International Clopidogrel Pharmacogenomics Consortium Genome Wide Association Study

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RIKEN Center for Integrative Medical Sciences

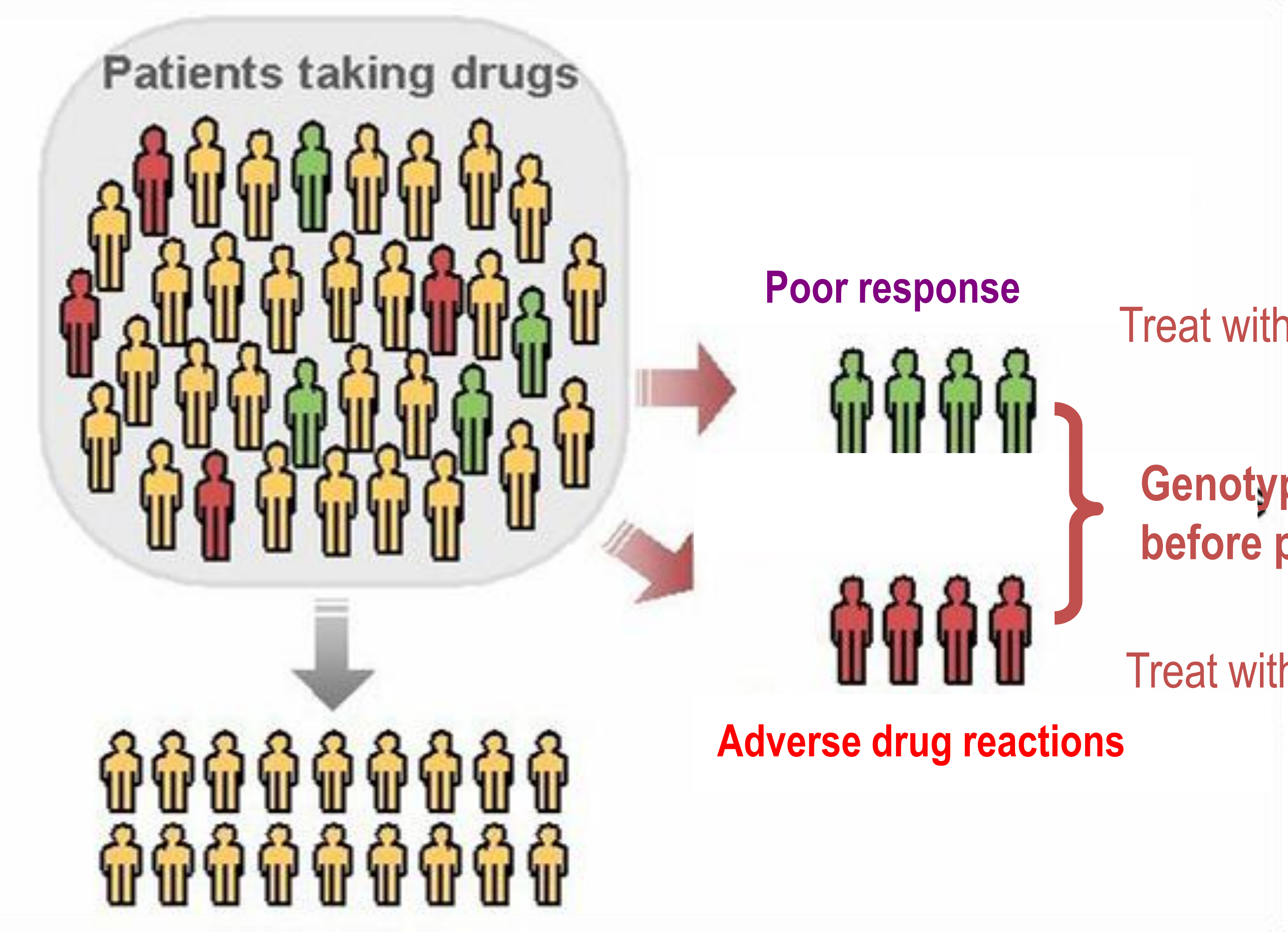
On behalf of

The International Clopidogrel Pharmacogenomics Consortium

The faces associated with one person's DNA sample

Lego

Pharmacogenomics



Poor response

Treat with alternative dose

Genotyping before prescribing

Treat with alternative drug

Adverse drug reactions

Annu. Rev. Genomics
Hum. Genet. 2001

Human Genome

↓

Sequence Variations

↓

1. **Restriction Fragment Length Polymorphism (RFLP)**
2. **Variable Number of Tandem Repeat (VNTR)**
3. **Short Tandem Repeat Polymorphism (STRP)**
4. **Single Nucleotide Polymorphism (SNP)**
5. **Copy Number Variation**

