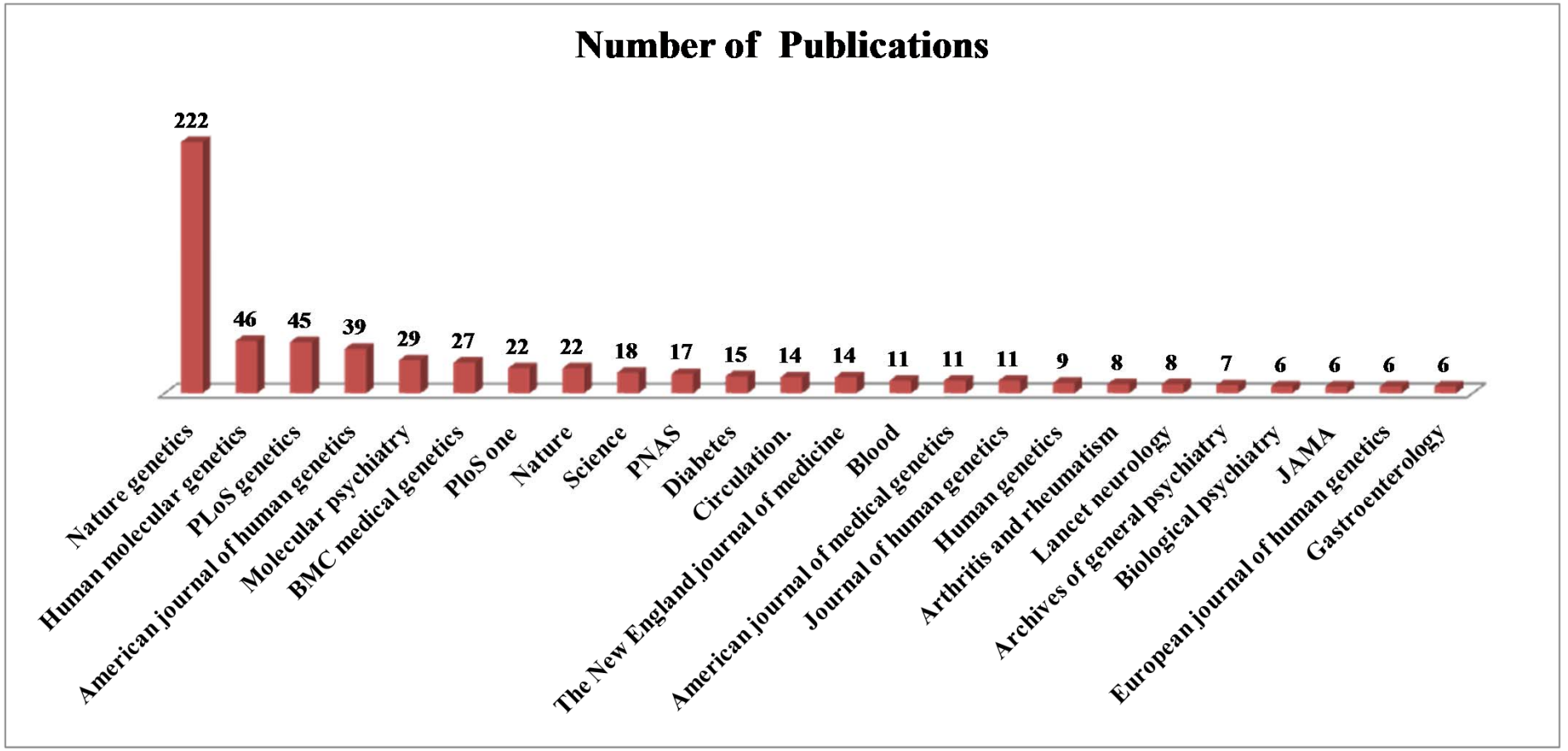
Trend of GWA studies-Publications: 847 papers, ~2010. Oct.13



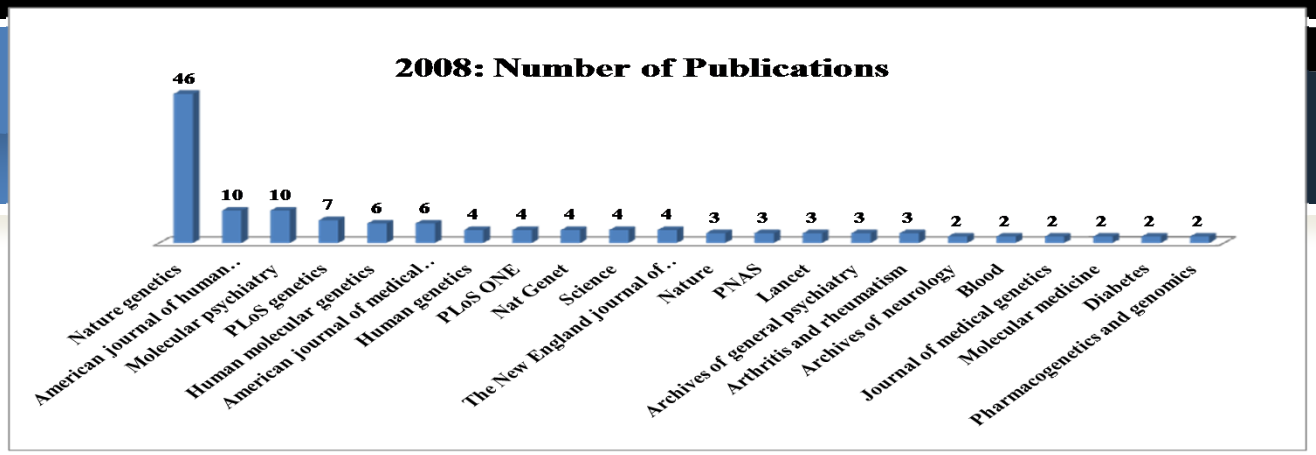
Modified data from HuGE Navigator

GWA studies are published in 160 Journals:

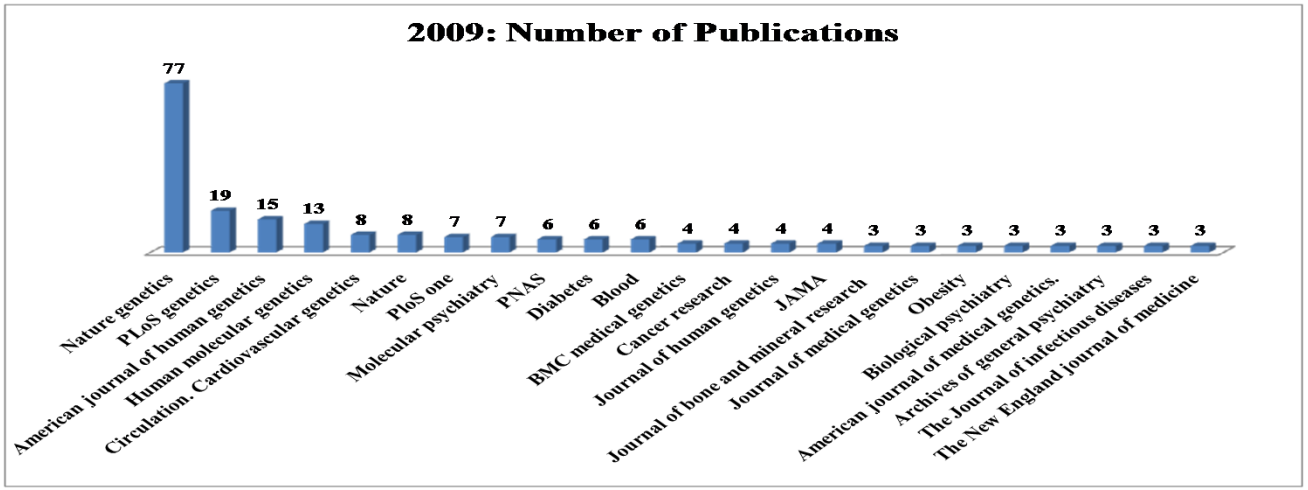
Nature genetics 222 papers, ~2010. Oct.13



