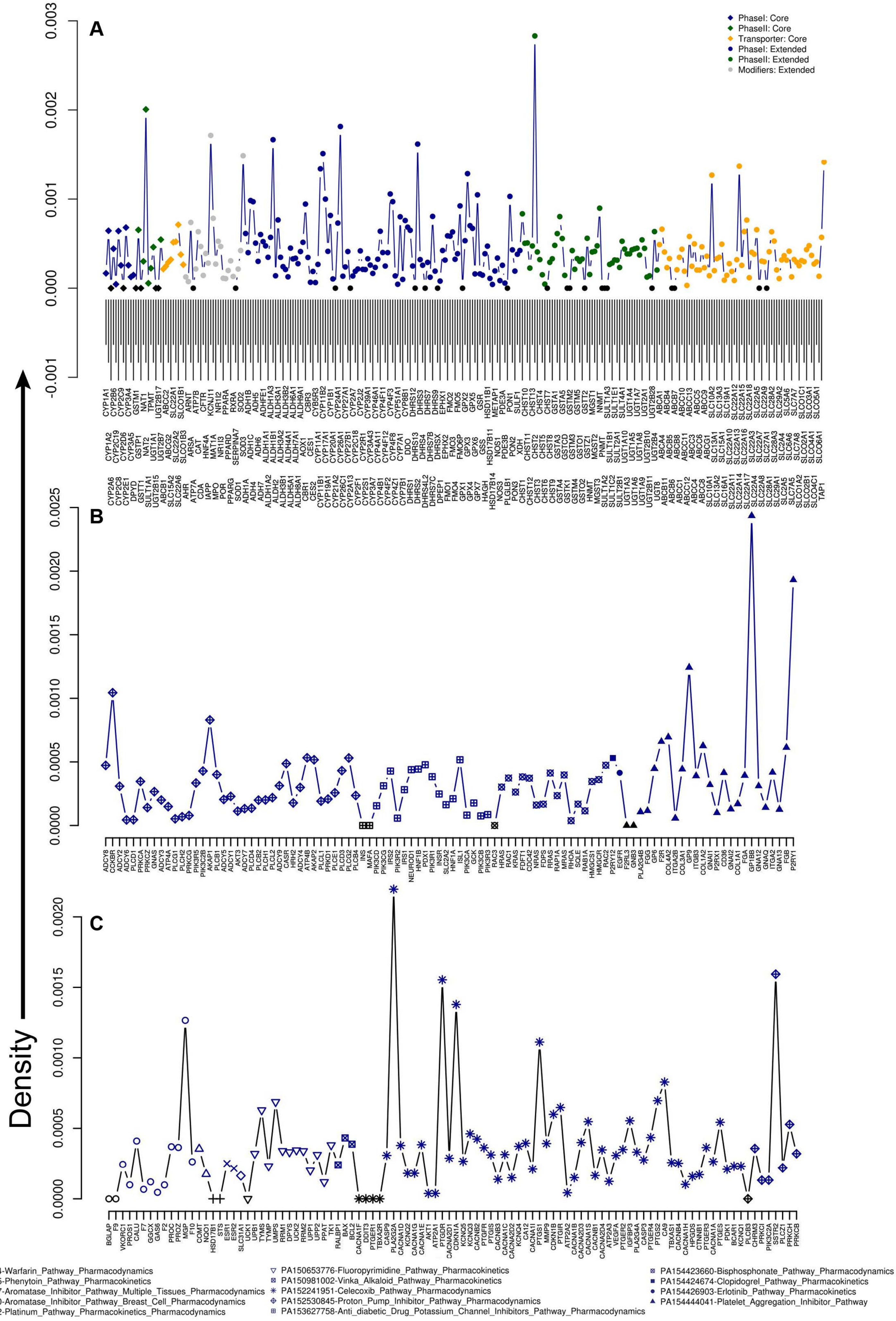
Figure S1: Density of the SNPs per base-pairs within the pharmacologically important genes. Genes having 0 SNPs in our dataset are given in black. A represents the density of SNPs in ADME genes while B, C, D, E F, G and H represents the density of SNPs in other pathway genes.