SNP

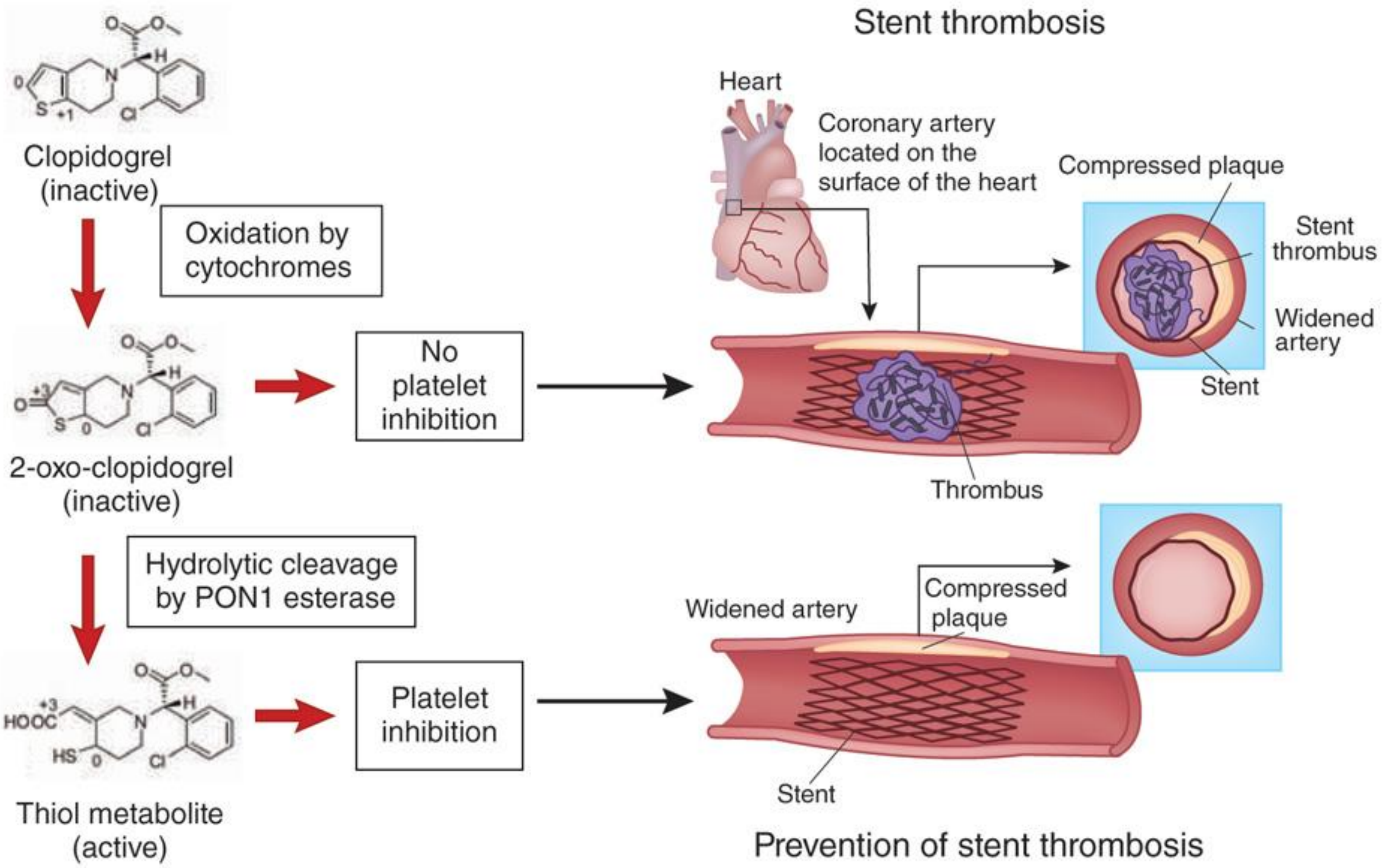
Example order of bases in a section of DNA on a chromosome:

...C C **A** T T G A C...
…G G **T** A A C T G…

...C C **G** T T G A C...
…G G **C** A A C T G…

Some people have a different base at a given location

International Clopidogrel Pharmacogenomics Consortium (ICPC)



Clopidogrel (inactive)

Oxidation by cytochromes

2-oxo-clopidogrel (inactive)

No platelet inhibition

Hydrolytic cleavage by PON1 esterase

Thiol metabolite (active)

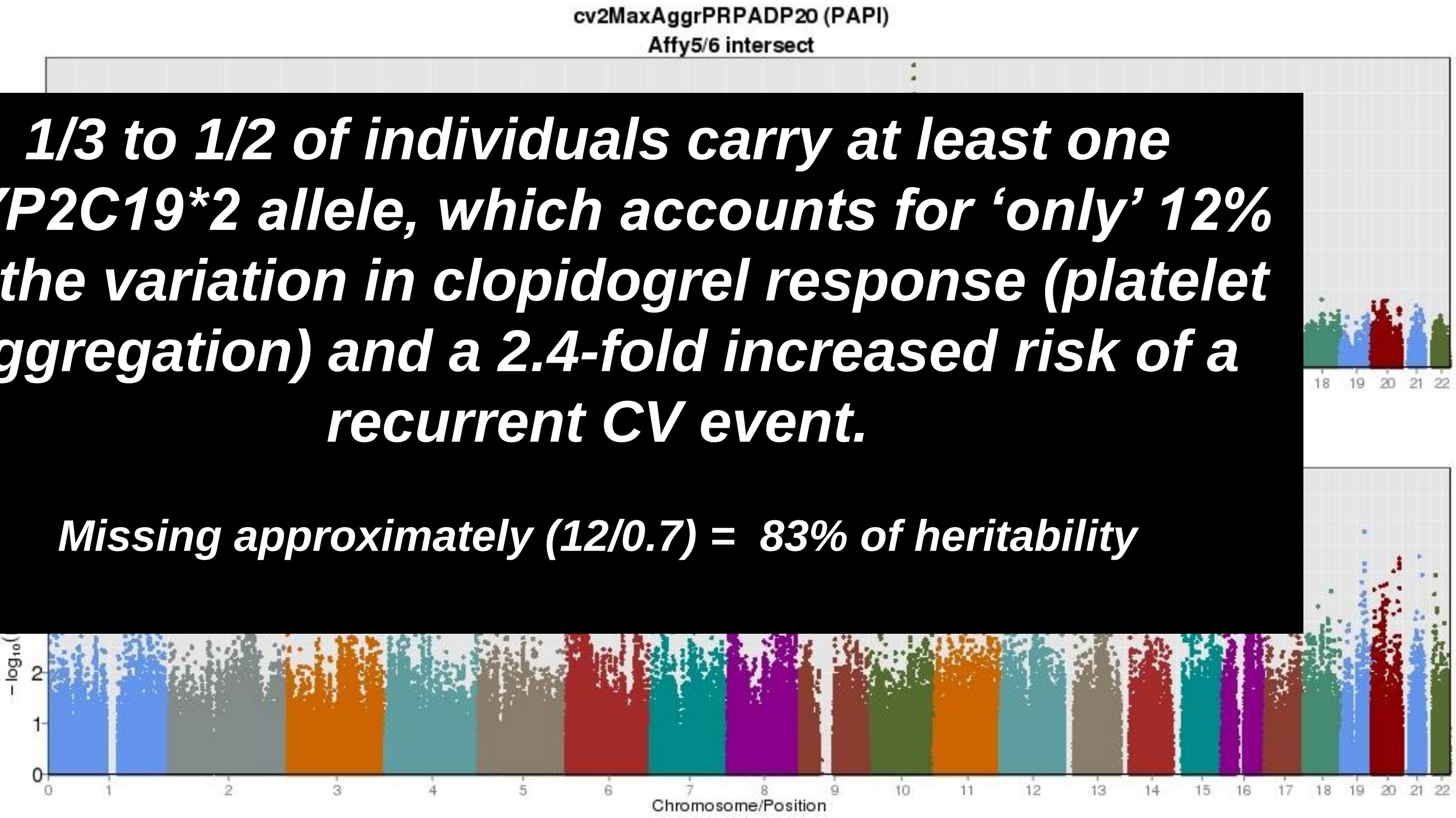
Platelet inhibition

Stent thrombosis

Prevention of stent thrombosis

Clopidogrel Response GWAS:
PAPI Study
(n=660)

Clopidog



1/3 to 1/2 of individuals carry at least one CYP2C19*2 allele, which accounts for 'only' 12% of the variation in clopidogrel response (platelet aggregation) and a 2.4-fold increased risk of a recurrent CV event.