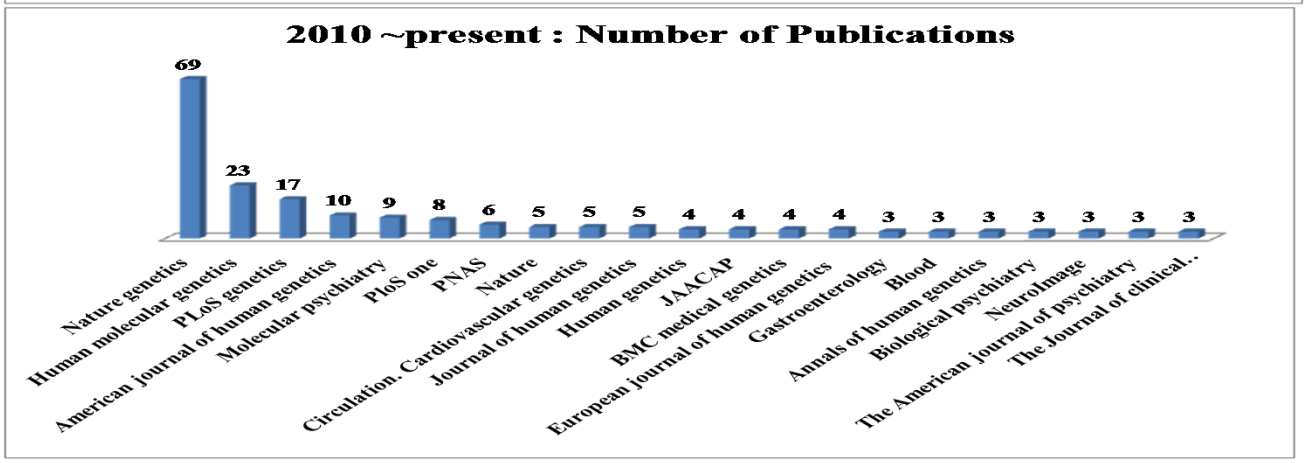
Modified data from HuGE Navigator



52 Journals

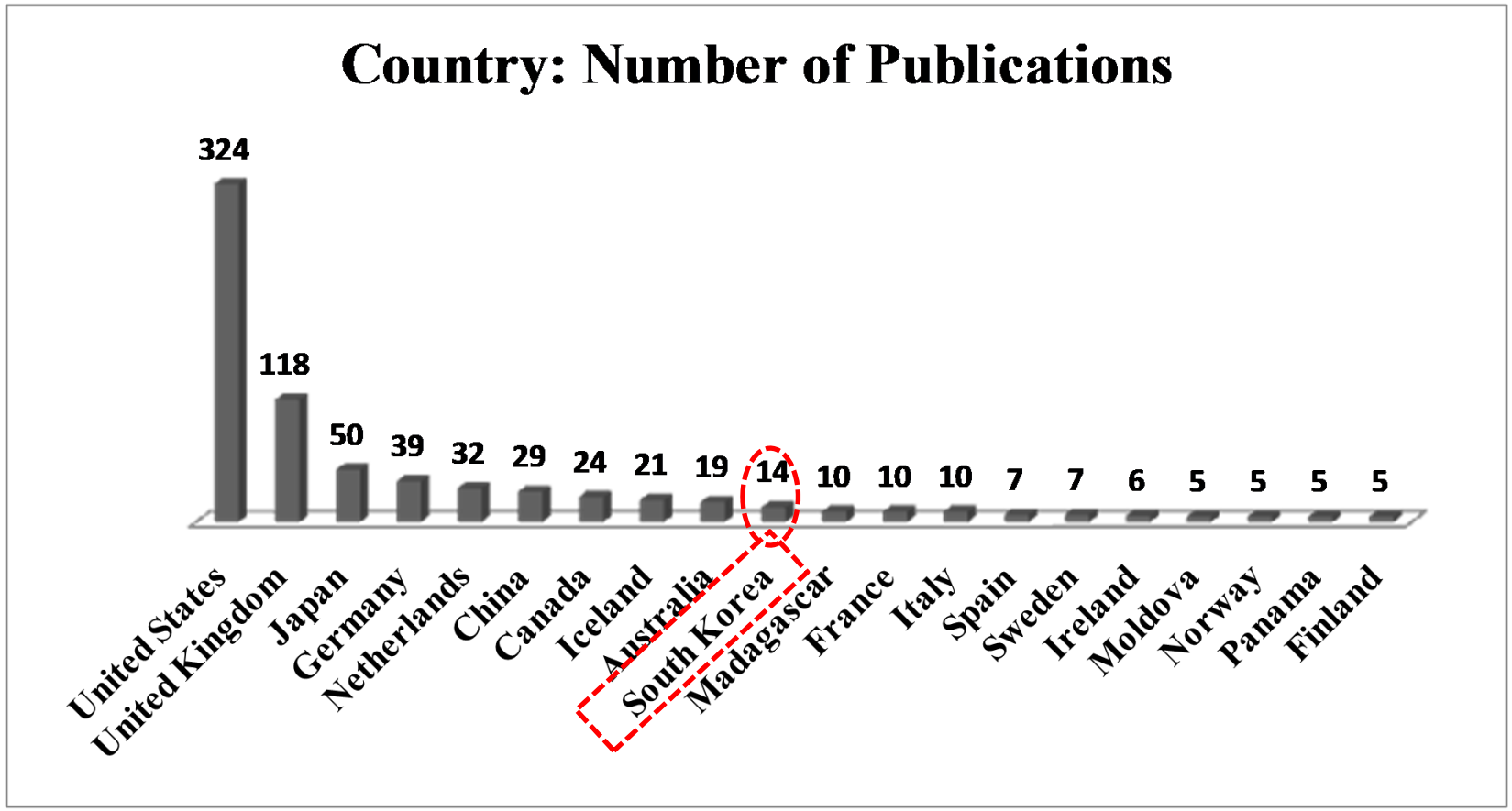


77 Journals



97 Journals

Trend of GWA studies-Publications: 847 papers, ~2010. Oct.13

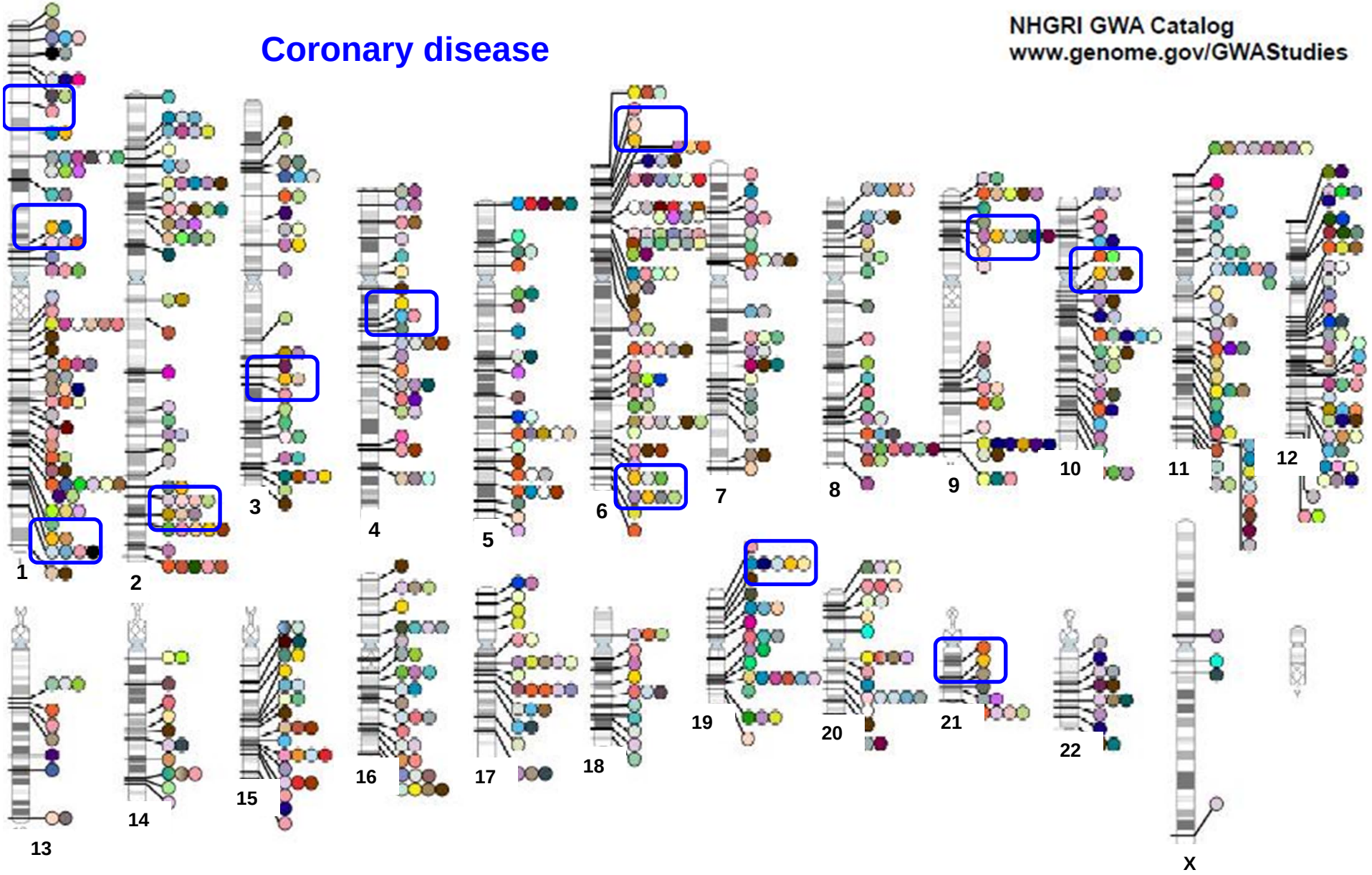


Modified data from HuGE Navigator

Published Genome-Wide Associations through 3/2010, 779 published GWA at $p \leq 5 \times 10^{-8}$ for 148 traits