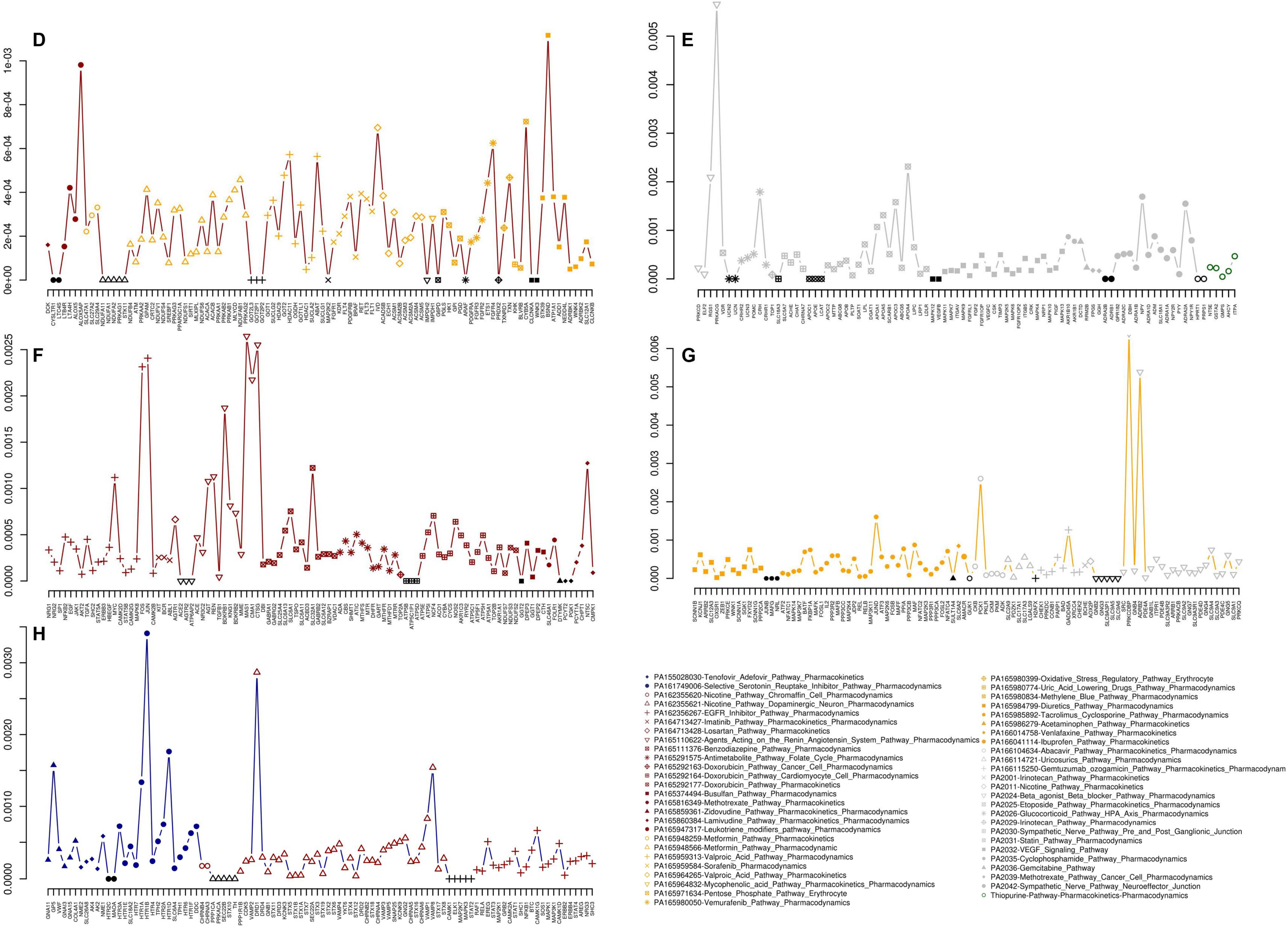

D
E
F
G
H
PA155028030-Tenofovir_Adefovir_Pathway_Pharmacokinetics
PA161749006-Selective_Serotonin_Reuptake_Inhibitor_Pathway_Pharmacodynamics
PA162355620-Nicotine_Pathway_Chromaffin_Cell_Pharmacodynamics
PA162355621-Nicotine_Pathway_Dopaminergic_Neuron_Pharmacodynamics
PA162356267-EGFR_Inhibitor_Pathway_Pharmacodynamics
PA164713427-Imatinib_Pathway_Pharmacokinetics_Pharmacodynamics
PA164713428-Losartan_Pathway_Pharmacokinetics
PA165110622-Agents_Acting_on_the_Renin_Angiotensin_System_Pathway_Pharmacodynamics
PA165111376-Benzodiazepine_Pathway_Pharmacodynamics
PA165291575-Antimetabolite_Pathway_Folate_Cycle_Pharmacodynamics
PA165292163-Doxorubicin_Pathway_Cancer_Cell_Pharmacodynamics
PA165292164-Doxorubicin_Pathway_Cardiomyocyte_Cell_Pharmacodynamics
PA165292177-Doxorubicin_Pathway_Pharmacokinetics
PA165374494-Busulfan_Pathway_Pharmacodynamics
PA165816349-Methotrexate_Pathway_Pharmacokinetics
PA165859361-Zidovudine_Pathway_Pharmacokinetics_Pharmacodynamics
PA165860384-Lamivudine_Pathway_Pharmacokinetics_Pharmacodynamics
PA165947317-Leukotriene_modifiers_pathway_Pharmacodynamics
PA165948259-Metformin_Pathway_Pharmacokinetics
PA165948566-Metformin_Pathway_Pharmacodynamic
PA165959313-Valproic_Acid_Pathway_Pharmacodynamics
PA165959584-Sorafenib_Pharmacodynamics
PA165964265-Valproic_Acid_Pathway_Pharmacokinetics
PA165964832-Mycophenolic_acid_Pathway_Pharmacokinetics_Pharmacodynamics
PA165971634-Pentose_Phosphate_Pathway_Erythrocyte
PA165980050-Vemurafenib_Pathway_Pharmacodynamics
PA165980399-Oxidative_Stress_Regulatory_Pathway_Erythrocyte
PA165980774-Uric_Acid_Lowering_Drugs_Pathway_Pharmacodynamics
PA165980834-Methylene_Blue_Pathway_Pharmacodynamics
PA165984799-Diuretics_Pathway_Pharmacodynamics
PA165985892-Tacrolimus_Cyclosporine_Pathway_Pharmacodynamics
PA166046279-Acetaminophen_Pathway_Pharmacokinetics
PA166014758-Venlafaxine_Pathway_Pharmacokinetics
PA166041114-Ibuprofen_Pathway_Pharmacokinetics
PA166104634-Abacavir_Pathway_Pharmacokinetics_Pharmacodynamics
PA166114721-Uricosurics_Pathway_Pharmacodynamics
PA166115250-Gemtuzumab_ozogamicin_Pathway_Pharmacokinetics_Pharmacodynam
PA2001-Irinotecan_Pathway_Pharmacokinetics
PA2011-Nicotine_Pathway_Pharmacokinetics
PA2024-Beta_agonist_Beta_blocker_Pathway_Pharmacodynamics
PA2025-Etoposide_Pathway_Pharmacokinetics_Pharmacodynamics
PA2026-Glucocorticoid_Pathway_HPA_Axis_Pharmacodynamics
PA2029-Irinotecan_Pathway_Pharmacodynamics
PA2030-Sympathetic_Nerve_Pathway_Pre_and_Post_Ganglionic_Junction
PA2031-Statin_Pathway_Pharmacodynamics
PA2032-VEGF_Signaling_Pathway
PA2035-Cyclophosphamide_Pathway_Pharmacodynamics
PA2036-Gemcitabine_Pathway
PA2039-Methotrexate_Pathway_Cancer_Cell_Pharmacodynamics
PA2042-Sympathetic_Nerve_Pathway_Neuroeffector_Junction
Thiopurine-Pathway-Pharmacokinetics-Pharmacodynamics