Missing approximately (12/0.7) = 83% of heritability

Clopidog
(adjusted fo
CYP2C19*2)

International Clopidogrel Pharmacogenomics Consortium (ICPC)

- Identify novel genetic determinants of clopidogrel response harnessing the power of large sample size, well-characterized clopidogrel-exposed subjects, and genome-wide approaches
  - GWAS
- *CYP2C19*
  - Gene dose effects
  - Other predictors and interactions (stratified and regression analyses including sex, age, smoking, indication, PPI use, etc.
  - Other *CYP2C19* variants?
- Probe deeper into less well-documented candidate genes (*ABCB1*, *CYP2B6*, *PON1*, *CES1*, *P2Y21*, others)
- DAPT/Aspirin response

ICPC Organization

- Overall coordination
    - University of Maryland (Shuldiner et al.)
    - PharmGKB (Klein/Gong)
- Committees
    - Coordinating committee
    - Phenotype committee
- Genotyping – RIKEN (Kubo, Lee)
- Analysis (Marylyn Richie/P-STAR; other sites)

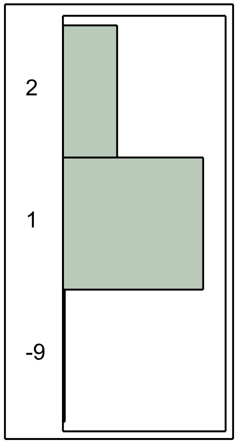
ICPC Status

- 19 Groups Participating in ICPC
  - 12 groups for GWAS phase (n=2734 + 678 PAPI)
- DNA (at UMD)
  - 6280 samples
- Phenotype deposits
  - 8829 subjects
- Additional 5+ groups for replication
  - G. Pare, et al.
    - [CURE (n=2549); ACTIVE (n=570)]
  - J. Mega, et al. [ELEVATE-TIMI (n=293)]
  - Roden, et al. [BioVU (n=199)]
  - J. ten Berg, et al. (n=1024)
  - D. Trenk, et al. [Excelsior (n=556)]
  - Others

ICPC Characteristics

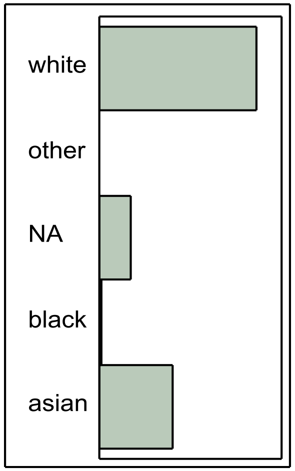
(n=8829)

Gender



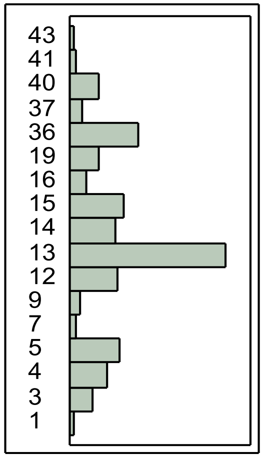
Level	Count	Prob
-9	77	0.00872
1	6291	0.71254
2	2461	0.27874
Total	8829	1.00000

Race_OMB



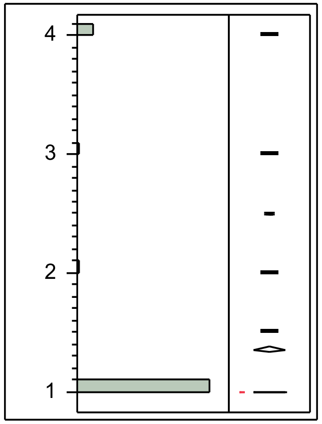
Level	Count	Prob
Asian	2457	0.27829
Black	77	0.00872
NA	1045	0.11836
other	5	0.00057
White	5245	0.59407
Total	8829	1.00000

Site



Level	Count	Prob
1	50	0.00566
3	325	0.03681
4	538	0.06094
5	736	0.08336
7	106	0.01201
9	160	0.01812
12	693	0.07849
13	2280	0.25824
14	687	0.07781
15	797	0.09027
16	234	0.02650
19	442	0.05006
36	1024	0.11598
37	192	0.02175
40	416	0.04712
41	79	0.00895
43	70	0.00793
Total	8829	1.00000

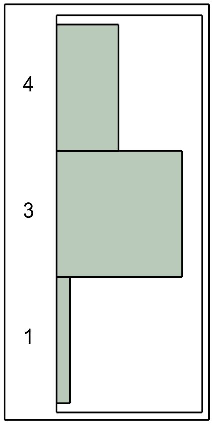
Indication clopidogrel



Mean	1.3541611
Std Dev	0.9370101
Std Err Mean	0.0108211
Upper 95% Mean	1.3753735
Lower 95% Mean	1.3329487
N	7498

1=Coronary artery disease
2=Peripheral arterial disease
3=Ischemic stroke
4=Healthy control