Coronary disease

NHGRI GWA Catalog
www.genome.gov/GWAStudies



Korean GWAS Vs Previous GWAS

			Korean GWAS					Previous GWAS				
SNP	Chromosome	Gene(s)	Type	Allele	maf	OR	*P*	Allele	maf	OR	*P*	Ref.
rs10757278	**9p21.3**	***CDKN2A-CDKN2B***	**I**	**G**	**0.485**	**1.269**	**1.91E-08**	**G**	**0.45**	**1.28**	**1.00E-20**	**Science 2007**
rs1333049	**9p21.3**	***CDKN2A-CDKN3B***	**O**	**C**	**0.494**	**1.263**	**3.30E-08**	**G**	**0.47**	**1.47**	**1.00E-13**	**Nature 2007**
rs4977574	**9p21.3**	***CDKN2A-CDKN2B***	**O**	**G**	**0.467**	**1.244**	**2.02E-07**	**G**	**0.56**	**1.29**	**3.00E-44**	**Nat Genet 2009**
rs4537545	**1q21.3**	***IL6R***	**O**	**T**	**0.417**	**0.809**	**1.20E-06**	**T**	**NR**	**11.5**	**2.00E-14**	**JAMA 2009**
rs599839	**1p13.3**	***PSRC1***	**O**	**G**	**0.06**	**0.725**	**0.00033**	**A**	**0.23**	**1.29**	**4.00E-09**	**N Engl J Med 2007**
rs646776	**1p13.3**	***CELSR2-PSRC1- SORT1***	**I**	**C**	**0.045**	**0.739**	**0.00295**	**T**	**0.81**	**1.19**	**8.00E-12**	**Nat Genet 2008**
rs501120	10q11.21	*CXCL12*	I	C	0.365	0.9193	0.05198	T	0.13	1.33	9.00E-08	N Engl J Med 2007
rs1000778	11q12.3	*FADS3*	I	A	0.3	0.9146	0.05651	A	0.32	0.62	7.00E-13	PLoS Genet 2009
rs1746048	10q11.21	*CXCL12*	O	A	0.328	0.9229	0.07304	C	0.84	1.17	7.00E-09	Nat Genet 2009
rs6725887	2q33.1	*WDR12*	O	C	0.014	1.357	0.08414	C	0.14	1.17	1.00E-08	Nat Genet 2009
rs17465637	1q41	*MIA3*	O	T	0.437	0.9323	0.09338	C	0.29	1.2	1.00E-06	N Engl J Med 2007
rs17465637	1q41	*MIA3*	O	T	0.437	0.9323	0.09338	C	0.72	1.14	1.00E-09	Nat Genet 2009

Boldfaces represent associations with $P < 0.05$ in Korean CAD GWAS
Abbreviation: I, imputed type; O, observed type

*Hugenavigator "**GWAS integrator**"*

Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls

Nature 2007

A Common Variant on Chromosome 9p21 Myo

oach to the

Anna Helg
Thorarinn
Adam Bak
Karl Ande
Thorbjorg
Arnaldur G
Christophe
Jeffrey R.
Augustine

The global
Here, we d
variant on
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cases. The

A Common Allele on Chromosome 9 Associated with Coronary Heart Disease

N Engl J Med. 2007

Science 2007

Ruth McPherson,[1]*† Alexander Pertsemlidis,[2]* Nihan Kavaslar,[1] Alexandre Stewart,[1] Robert Roberts,[1] David R. Cox,[3] David A. Hinds,[3] Len A. Pennacchio,[4,5] Anne Tybjaerg-Hansen,[6] Aaron R. Folsom,[7] Eric Boerwinkle,[8] Helen H. Hobbs,[2,9] Jonathan C. Cohen[2,10]†

Coronary heart disease (CHD) is a major cause of death in Western countries. We used genome-wide association scanning to identify a 58-kilobase interval on chromosome 9p21 that was consistently associated with CHD in six independent samples (more than 23,000 participants) from four Caucasian populations. This interval, which is located near the *CDKN2A* and *CDKN2B* genes, contains no annotated genes and is not associated with established CHD risk factors such as plasma lipoproteins, hypertension, or diabetes. Homozygotes for the risk allele make up 20 to 25% of Caucasians and have a ~30 to 40% increased risk of CHD.

Associations of *IL6R* variants at 1q21.3

Genetic Loci Associated With C-Reactive Protein Levels and Risk of Coronary Heart Disease

Paul Elliott, FRCP
John C. Chambers, PhD
Weihua Zhang, PhD
Robert Clarke, MD
Jemma C. Hopewell, PhD
John F. Peden, PhD
Jeanette Erdmann, PhD
Peter Braund, MSc
James C. Engert, PhD
Derrick Bennett, PhD
Lachlan Coin, PhD
Deborah Ashby, PhD
Ioanna Tzoulaki, PhD
Ian J. Brown, PhD
Shahrul Mt-Isa, BSc
Mark I. McCarthy, FRCP
Leena Peltonen, MD, PhD
Nelson B. Freimer, MD
Martin Farrall, FRCPath
Aimo Ruokonen, MD, PhD
Anders Hamsten, MD
Noha Lim, PhD
Philippe Froguel, MD
Dawn M. Waterworth, PhD
Peter Vollenweider, MD
Gerard Waeber, MD
Marjo-Riitta Jarvelin, MD
Vincent Mooser, MD

Context Plasma levels of C-reactive protein (CRP) are independently associated with risk of coronary heart disease, but whether CRP is causally associated with coronary heart disease or merely a marker of underlying atherosclerosis is uncertain.

Objective To investigate association of genetic loci with CRP levels and risk of coronary heart disease.

Design, Setting, and Participants We first carried out a genome-wide association (n=17 967) and replication study (n=13 615) to identify genetic loci associated with plasma CRP concentrations. Data collection took place between 1989 and 2008 and genotyping between 2003 and 2008. We carried out a mendelian randomization study of the most closely associated single-nucleotide polymorphism (SNP) in the *CRP* locus and published data on other *CRP* variants involving a total of 28 112 cases and 100 823 controls, to investigate the association of *CRP* variants with coronary heart disease. We compared our finding with that predicted from meta-analysis of observational studies of CRP levels and risk of coronary heart disease. For the other loci associated with CRP levels, we selected the most closely associated SNP for testing against coronary heart disease among 14 365 cases and 32 069 controls.

Main Outcome Measure Risk of coronary heart disease.

Results Polymorphisms in 5 genetic loci were strongly associated with CRP levels (% difference per minor allele): SNP rs6700896 in *LEPR* (−14.8%; 95% confidence interval [CI], −17.6% to −12.0%; $P=6.2\times10^{-22}$), rs4537545 in *IL6R* (−11.5%; 95% CI, −14.4% to −8.5%; $P=1.3\times10^{-12}$), rs7553007 in the *CRP* locus (−20.7%; 95% CI, −23.4% to −17.9%; $P=1.3\times10^{-38}$), rs1183910 in *HNF1A* (−13.8%; 95% CI, −16.6% to −10.9%; $P=1.9\times10^{-18}$), and rs4420638 in *APOE-CI-CII* (−21.8%; 95% CI, −25.3% to −18.1%; $P=8.1\times10^{-26}$). Association of SNP rs7553007 in the *CRP* locus with coronary heart disease gave an odds ratio (OR) of 0.98 (95% CI, 0.94 to 1.01) per 20% lower CRP level. Our mendelian randomization study of variants in the *CRP* locus showed no association with coronary heart disease: OR, 1.00; 95% CI, 0.97 to 1.02; per 20% lower CRP level, compared with OR, 0.94; 95% CI, 0.94 to 0.95; predicted from meta-analysis of the observational studies of CRP levels and coronary heart disease (z score, −3.45; $P<.001$). SNPs rs6700896 in *LEPR* (OR, 1.06; 95% CI, 1.02 to 1.09; per minor allele), rs4537545 in *IL6R* (OR, 0.94; 95% CI, 0.91 to 0.97), and rs4420638 in the *APOE-CI-CII* cluster (OR, 1.16; 95% CI, 1.12 to 1.21) were all associated with risk of coronary heart disease.