Figure S2. Number of SNPs per 200,000 base-pairs along all chromosomes. The number of SNPs are equal to number of chances to find extreme std-z score.

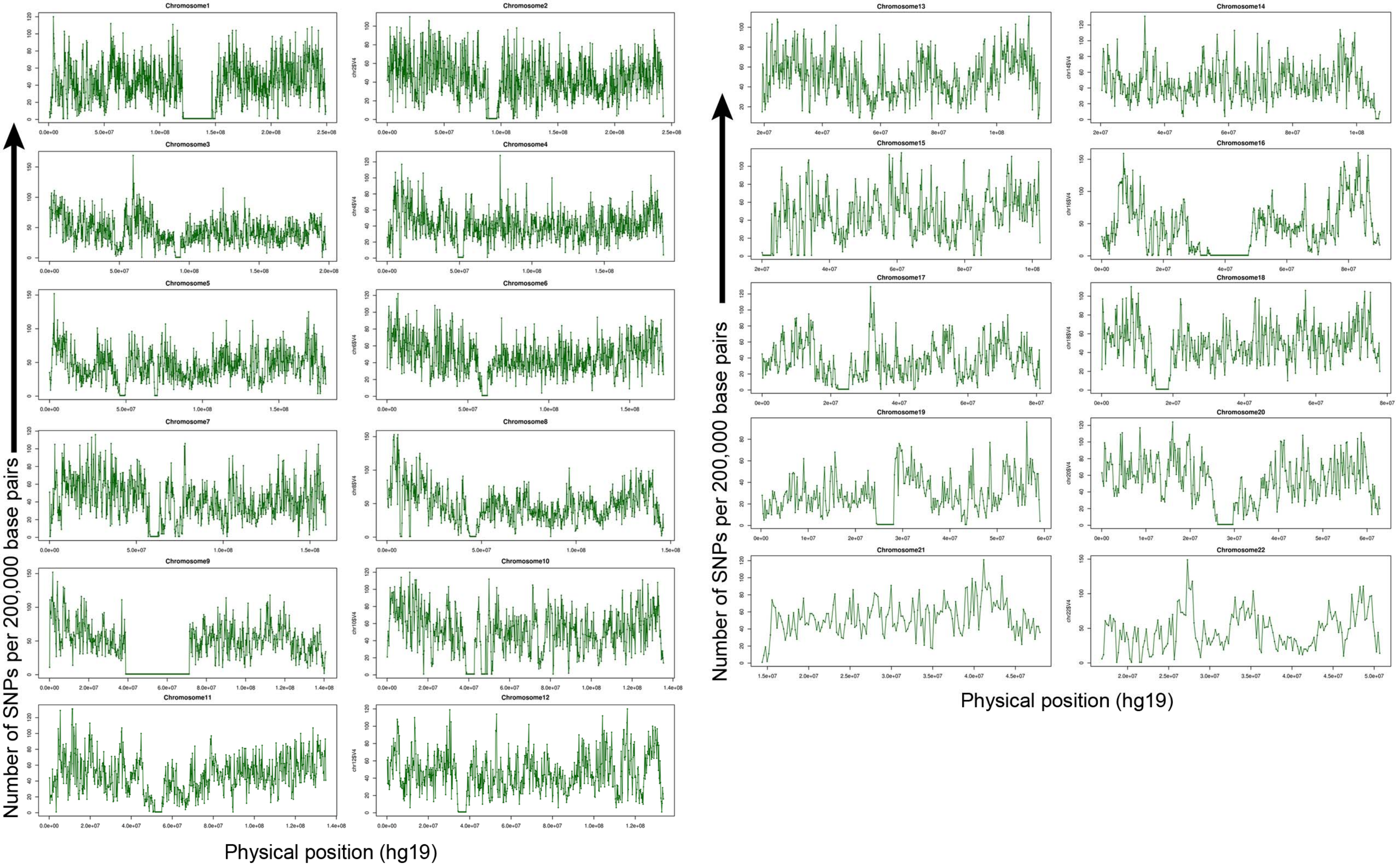