PCI information

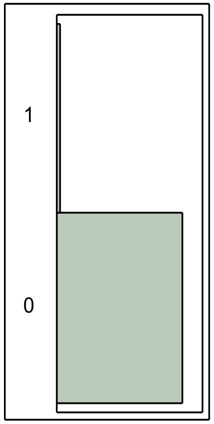


Level	Count	Prob
1	441	0.06734
3	4071	0.62162
4	2037	0.31104
Total	6549	1.00000

1=Stable and no PCI
2=ACS and no PCI
3=Stable and PCI
4= ACS and PCI

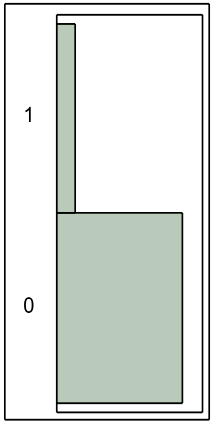
Clinical Phenotypes

All_cause mortality



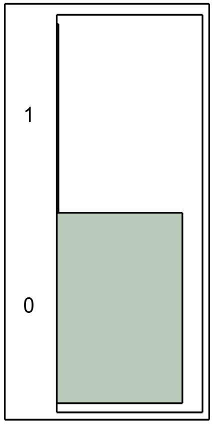
Level	Count	Prob
0	7689	0.97341
1	210	0.02659
Total	7899	1.00000

CV_events



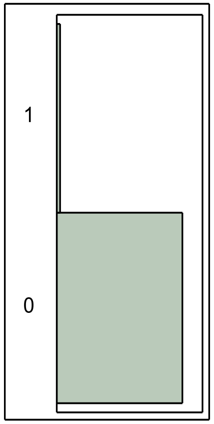
Level	Count	Prob
0	6318	0.86738
1	966	0.13262
Total	7284	1.00000

Major bleeding



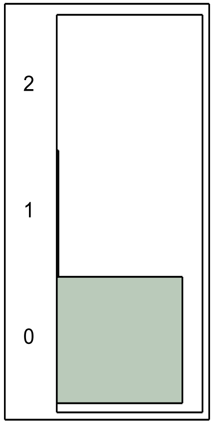
Level	Count	Prob
0	6789	0.98520
1	102	0.01480
Total	6891	1.00000

Minor bleeding



Level	Count	Prob
0	5366	0.97069
1	162	0.02931
Total	5528	1.00000

Stent thrombosis



Level	Count	Prob
0	7959	0.98563
1	113	0.01399
2	3	0.00037
Total	8075	1.00000

ADP-Stimulated Platelet Aggregation

- 31 Different ADP platelet aggregation traits across the 19 studies

Project Site (F)	Total sample size with 1 or more ADP platelet aggregation traits	Verify Now ADP stimulated	PFA ADP/Collagen closure time	PAP-8 PRP ADP 5 µM	Chronolog whole blood ADP 20 µM	VASP	Multiplate ADP test	CARAT TX4 ADP 5uM AGGlate
1	50	44	0	0	0	0	0	0
12	693	0	0	0	0	0	0	693
13	2280	279	0	0	92	0	0	0
14	687	0	668	669	669	0	0	0
15	797	0	0	760	0	0	0	0
16	234	234	0	0	0	0	0	234
19	442	0	0	0	0	0	100	0
3	325	0	0	325	0	325	0	0
36	1024	874	535	618	0	0	0	0
37	192	0	0	0	0	0	0	192
4	538	0	0	535	0	536	0	0
40	416	0	415	0	0	408	0	0
41	79	0	0	64	0	0	0	0
43	70	0	0	0	0	0	0	0
5	736	0	0	0	0	0	0	0
7	106	0	0	0	0	0	106	0
9	160	160	0	0	0	0	0	0
Totals	**8829**	**1591**	**1618**	**2971**	**761**	**1269**	**206**	**111**

Harmonization of ICPC Platelet Function Data

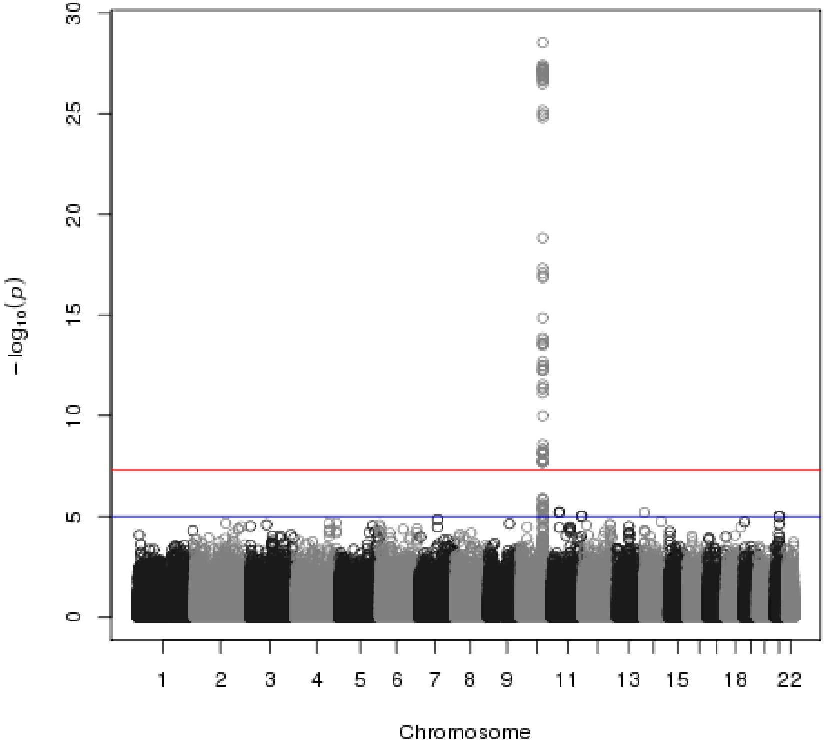
- Platelet function phenotype priorities based on:
  - Preliminary analyses of *CYP2C19**2
  - Knowledge of platelet function traits (pathways, reproducibility, etc.)
    - VASP > VerifyNow > PAP8/Multiplate
- Compared standardized mean difference (SMD) to a standardized phenotype by platform and site
  - Results are highly comparable
  - SMD is a more computationally intensive method