Conclusion The lack of concordance between the effect on coronary heart disease risk of *CRP* genotypes and CRP levels argues against a causal association of CRP with coronary heart disease.

JAMA. 2009;302(1):37-48 www.jama.com

***JAMA* 2009**

Genomewide Association Analysis of Coronary Artery Disease

N Engl J Med. 2007

Nilesh J. Samani, F.Med.Sci., Jeanette Erdmann, Ph.D., Alistair S. Hall, F.R.C.P., Christian Hengstenberg, M.D., Ma
Thomas Meitinger, M.D.,
Ph.D., Inke R. König, Ph
Alexandre Tregouet, Ph.
M.Sc., Wolfgang Lieb, M
Ouwehand, F.R.C.Path.,
Baessler, M.D., Stephen
Gieger, Ph.D., Panos De
John R. Thompson, Ph.D
*for the WTCCC and the C

Six new loci associated with blood low-density lipoprotein cholesterol, high-density lipoprotein cholesterol or triglycerides in humans

Nat. Genet. 2008

Sekar Kathiresan[1–3], Olle Melander[4], Candace Guiducci[2], Aarti Surti[2], Noël P Burtt[2], Mark J Rieder[5], Gregory M Cooper[5], Charlotta Roos[6], Benjamin F Voight[2,7,8], Aki S Havulinna[9], Björn Wahlstrand[10], Thomas Hedner[10], Dolores Corella[11], E Shyong Tai[12], Jose M Ordovas[13], Göran Berglund[14], Erkki Vartiainen[9], Pekka Jousilahti[9], Bo Hedblad[15], Marja-Riitta Taskinen[16], Christopher Newton-Cheh[1–3], Veikko Salomaa[9], Leena Peltonen[2,9,17,18], Leif Groop[6,19], David M Altshuler[2,3,7,8,20] & Marju Orho-Melander[6]

Abstract

BACKGROUND—Mc
components of complex
studies of coronary arte

METHODS—We first
artery disease in the We
1926 case subjects with
German MI [Myocardia
myocardial infarction a
that were significantly a
combined to identify ad
studies was performed v

RESULTS—Of thousa
with coronary artery dis
rs1333049) (P=1.80×10

Blood concentrations of lipoproteins and lipids are heritable[1] risk factors for cardiovascular disease[2,3]. Using genome-wide association data from three studies (n = 8,816 that included 2,758 individuals from the Diabetes Genetics Initiative specific to the current paper as well as 1,874 individuals from the FUSION study of type 2 diabetes and 4,184 individuals from the SardiNIA study of aging-associated variables reported in a companion paper in this issue[4]) and targeted replication association analyses in up to 18,554 independent participants, we show that common SNPs at 18 loci are reproducibly associated with concentrations of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and/or triglycerides. Six of these loci are new ($P < 5 \times 10^{-8}$ for each new locus). Of the six newly identified chromosomal regions, two were associated with LDL cholesterol (1p13 near *CELSR2*, *PSRC1* and *SORT1* and 19p13 near *CILP2* and *PBX4*), one with HDL cholesterol (1q42 in *GALNT2*) and five with triglycerides (7q11 near *TBL2* and *MLXIPL*, 8q24 near *TRIB1*, 1q42 in *GALNT2*, 19p13 near *CILP2* and *PBX4* and 1p31 near *ANGPTL3*). At 1p13, the LDL-associated SNP was also strongly correlated with *CELSR2*, *PSRC1*, and *SORT1* transcript levels in human liver, and a proxy for this SNP was recently shown to affect risk for coronary artery disease[5]. Understanding the molecular, cellular and clinical consequences of the newly identified loci may inform therapy and clinical care.

We recently conducted the Diabetes Genetics Initiative (DGI) genome-wide association study for type 2 diabetes and 18 other traits, including blood lipoprotein and lipid concentrations[6]. Here, we focus on replication analyses related to three traits—concentrations of LDL cholesterol, HDL cholesterol and triglycerides. In DGI, we analyzed the association of 389,878 markers with blood lipoproteins and lipids in 2,758 individuals. From these results, we selected an initial 196 SNPs for replication on the basis of the strength of statistical evidence. We then combined the DGI results with those from two other genome-wide association studies—the Finland–United States Investigation of NIDDM Genetics (FUSION) and the SardiNIA Study of Aging (see companion manuscript for meta-analytic methods[4])—and selected an additional 30 SNPs for replication on the basis of the combined evidence (see **Supplementary Fig. 1** online for study design). The 226 SNPs selected for replication were tested in up to 18,554 separate participants from three studies, (**Table 1**). Statistical evidence from the DGI

Most loci with associations with CAD have been confirmed primarily in large European populations

In Asian Populations,

• New associations of ***BRAP*** variants with myocardial infarction at 12q24.12 in Japanese populations Ozaki K *et al. Nat.Genet* 2009

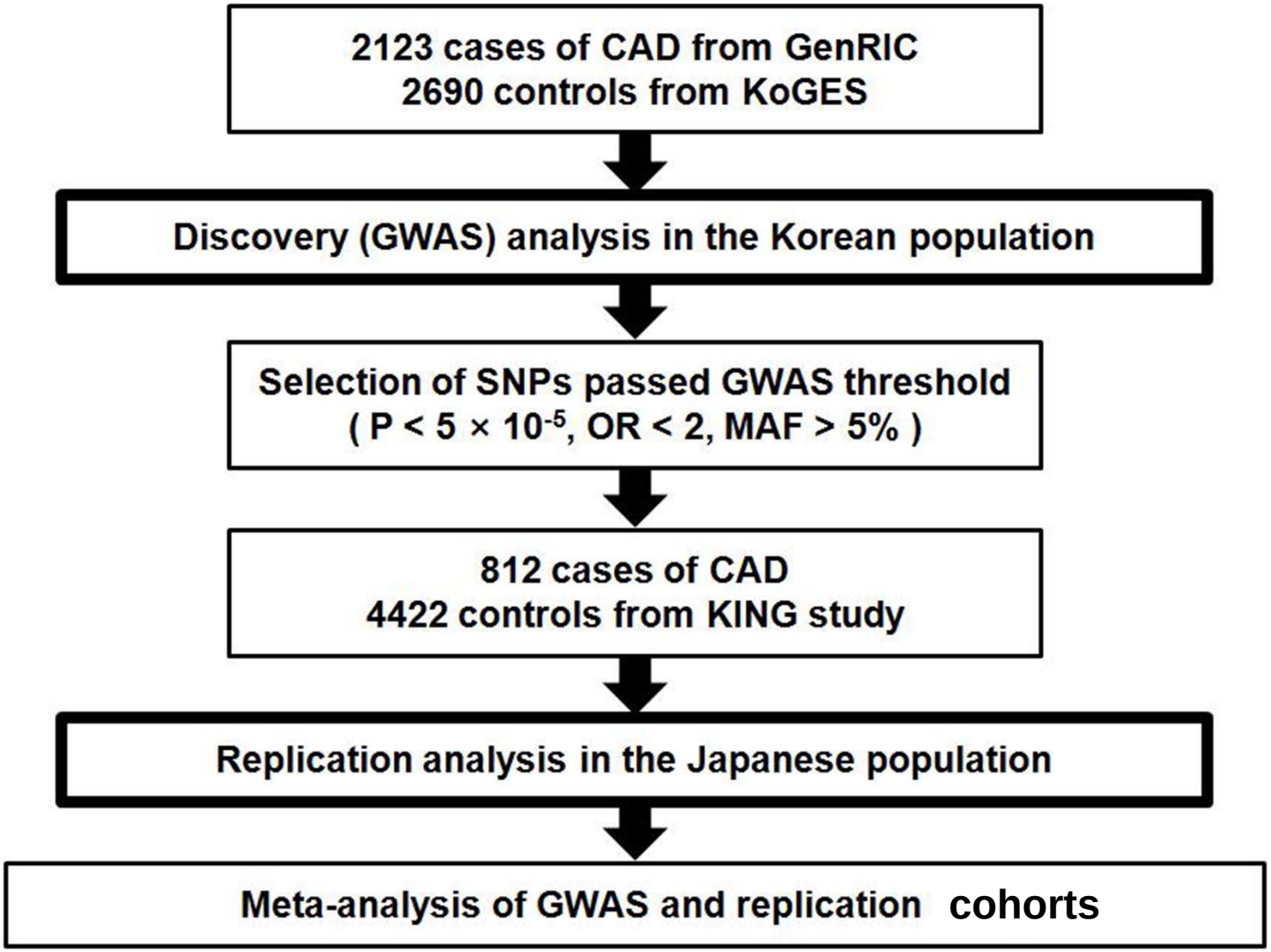
• Replication for associations of ***BRAP*** variants Hinohara K *et al. J Hum Genet*. 2009