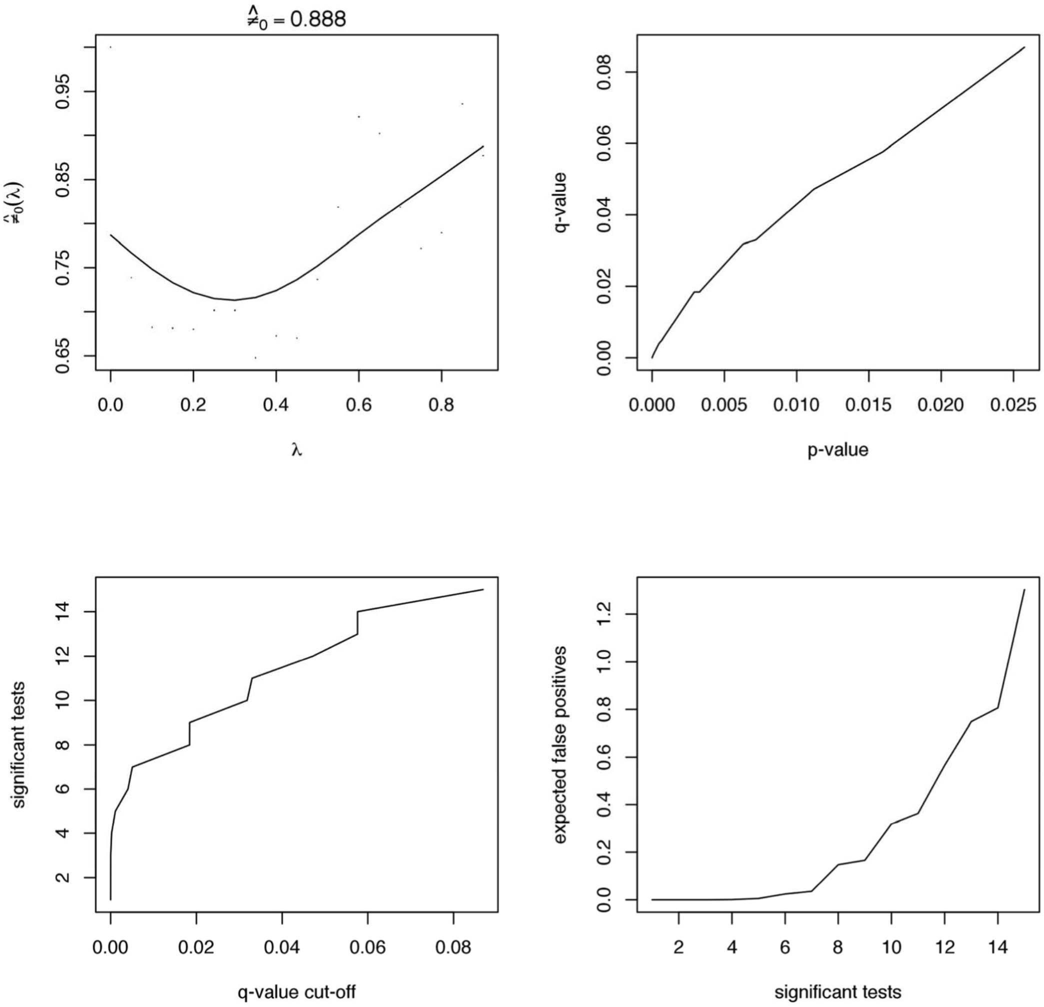
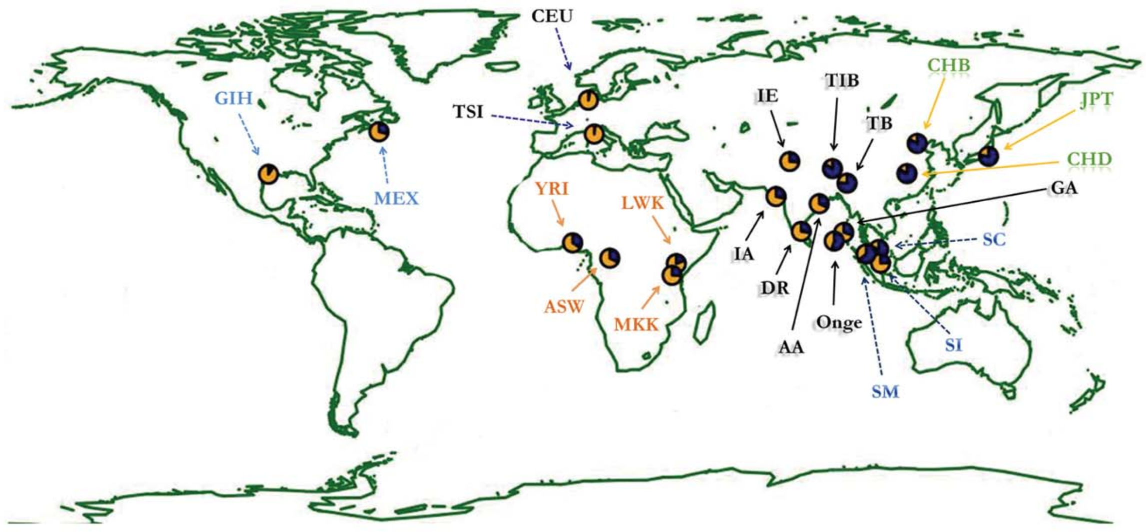


Figure S3: Multiple test correction for pathway-analysis with q-value.