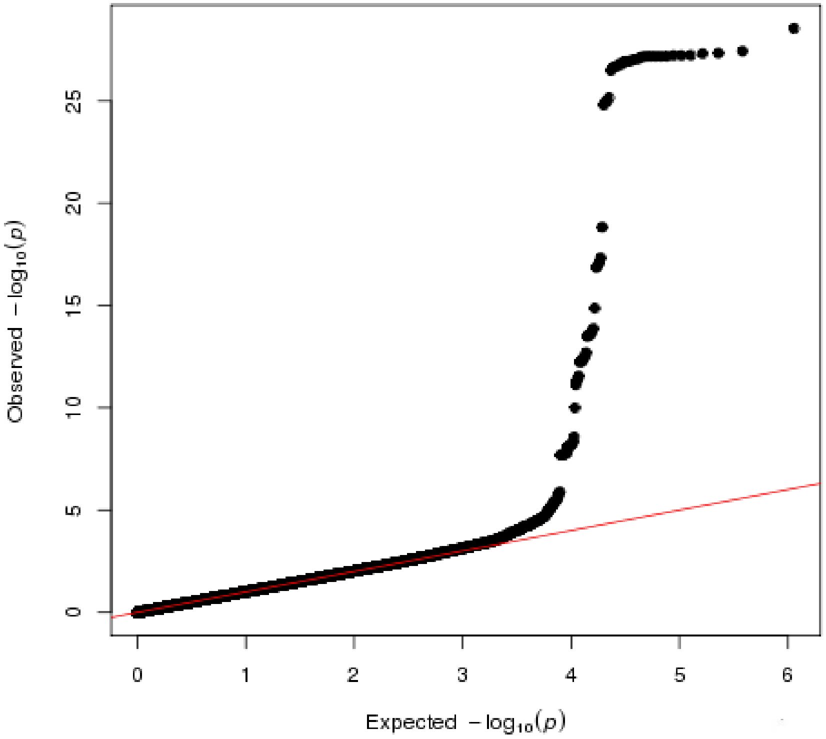
ICPC GWAS Genotype Data (RIKEN)

- 2781 samples (all Caucasian with at least 1 platelet aggregation trait and CV outcomes)
  - 2074 males
  - 647 females
  - 2721 are unique and 60 are duplicates
- Platform = Illumina Omni Express with Exome (OEE)
  - 964,193 markers (717,214 map to dbSNP plus exome coverage)
  - QC measures
    - Sex checks (Dropped 29 samples)
    - Call rates >99% all samples
    - H-W equilibrium (flagged, not dropped)
    - PC analysis
  - Imputation to 1,000 genomes

First-pass GWAS Result (1)

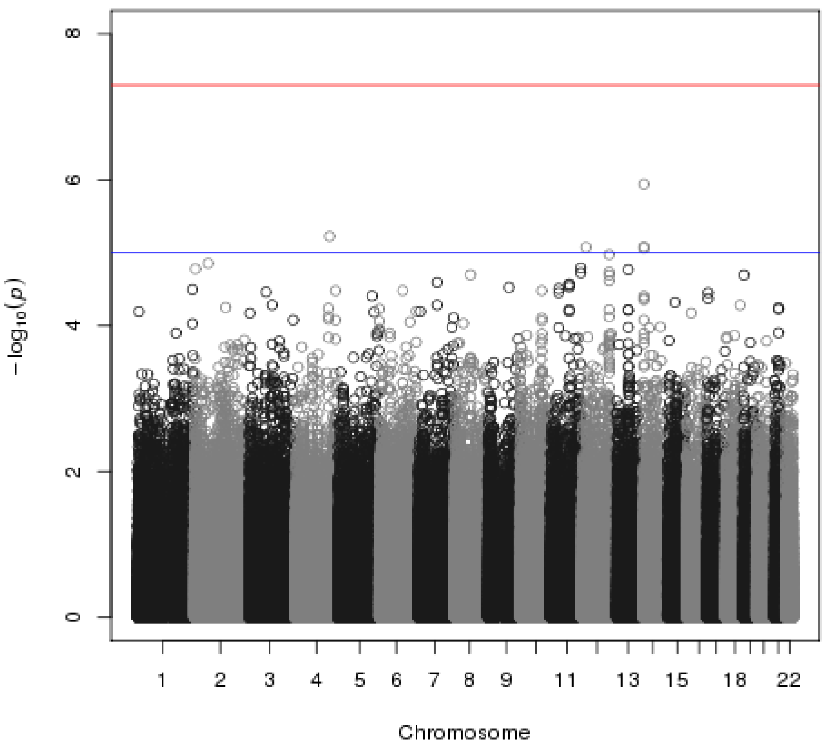
- Standardized phenotypes by site (w/o site 14)
- Linear regression adjusted by Project Site, Sex, Age, PC1, PC2

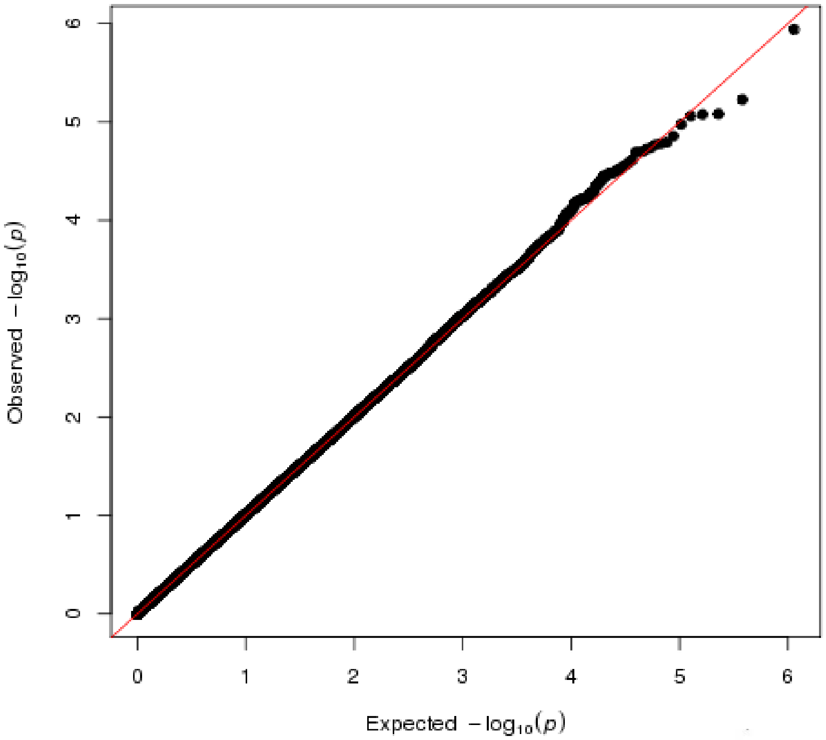




First-pass GWAS Result (2)

- Standardized phenotypes by site (w/o site 14)
- Linear regression adjusted by Project Site, Sex, Age, PC1, PC2 and rs4244285