• Replication for associations of variants at **9p21.3** in Chinese, Japanese and Korean populations Ding *H et al. Circ Cardiovasc Genet*. 2009 ,
•Hinohara K et al. J Hum Genet. 2008

• Replication for associations of ***MIA3*** variants at 1q41 in Japanese Hiura Y *et al Circ J.* 2008

Genome-wide association study of CAD in East Asian populations

Schematic Overview of CAD GWAS



Samples in The Discovery Stage

- Cases with coronary artery disease
  - Samples were collected by **GenRIC Working Group**
    - Samsung Medical Center
    - Seoul National University Hospital
    - Yonsei University College of Medicine, Seoul, Korea

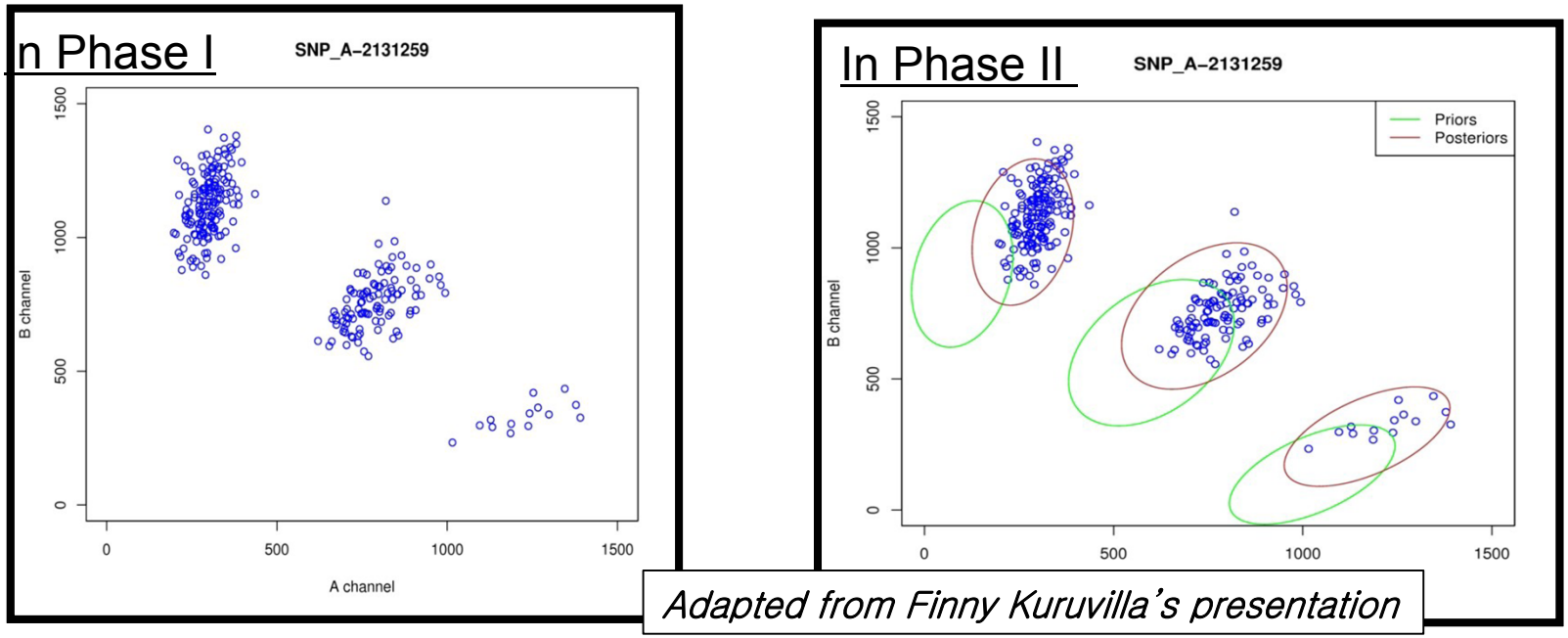
  - Age of men and women was younger than 55 and 65, respectively
  - Collected Between 2005 and 2009

- Controls
  - Samples recruited from a large urban cohort, part of the **Korea Genome Epidemiology Study (KoGES)**
    - KoGES is an ongoing cohort study in Korea that started in 2001
    - Samples of urban cohorts were collected in centers of Seoul and Busan for health examination

  - Age of men and women was older than 40

Genotype for Discovery Stage

- Samples
  - **2,317 cases** with **stable angina**, **unstable angina** and **myocardial infarction** from 3 hospitals
  - **4,302 controls** from urban cohort
- Platform
  - Affymetrix Genome-Wide Human SNP Array 6.0
- genotyping algorithm
  - **Birdseed** is a new tool to genotype SNPs on the Affymetrix SNP 6.0 arrays (Downloaded from "**Affymetrix Power Tools**")



Adapted from Finny Kuruvilla's presentation

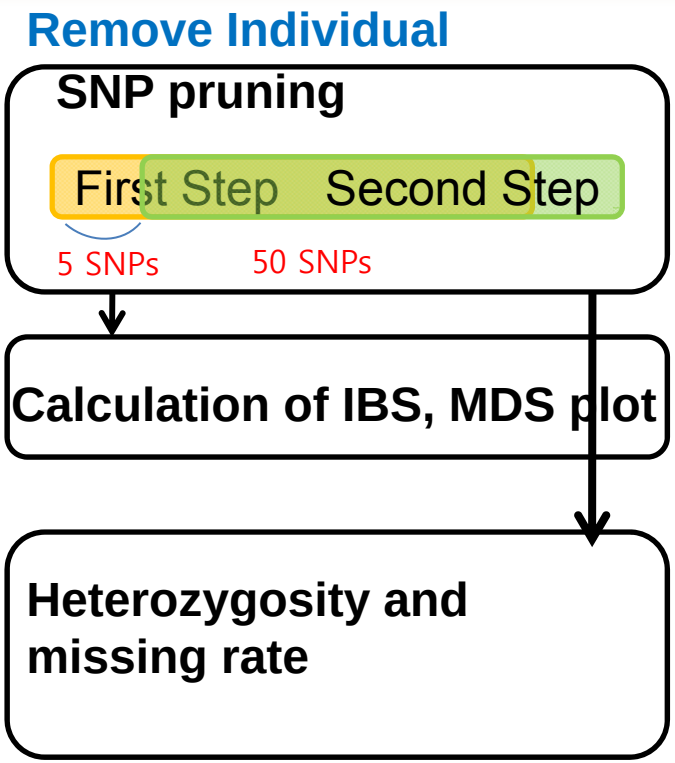
Quality Control Procedure

Sample quality control

	Case	Control
At beginning	**2,317**	**4,302**
Gender discrepancy	-28	-8
Low call rate >= 95 %	-108	-443
Excessive heterozygosity	-51	-25
Cryptic first degree relative	-9	-33
outlier (MDS)	-3	-26
Cancer history		-64
After filtering	**2,123**	**3,703**

SNP quality control

	Case	Control
At beginning	**909,622**	**909,622**
Minor allele frequency	-175,249	-112,231
Missing rate	-97,776	-170,631
Hardy-weinberg		-39,456
After filtering	**644,502**	**627,659**



Samples and SNPs quality control

- **Case** : At beginning 2,317 samples and 909,622 SNPs
  after filtering 2,123 samples and 644,502 SNPs
- **Control** : At beginning 4,304 samples and 909,622 SNPs
  after filtering 3,703 samples and 627,659 SNPs