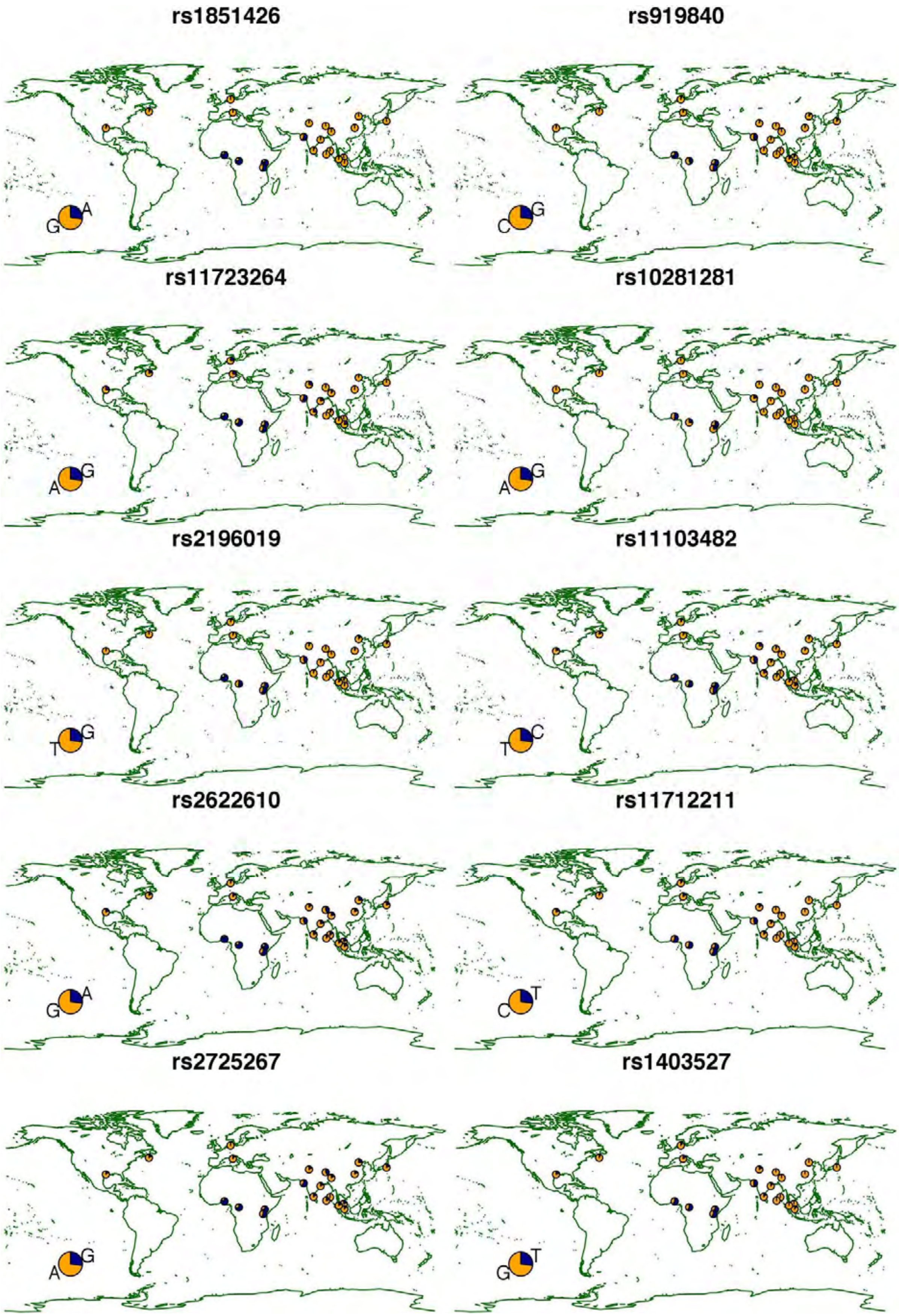


	<1e-04	<0.001	<0.01	<0.025	<0.05	<0.1	<1
p-value	4	7	11	14	17	22	57
q-value	3	4	7	9	12	15	57

Figure S4: Distribution of allele frequency of hard-sweep signals in world populations.



GIH: Gujarati Indians; MEX: Mexicans; YRI: Yoruba; ASW: African ancestry in South-West USA; MKK: Maasai; IA: Indo-Africans; DR: Dravidian; AA: Austro-Asiatic; IE: Indo-Europeans; TIB: Tibetans; TB: Tibeto-Burman; SM: Singapore-Malaysians; SI: Singapore-Indians; SC: Singapore-Chinese; GA: Great-Andamanese; CHD: Chinese-Denver; JPT: Japanese; CHB: Chinese-Beijing; LWK: Luhya; TSI: Toscans; CEU: Utah residents with European ancestry



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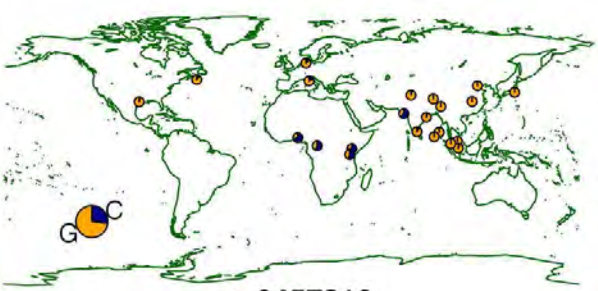
G T

rs6008197



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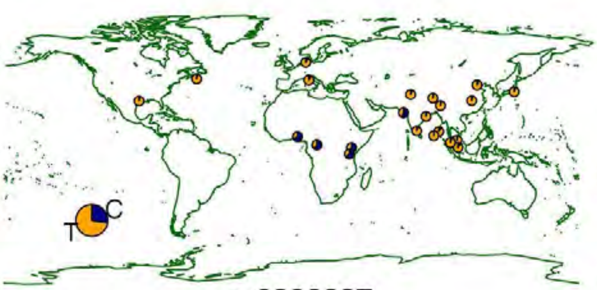