Top 35 Hits when adjusted for Sex, PCs, Project, rs4244285, and Age

CHR	SNP	BP	Beta	P-Val	In-Gene	Upstream Gene	Downstream Gene
1	RS10864305	7567346	-0.118	6.17E-05	CAMTA1	LOC101928836	VAMP3
1	RS4658825	242726365	0.1126	6.25E-05		PLD5	RSL24D1P4
1	RS2298900	169669020	-0.124	8.09E-05	SELL	SELP	SELE
1	RS6675916	157151523	-0.111	0.0001383		ETV3	LOC101928202
1	RS4233496	45763650	-0.122	0.0001472		ZSWIM5	LINC01144
1	RS945652	244374051	-0.113	0.0001556		LOC440742	C1orf100
2	RS3924400	62694693	-0.144	1.92E-005	TMEM17	LOC101928724	RPL37P13
2	RS2693932	6187107	0.2426	4.56E-05		LOC400940	LINC01247
2	RS13395505	191838514	-0.117	5.24E-05	STAT1	GLS	LOC100420571
2	RS881639	138398906	0.1101	8.59E-05	THSD7B	RNA5SP105	LOC101928273
2	RS10928450	134086271	0.1267	0.0001061	NCKAP5	LOC101928161	MGAT5
2	RS6720388	192604268	-0.114	0.0001103		NABP1	SDPR
2	RS13000695	220703292	-0.172	0.0001122		RPL23P4	LOC101928639
3	RS1214375	100065632	0.123	1.93E-005	NIT2	TBC1D23	TOMM70A
3	RS6797484	73475521	-0.135	2.65E-005	PDZRN3	LOC101927321	LOC101927296
3	RS2399046	105189978	0.124	0.0001167	ALCAM	LOC391562	CBLB
4	RS12651351	153979941	-0.133	1.28E-005		FHDC1	TRIM2
4	RS1017710	180700264	0.2251	4.55E-05		RNA5SP173	LOC100288337
4	RS992556	149269636	-0.11	0.0001334	NR3C2	LOC102724672	LOC101929065
4	RS10050320	31941906	0.1113	0.0001337		LOC102723778	LOC102723828
5	RS919751	149505489	0.1232	3.34E-005	PDGFRB	CSF1R	CDX1
5	RS12513480	159261636	-0.155	5.23E-05	LOC101927766	LOC285627	ADRA1B
5	RS12656368	179653428	-0.112	0.0001202	RPS8P7	RASGEF1C	MAPK9
5	RS4569891	171480055	-0.111	0.0001344	STK10	FBXW11	EFCAB9
6	RS7771614	45975798	0.1144	6.60E-05	CLIC5	RUNX2	ENPP4
6	RS3995732	102603013	0.1129	0.0001171		GRIK2	LOC100996860
6	RS2473479	530459	0.1331	0.0001204	EXOC2	IRF4	HUS1B
6	RS6940101	134740760	0.2206	0.0001207		LOC102723463	LOC101928231
7	RS10954734	83385765	0.1459	1.49E-005		RAD23BP2	SEMA3A
7	RS10278502	148044472	-0.143	8.65E-05	CNTNAP2	RNA5SP249	LOC392145
7	RS657664	129146415	0.1229	9.41E-05	SMKR1	STRIP2	NRF1
7	RS7807731	155755336	0.1103	9.99E-05	LOC389602	SHH	LOC285889
7	RS4725143	8935674	-0.136	0.0001023		NXPH1	RPL9P19
7	RS10231911	154001559	0.1091	0.0001376	DPP6	LOC101929998	PAXIP1OS
8	RS10448034	70588878	-0.148	7.01E-05	SLCO5A1	SULF1	LOC100101127

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1	RS4658825	242726365	0.1126	6.25E-05		PLD5	RSL24D1P4
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1	RS6675916	157151523	-0.111	0.0001383		ETV3	LOC101928202
1	RS4233496	45763650	-0.122	0.0001472		ZSWIM5	LINC01144
1	RS945652	244374051	-0.113	0.0001556		LOC440742	C1orf100
2	RS3924400	62694693	-0.144	1.92E-005	TMEM17	LOC101928724	RPL37P13
2	RS2693932	6187107	0.2426	4.56E-05		LOC400940	LINC01247
2	RS13395505	191838514	-0.117	5.24E-05	STAT1	GLS	LOC100420571
2	RS881639	138398906	0.1101	8.59E-05	THSD7B	RNA5SP105	LOC101928273
2	RS10928450	134086271	0.1267	0.0001061	NCKAP5	LOC101928161	MGAT5
2	RS6720388	192604268	-0.114	0.0001103		NABP1	SDPR
2	RS13000695	220703292	-0.172	0.0001122		RPL23P4	LOC101928639
3	RS1214375	100065632	0.123	1.93E-005	NIT2	TBC1D23	TOMM70A
3	RS6797484	73475521	-0.135	2.65E-005	PDZRN3	LOC101927321	LOC101927296
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4	RS12651351	153979941	-0.133	1.28E-005		FHDC1	TRIM2
4	RS1017710	180700264	0.2251	4.55E-05		RNA5SP173	LOC100288337
4	RS992556	149269636	-0.11	0.0001334	NR3C2	LOC102724672	LOC101929065
4	RS10050320	31941906	0.1113	0.0001337		LOC102723778	LOC102723828
5	RS919751	149505489	0.1232	3.34E-005	PDGFRB	CSF1R	CDX1
5	RS12513480	159261636	-0.155	5.23E-05	LOC101927766	LOC285627	ADRA1B
5	RS12656368	179653428	-0.112	0.0001202	RPS8P7	RASGEF1C	MAPK9
5	RS4569891	171480055	-0.111	0.0001344	STK10	FBXW11	EFCAB9
6	RS7771614	45975798	0.1144	6.60E-05	CLIC5	RUNX2	ENPP4
6	RS3995732	102603013	0.1129	0.0001171		GRIK2	LOC100996860
6	RS2473479	530459	0.1331	0.0001204	EXOC2	IRF4	HUS1B
6	RS6940101	134740760	0.2206	0.0001207		LOC102723463	LOC101928231
7	RS10954734	83385765	0.1459	1.49E-005		RAD23BP2	SEMA3A
7	RS10278502	148044472	-0.143	8.65E-05	CNTNAP2	RNA5SP249	LOC392145
7	RS657664	129146415	0.1229	9.41E-05	SMKR1	STRIP2	NRF1
7	RS7807731	155755336	0.1103	9.99E-05	LOC389602	SHH	LOC285889
7	RS4725143	8935674	-0.136	0.0001023		NXPH1	RPL9P19
7	RS10231911	154001559	0.1091	0.0001376	DPP6	LOC101929998	PAXIP1OS