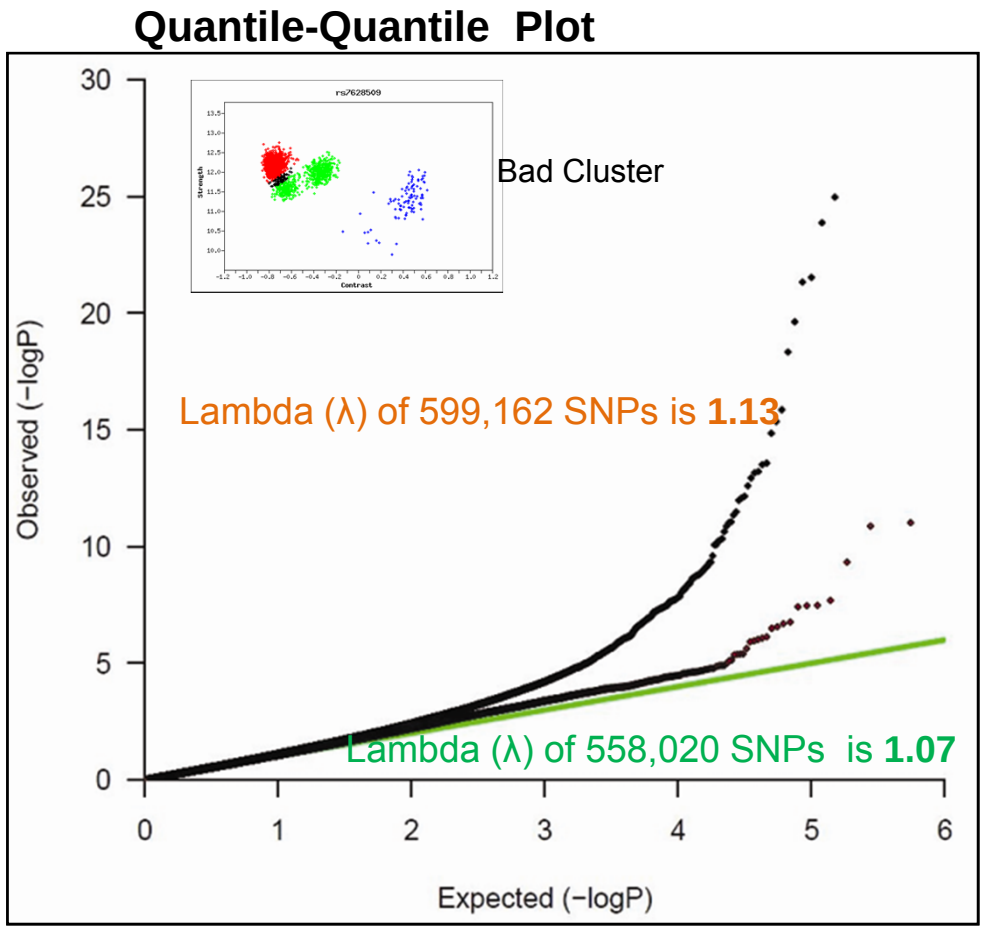
Association Analysis

• The logistic regression with adjust ment for age, gender under additive model

• 599,162 SNPs in **2,123 cases** (in men < 55 y old and in women < 65 y old) and **2,690 gender-matched controls** among 3,703 subjects pa ssed by quality control criteria

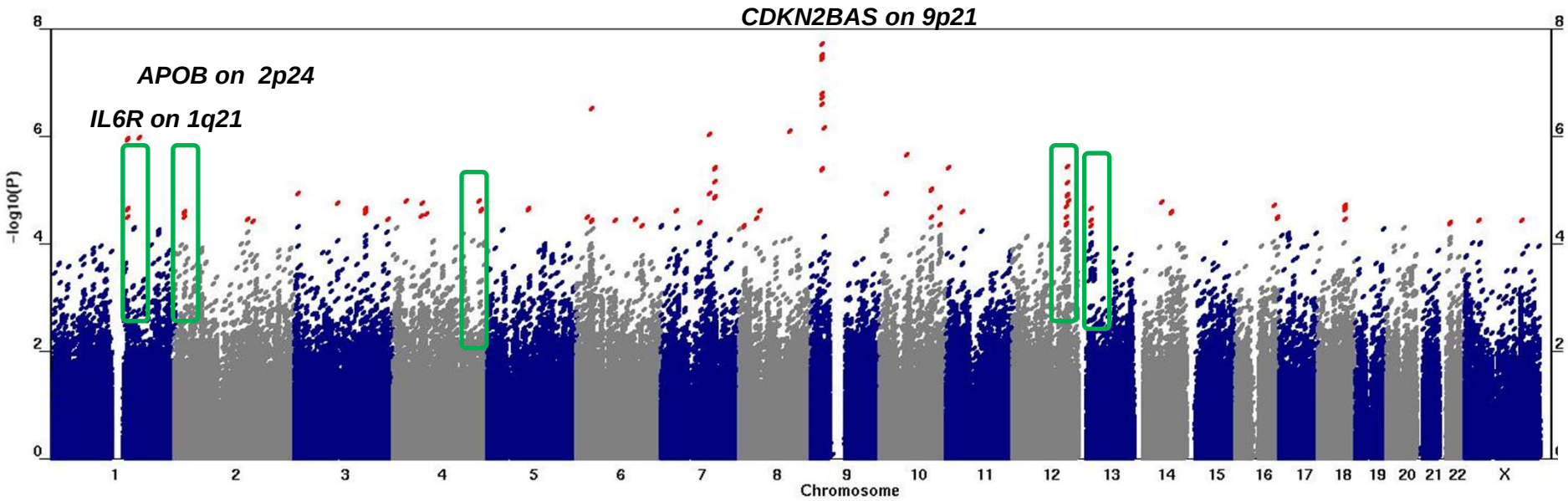
• To reduce inflation generated by confounding effects, remove with SNPs,

- Different missing proportions in cases and controls
  - -- Case missing rate >1% or control missing rate >1%,
  - -- Missing P<5X10-5
- Or with ambiguous cluster plots



Association Results

For the 558,020 markers in 2,123 cases and 2,690 gender-matched controls from discovery stage



SNP selection for replication

Loci replicated with $P < 0.05$

- 62 SNPs with $P < 5 \times 10^{-5}$
- Lead 36 SNPs with lowest *P* value in Linkage Disequilibrium(LD) block
- **18 loci** were selected for replication test in the Japanese population
  - P < 5 X 10-5, Minor allele frequency > 5%, OR < 2,
  - Robust cluster plot
  - supporting evidence for association in LD block

Replication Stage

- Subjects
  - The samples of cases and controls were collected from from KING (KItaNagoya Genome) study
  - Age of men and women is younger than 80
  - Between May 2005 and December 2007

- Genotype of subjects in cases and controls
  -18 SNPs were genotyped in **812 cases** and **4,422 gender-matched controls** (in men < 55 y old and in women < 65 y old) using TaqMan® SNP genotyping assays

Previously published loci associated with CAD

SNP	Gene	Chromosome	Risk Allele	Risk Allele Freq.	OR
rs9818870	*MRAS*	3q22.3	T	17.3	1.15
Hap	*SLC22A3, LPAL2,LPA*	6q25.3		0.02	1.82
rs646776	***CELSR2, PSRC1, SORT1***	**1p13.3**	**T**	**0.81**	**1.19**
rs11206510	*PCSK9*	1p32.3	T	0.81	1.15
rs17465637	*MIA3*	1q41	C	0.72	1.14
rs6725887	*WDR12*	2q33.1	C	0.14	1.17
rs12526453	*PHACTR1*	6p24.1	C	0.65	1.12
rs4977574	***CDKN2A, CDKN2B***	**9p21.3**	**G**	**0.56**	**1.29**
rs1746048	*CXCL12*	10q11.21	C	0.84	1.17
rs11066001	*BRAP*	12q24.12	G	0.34	1.47
rs1122608	*LDLR*	19p13.2	G	0.75	1.15
rs9982601	*SLC5A3, MRPS6, KCNE2*	21q22.11	T	0.13	1.2