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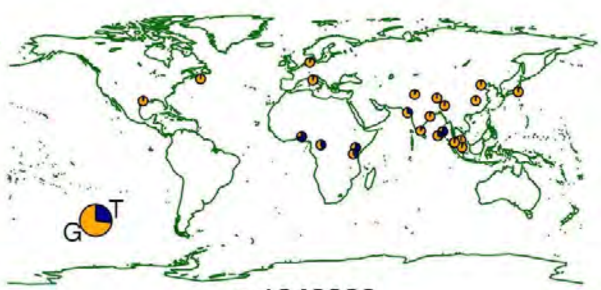

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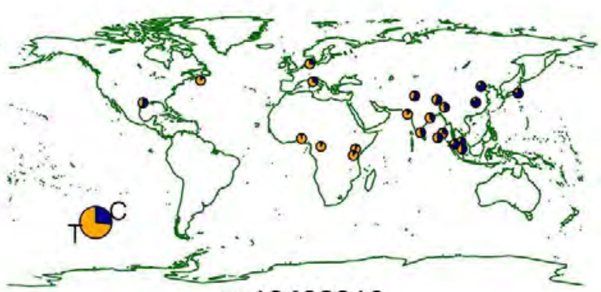

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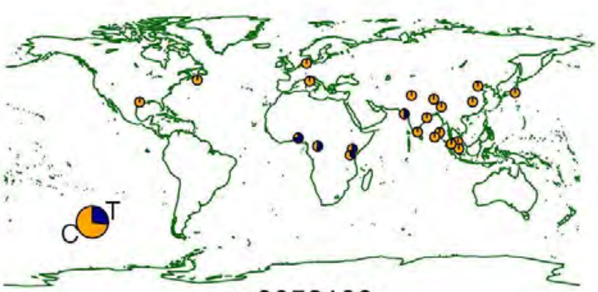

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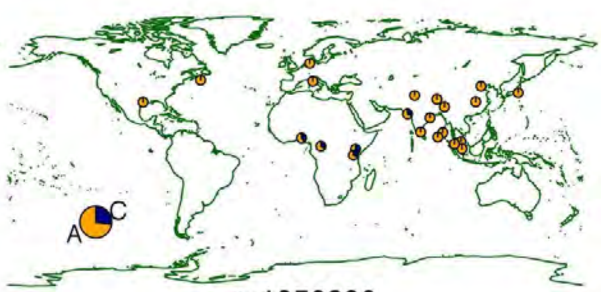

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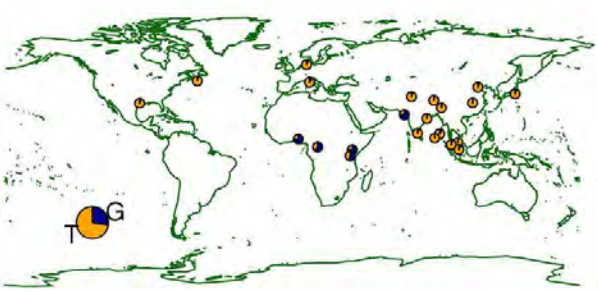

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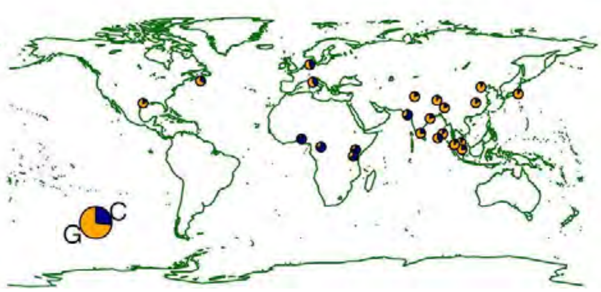