Replication of Top Hits in Site 14

CHR	SNP	BP	Beta	P-Val	Amish_Beta	Amish_PVAL
1	RS6675916	1.57E+08	-0.1107	0.000138	-0.10957236	0.083291551
1	RS4233496	45763650	-0.1217	0.000147	-0.070134034	0.17906763
1	RS4658825	2.43E+08	0.1126			
1	RS2298900	1.7E+08				
1	RS10864305	7567346				
1	RS945652	2.44E+08				
2	RS881639	1.38E+08				
2	RS2693932	6187107				
2	RS3924400	62694693				
2	RS10928450	1.34E+08				
2	RS6720388					
2	RS13000695					
2	RS13395505		-0.1168			
3	RS2399046	1.05E+08	0.124	0.000117	0.18650698	0.002295542
3	RS1214375	1E+08	0.123	1.93E-05	0.027457686	0.598030959
3	RS6797484				0.007049372	0.919456428
4	RS12651351				0.06347722	0.354959023
4	RS1017710				-0.049393407	0.75776735
4	RS10050320				0.015392902	0.821650733
4	RS992556				-0.003921003	0.942153555
5	RS12656368	1.8E+08	-0.1116	0.00012	0.10766364	0.026485475
5	RS919751	1.5E+08	0.1232	3.34E-05	0.025884099	0.683676787
5	RS4569891	1.71E+08	-0.1109	0.000134	0.013887712	0.822097556
5	RS12513480	1.59E+08	-0.1551	5.23E-05	-0.019738181	0.82491629
6	RS7771614	45975798	0.1144	0.000066	-0.01861321	0.73608686
6	RS6940101	1.35E+08	0.2206	0.000121	0.077519135	0.749297672
6	RS2473479	530459	0.1331	0.00012	-0.014180702	0.826530993
6	RS3995732	1.03E+08	0.1129	0.000117	0.005227161	0.910613217
7	RS10231911	1.54E+08	0.1091	0.000138	-0.04764964	0.29693875
7	RS7807731	1.56E+08	0.1103	9.99E-05	-0.048316823	0.316671082
7	RS10954734	83385765	0.1459	1.49E-05	-0.054899695	0.359054746
7	RS4725143	8935674	-0.1364	0.000102	-0.01944462	0.763546361
7	RS657664	1.29E+08	0.1229	9.41E-05	-0.010911895	0.816615101

X

ALCAM: Activated leukocyte cell adhesion molecule (also known as CD166). Binds to T-cell differentiation antigene CD6, and is implicated in the processes of cell adhesion and migration.

RPS8P7

Replication of Top Hits in Site 14

	CHR	SNP	BP	Beta	P-Val	Amish_Beta	Amish_PVAL
	7	RS10278502	148044472	-0.1428	0.0000865	0.000728287	0.990992644
	8	RS10448034	70588878	-0.1481	0.0000701	0.045245903	0.360940994
	8	RS2543053	39821715	0.2221	0.0000726	0.003266302	0.982545269
	9	RS10988625	[illegible]	[illegible]	0.0001142	-0.25097729	0.313472497
	9	RS964912	[illegible]	[illegible]	0.0000328	-0.025870822	0.630496054
	10	RS2901783	[illegible]	[illegible]	0.0000815	0.14627698	0.005706499
	10	RS2104543	[illegible]	[illegible]	0.0000441	0.14590569	0.020734334
	10	RS1998591	96407978	0.2205	0.0000167	0.1459057	0.020734334
	10	RS11188256	97037578	0.1383	0.0000453	-0.099116136	0.117121406
	10	RS17878673	96539144	0.2319	0.0000417	0.042019389	0.595341662
	10	RS2892351	6941310	0.2123	0.0001372	0.043930744	0.753613013
	10	RS17542837	36562514	-0.1656	0.000147	-0.007231738	0.898274548
	10	RS10826566	29364697	0.151	0.0001454	0.005087658	0.949286415
	11	RS1909138	[illegible]	[illegible]	0.00003	-0.025990964	0.590125514
	11	RS5028798	[illegible]	[illegible]	0.0000359	0.043530318	0.613868903
	11	RS4578397	[illegible]	[illegible]	0.0000109	0.011886652	0.810697243
X	12	RS7979473	[illegible]	[illegible]	0.0000732	-0.1235465	0.019222431
	12	RS2251468	121405126	0.1292	0.00000628	-0.069691621	0.20604963
	12	RS6553	121202362	-0.1128	0.0001379	0.073288229	0.227919156
	12	RS11065286	121271734	-0.1252	0.0000183	0.064098006	0.337783003
	12	RS11060592	[illegible]	[illegible]	0.0000666	-0.047333151	0.540268771
	12	RS10505836	[illegible]	[illegible]	0.0000059	0.046857203	0.618218512
	13	RS1887827	[illegible]	[illegible]	0.0000261	-0.055451388	0.41228866
	14	RS8022742	[illegible]	[illegible]	0.0000884	-0.17351447	0.002866396
	14	RS10136508	24764114	-0.1338	0.00000499	0.063210568	0.237840494
	14	RS1806787	47797402	0.1309	0.0000647	0.050875099	0.270956743
	14	RS2295300	24805117	-0.1355	0.0000921	0.044963032	0.47445377
	14	RS2180196	24734645	-0.1611	0.0001468	-0.12773891	0.507141499
	14	RS4280164	[illegible]	[illegible]	0.0000673	0.042310417	0.512251055
	15	RS1156233	[illegible]	[illegible]	0.000024	0.097667092	0.157058655
	16	RS10521117	[illegible]	[illegible]	0.0000609	0.14065525	0.440276489
X	17	RS218697	[illegible]	[illegible]	0.0000253	0.18011008	0.018118274
	18	RS7237209	[illegible]	[illegible]	0.0000359	0.21987116	0.016541014
	19	RS10415651	[illegible]	[illegible]	0.0000201	-0.044292775	0.476688478
	21	RS607020	[illegible]	[illegible]	0.0000719	0.016757119	0.719024288
	21	RS845017	[illegible]	[illegible]	0.0000325	0.008693067	0.853826089