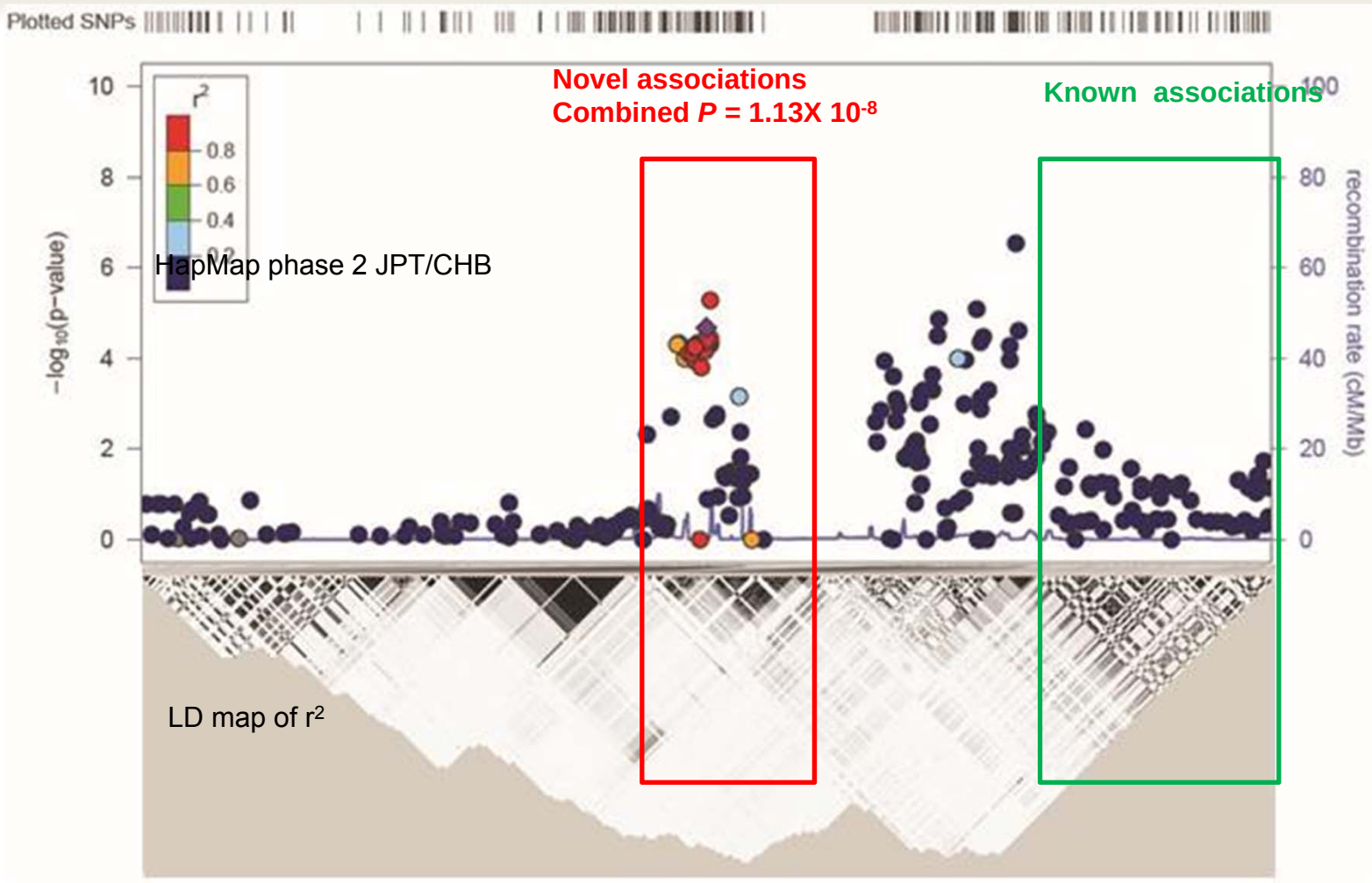
SNPs with *P* value < 5×10^{-8}

Dan E. Arking and Aravinda Chakravarti, *Trends in Genetics* 2009

Results of a meta-analysis for SNPs identified from both the GWAS and the replication cohorts

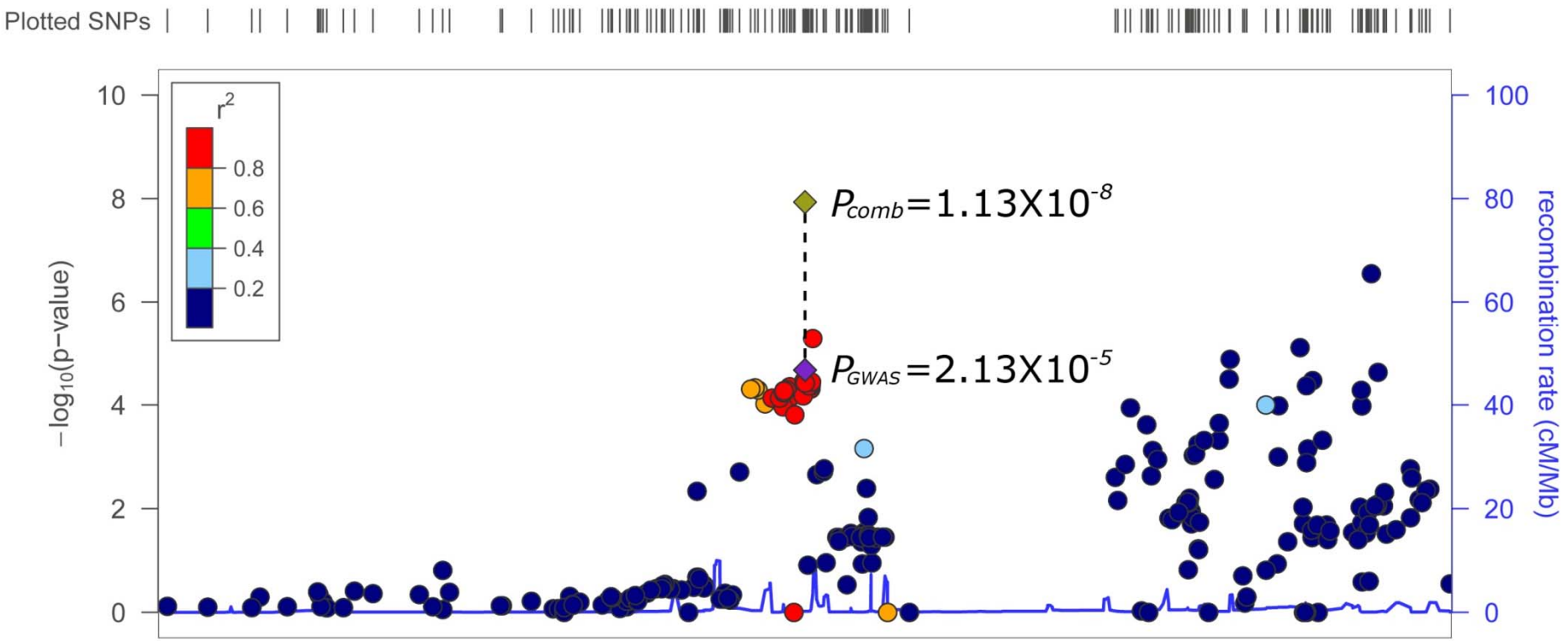
				GWAS - Korea				Replication - Japan				Combined analysis		
SNP	Chromosome	Gene	Func	Allele	N	OR	P	Allele	N	OR	P	OR	p	het.(*P*)
Previous publications														
rs4537545	**1q21.3e**	***IL6R***	**i**	**T**	**4735**	**0.8356**	**2.39E-05**	**T**	**5234**	**0.8936**	**0.04297**	**0.8659**	**4.74E-05**	**0.3376**
rs7588415	**2p24.1c**	***APOB***		**A**	**4778**	**0.7578**	**2.74E-05**	**A**	**5233**	**0.8232**	**0.02587**	**0.7914**	**2.47E-05**	**0.4498**
New identified loci														
rs1111782	9p21.2a	*TEK*	i	A	4716	0.8101	7.32E-07	T	5234	0.952	0.3684	0.8816	3.46E-04	0.0198
rs12114277	8q22.3b	*UBR5*	i	A	4674	0.8082	8.43E-07	A	5233	1.016	0.764	0.912	8.70E-03	9.00E-04
rs219822	7q22.1a	*TRRAP*	i	A	4783	1.229	9.64E-07	A	5232	1.068	0.2277	1.1422	1.35E-04	4.12E-02
rs12705702	7q31.1b			T	4781	0.8263	4.17E-06	G	5232	1.039	0.4792	0.9314	4.06E-02	8.00E-04
rs1163072	10q24.33			T	4780	1.203	1.04E-05	G	5231	1.051	0.3571	1.1208	9.86E-04	0.0487
rs41391154	3p26.1a	*GRM7*	i	T	4775	0.7166	1.24E-05	T	5233	0.9898	0.9076	0.8487	5.05E-03	0.0055
rs886126	12q24.11d	*CUX2*	i	C	4756	0.8244	1.31E-05	C	5232	0.9654	5.45E-01	0.8958	2.92E-03	0.0309
rs10012505	4q34.1b	*GALNT17*	i	G	4662	0.7661	1.67E-05	C	5233	0.9422	0.4594	0.8547	2.35E-03	0.0416
rs2122149	4q13.1a			A	4674	1.277	1.87E-05	A	5231	1.03	0.6516	1.14	2.96E-03	0.0138
rs9944810	18q21.31	*ALPK2*	cn	C	4783	0.8326	2.08E-05	C	5234	0.9488	0.3364	0.8914	1.09E-03	0.0603
SNP2	**12**	***gene2***	**i**	**C**	**4762**	**1.255**	**2.13E-05**	**G**	**5232**	**1.262**	**9.85E-05**	**1.2586**	**1.13E-08**	**0.9446**
rs17101534	10q26.12b			C	4780	0.8218	2.26E-05	C	5232	0.9621	0.5224	0.8923	3.13E-03	0.0384
rs2068230	3q23c	*ATP1B3*	i	A	4759	0.834	2.33E-05	T	5231	0.9775	0.6776	0.9063	5.25E-03	0.0226
SNP3	**13**	***gene3***	**i**	**C**	**4789**	**1.192**	**2.34E-05**	**G**	**5231**	**1.148**	**1.09E-02**	**1.1688**	**6.35E-06**	**0.5817**
SNP4	**4**	***gene4***	**i**	**G**	**4781**	**1.187**	**3.27E-05**	**C**	**5233**	**1.116**	**0.04156**	**1.1491**	**4.91E-05**	**0.3625**
rs9368386	6p22.3b			T	4779	0.7383	3.33E-05	T	5232	0.9921	0.928	0.8616	9.85E-03	0.0098