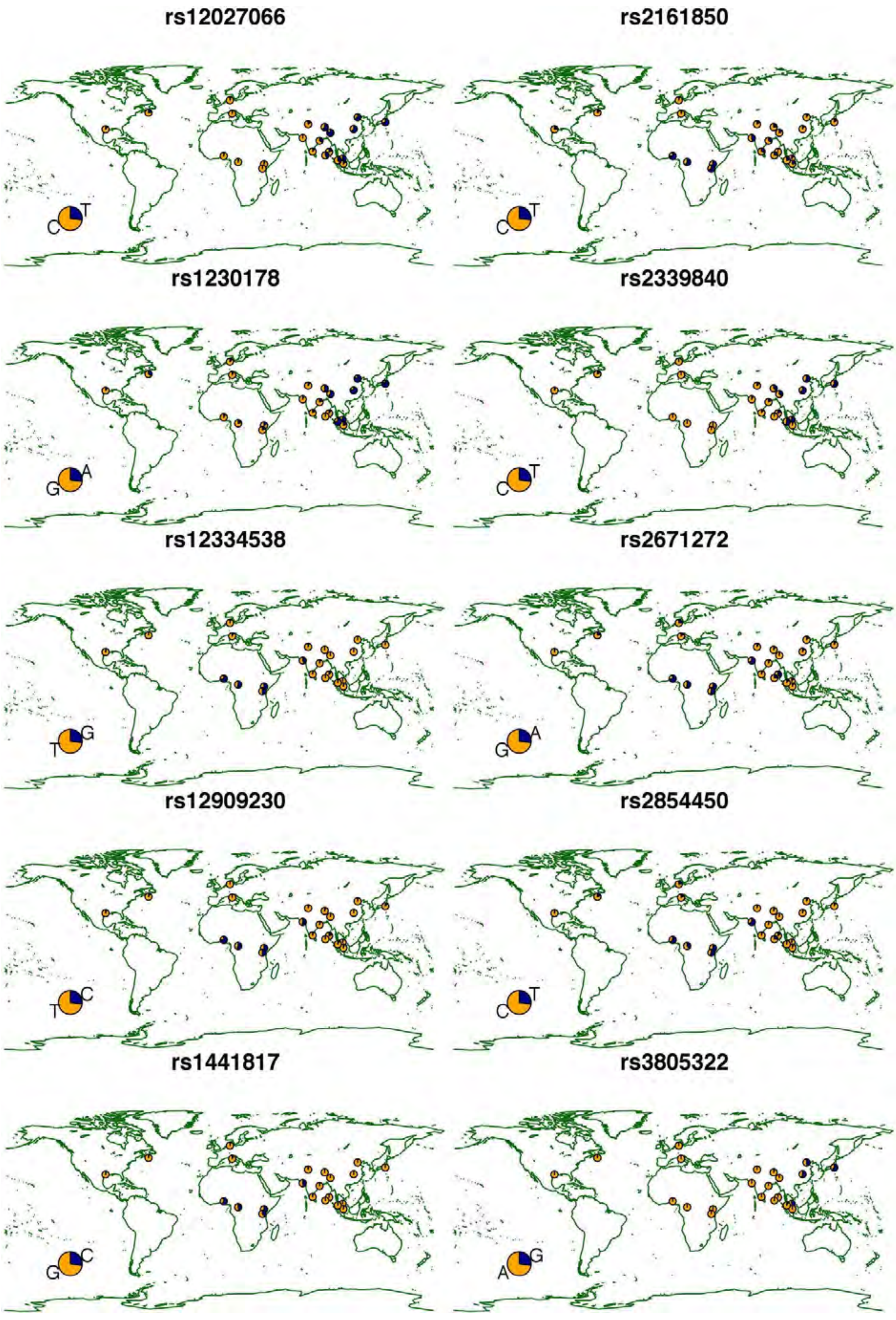
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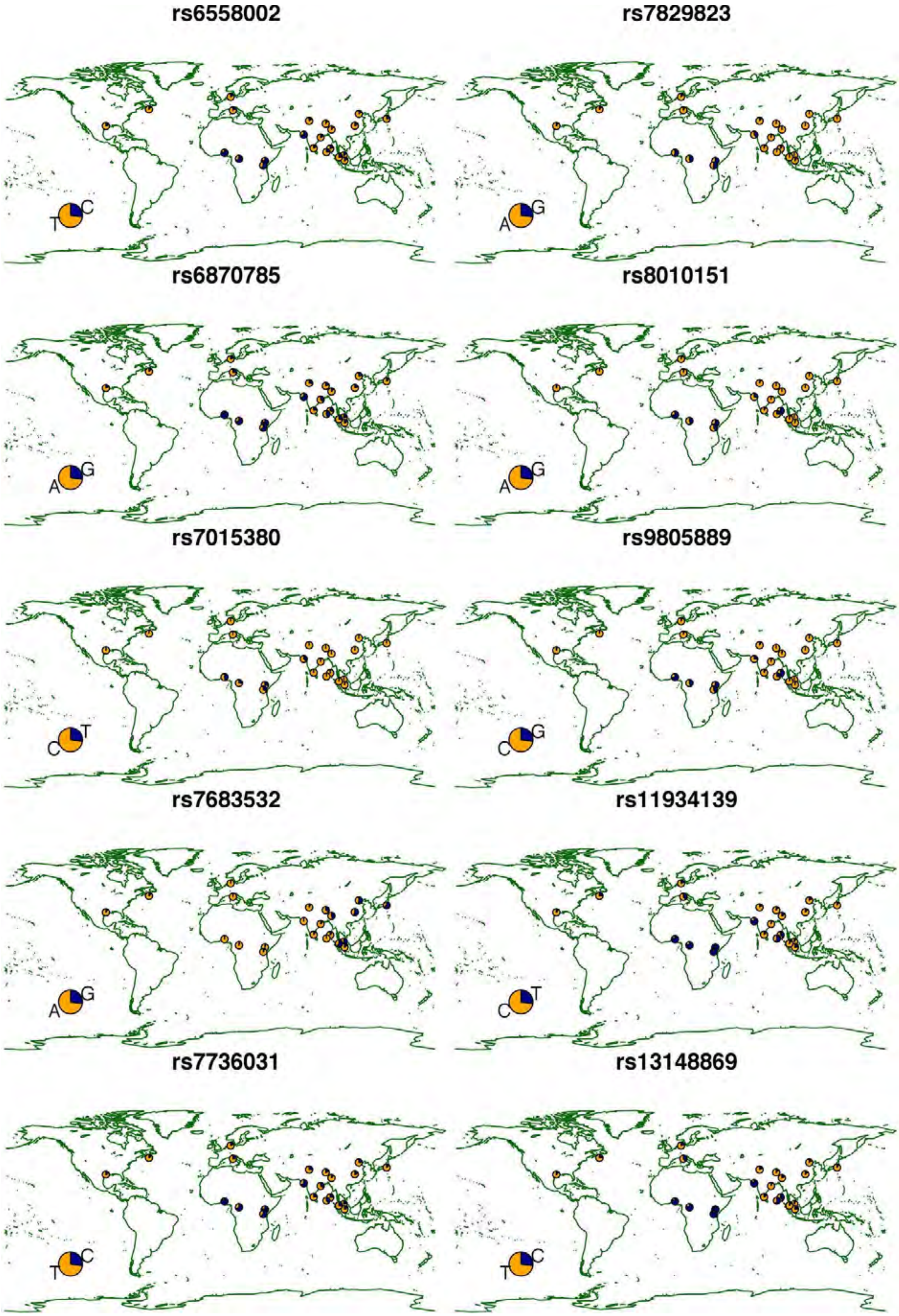
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C
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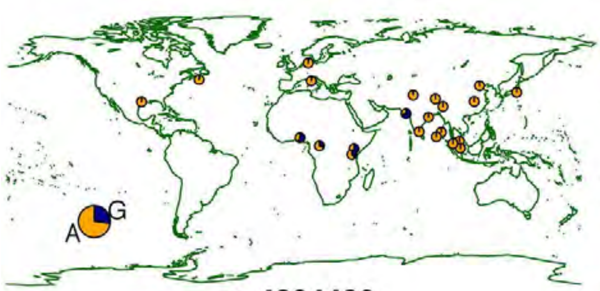
C