CYP2C18

HNF1A

LINC00618

TGM1

LOC643542

GWAS Next Steps

- GWAS of CV event traits
- LD maps
- Informatics
- Follow-up genotyping
  - Imputed SNPs (ICPC and PAPI)
  - Replication sample

Candidate Gene Study Summary

- 28 of 32 SNPs were polymorphic and passed QC
- Of 2621 samples, approximately 2,050 passed qc for any given SNP
- Association analyses performed using standard mean differences of ADP-stimulated platelet aggregation traits

Genotype concordance rates for 2452 samples genotyped in both the ICPC Candidate Gene Study and the RIKEN GWAS

Assay	Rs id	MAF - RIKEN GWAS	Concordance* %	Call rate per SNP across, all samples (Candidate gene study)	Call rate per SNP across, all samples (ICPC RIKEN GWAS)
C___7586657_20	rs1045642	0.49	99.93	99.50	98.24
C___7586662_10	rs1128503	0.43	100	99.54	98.24
C__31432615_10	rs12041331	0.11	95.74	94.62	98.24
C___1941833_10	rs1472122	0.50	99.89	98.36	98.24
AHUAF18	rs2244613	0.20	99.34	98.89	97.60
C__30634132_70	rs28371685	0.00	99.96	96.34	98.24
C__30634136_10	rs28399504	0.00	99.96	95.92	98.21
C__25986767_70	rs4244285	0.17	99.88	96.68	98.21
C__27861809_10	rs4986893	0.00	100	99.20	98.24
C____818008_30	rs5918	0.15	99.97	97.18	98.24
C___2548962_20	rs662	0.28	100	97.86	98.24
C__11507727_10	rs7254579	0.33	99.69	98.89	98.09
C__22275631_10	rs8192719	0.25	99.62	91.38	98.21

*- excluded genotypes reported as missing, while calculating mismatches

Candidate Gene Association Analysis Results

	Gene	Reference allele	Reference allele frequency	Call rate	HW p: value	BETA	STAT	Age sex	Age Sex & rs4244285
rs1045642	ABCB1	A	0.504	1	0.352	-0.0509	-1.475	1.40E-01	1.07E-01
rs1128503	ABCB1	A	0.433	1	0.509	0.02758	0.7992	4.24E-01	2.73E-01
rs71647871	**CES1**	**C**	**0.984**	**1**	**0.459**	**-0.5872**	**-4.217**	**2.61E-05**	**1.70E-05**
rs2244613	CES1	T	0.806	1	0.61	0.05566	1.3	1.94E-01	1.01E-01
rs762551	CYP1A2	A	0.684	1	0.565	-0.0101	-0.2766	7.82E-01	7.07E-01
rs2302429	CYP1A2*1	G	0.832	0.98	0.333	-0.05597	-1.226	2.21E-01	2.82E-01
rs4803419	CYP2B6;CYP2A7P1	T	0.317	1	0.37	0.006793	0.1858	8.53E-01	6.60E-01
rs3745274	*CYP2B6;CYP2A7P1*	*T*	*0.236*	*0.96*	*0.011*	*0.07223*	*2.125*	*3.37E-02*	*1.67E-02*
rs7254579	CYP2B6;CYP2A7P1	C	0.325	1	0.159	0.04352	1.424	1.55E-01	1.34E-01
rs8192719	*CYP2B6;CYP2A7P1*	*C*	*0.75*	*0.99*	*0.014*	*0.07164*	*2.173*	*2.99E-02*	*1.35E-02*
rs4803418	CYP2B6;CYP2A7P1	C	0.686	0.97	0.326	0.03677	0.9906	3.22E-01	1.38E-01
rs12248560	**CYP2C19**	**C**	**0.793**	**0.99**	**0.217**	**-0.1885**	**-5.205**	**2.14E-08**	**3.10E-03**
rs4244285	**CYP2C19**	**G**	**0.833**	**1**	**0.407**	**0.4745**	**10.74**	**4.09E-26**	**NA**
rs72552267	CYP2C19	G	0.999	1	0.947	0.2792	0.6813	4.96E-01	4.79E-01
rs41291556	CYP2C19	C	0.003	0.99	0.903	0.0636	0.1796	8.58E-01	9.90E-01
rs28399504	CYP2C19	A	0.996	1	0.842	-0.1828	-0.7258	4.68E-01	7.72E-01
rs1799853	CYP2C9	C	0.841	0.97	0.162	-0.0547	-1.141	2.54E-01	7.72E-01
rs1057910	*CYP2C9*	*C*	*0.089*	*0.98*	*0.951*	*0.04617*	*0.8962*	*3.70E-01*	*1.48E-02*
rs28371685	CYP2C9	C	0.996	0.99	0.841	0.367	1.457	1.45E-01	9.19E-01
rs168753	F2R	T	0.16	0.98	0.202	0.03491	0.7699	4.42E-01	4.77E-01
rs5918	ITGB3	T	0.85	0.99	0.179	-0.00764	-0.1573	8.75E-01	8.82E-01
rs2046934	P2RY12	A	0.849	0.98	0.002	0.03368	0.7204	4.71E-01	3.63E-01
rs1472122	**P2RY12**	**A**	**0.5**	**1**	**0.402**	**0.1033**	**3.021**	**2.56E-03**	**1.76E-03**
rs12041331	PEAR1	G	0.869	0.97	0.003	-0.0422	-0.8087	4.19E-01	3.17E-01
rs854560	PON1	A	0.631	0.98	0.282	-0.0217	-0.582	5.61E-01	3.31E-01
rs662	PON1	C	0.28	1	0.56	-0.00238	-0.06256	9.50E-01	8.03E-01
rs1057868	TMEM120A;POR	C	0.718	1	0.282	0.03123	0.8369	4.03E-01	4.70E-01
rs2286823	TMEM120A;POR	G	0.701	0.99	0.535	-0.01432	-0.3891	6.97E-01	6.66E-01

Candidate Gene Study Next Steps

- WGA completed
- 1692 additional samples genotyped
- Finalize analysis with combined set