Novel association at 12q24 confirmed in the present study

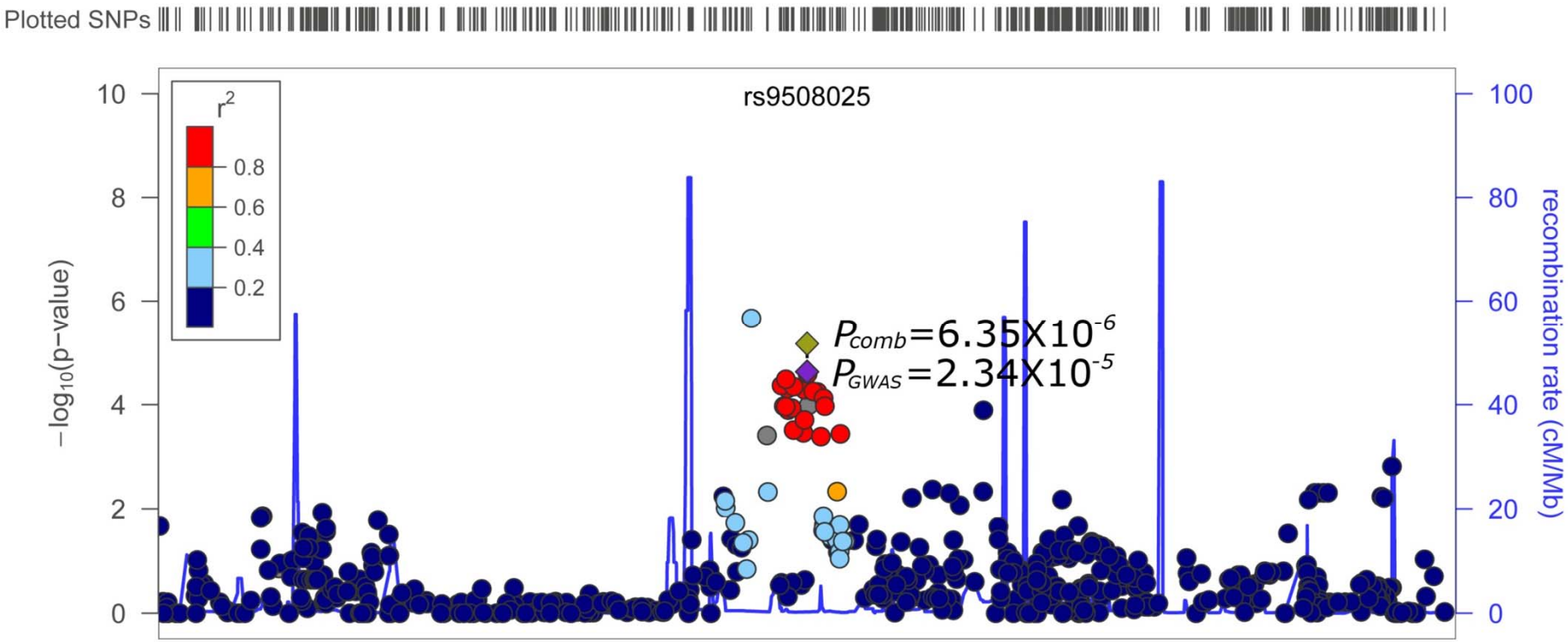


Novel locus is about 700kb apart from known locus

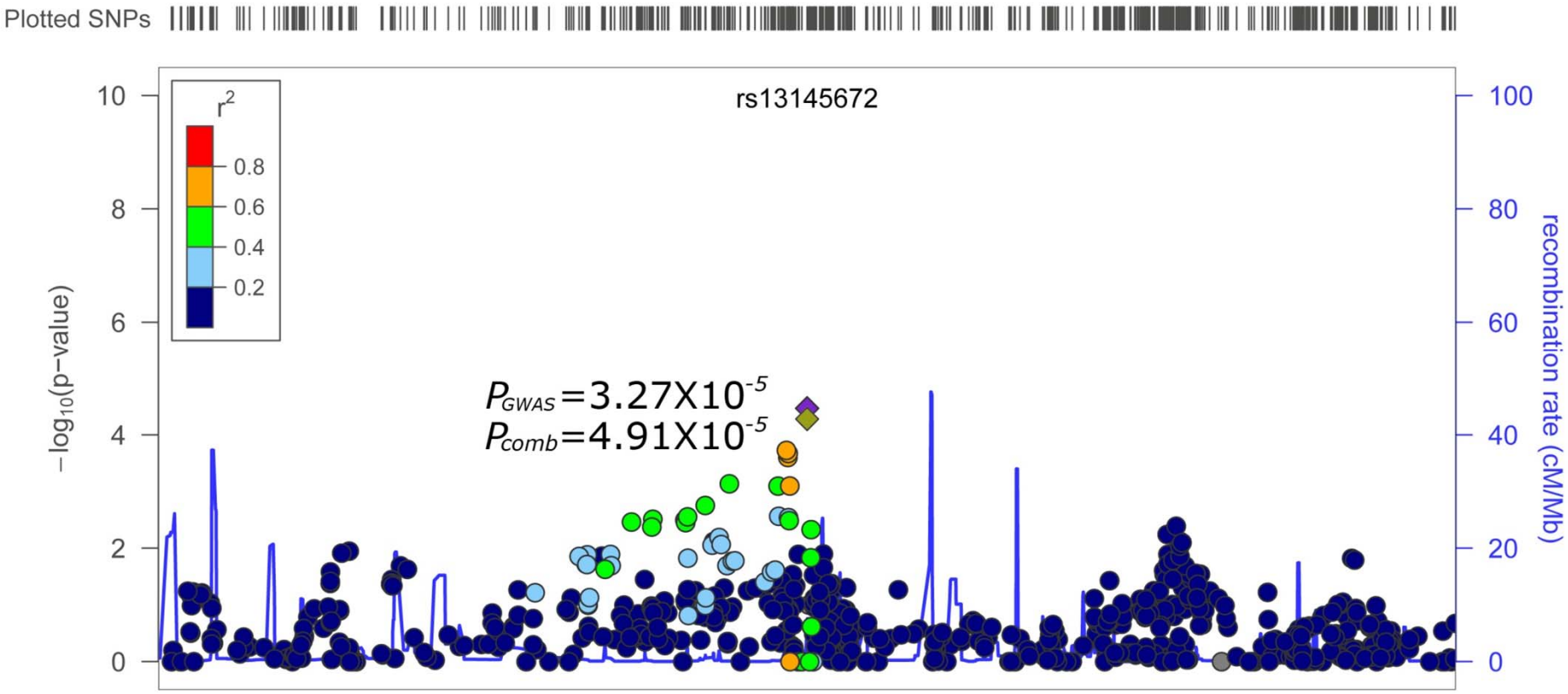
Signal plot at chromosome 12



Signal plot at chromosome 13



Signal plot at chromosome 4



Summary and Future Works

• We undertook a GWAS in large Korean population followed by replication studies in an independent Japanese population to discover novel susceptibility loci associated with CAD in East Asian populations

• We identified One new susceptibility locus on 12q24.11 supported by compelling statistical evidence, together with two additional statistically significant loci on 13q12.3 and 4q12.

• Meta-analysis and replication should be required to discover more novel risk genetic factors for CAD in different large-scale populations.

• Fine mapping will be conducted to detect some novel loci and functional rare variants that have been missed completely.

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감사합니다!