rs4834424 **rs6831964**



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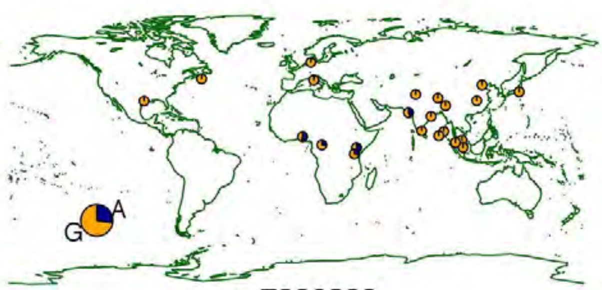

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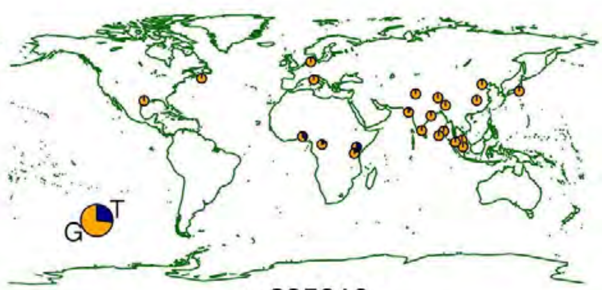

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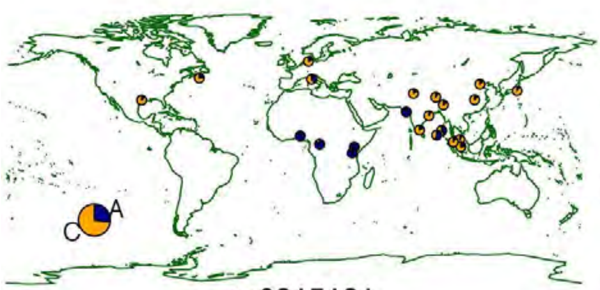

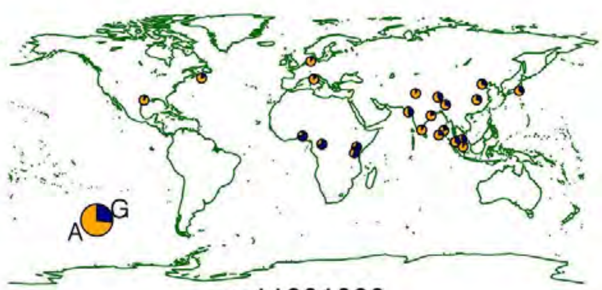

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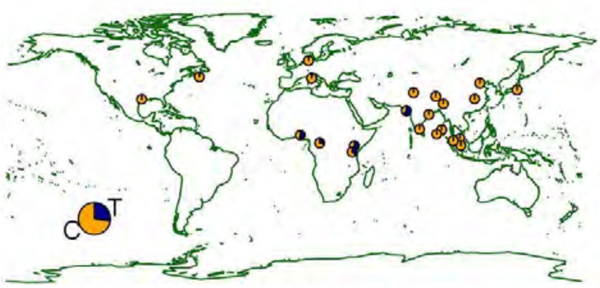

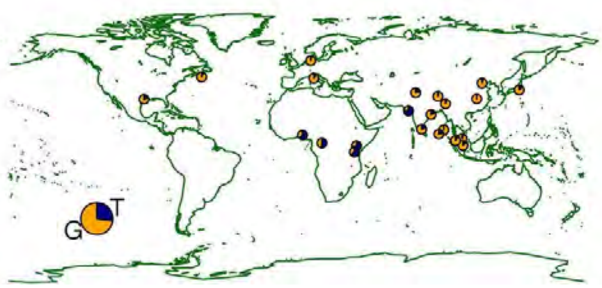

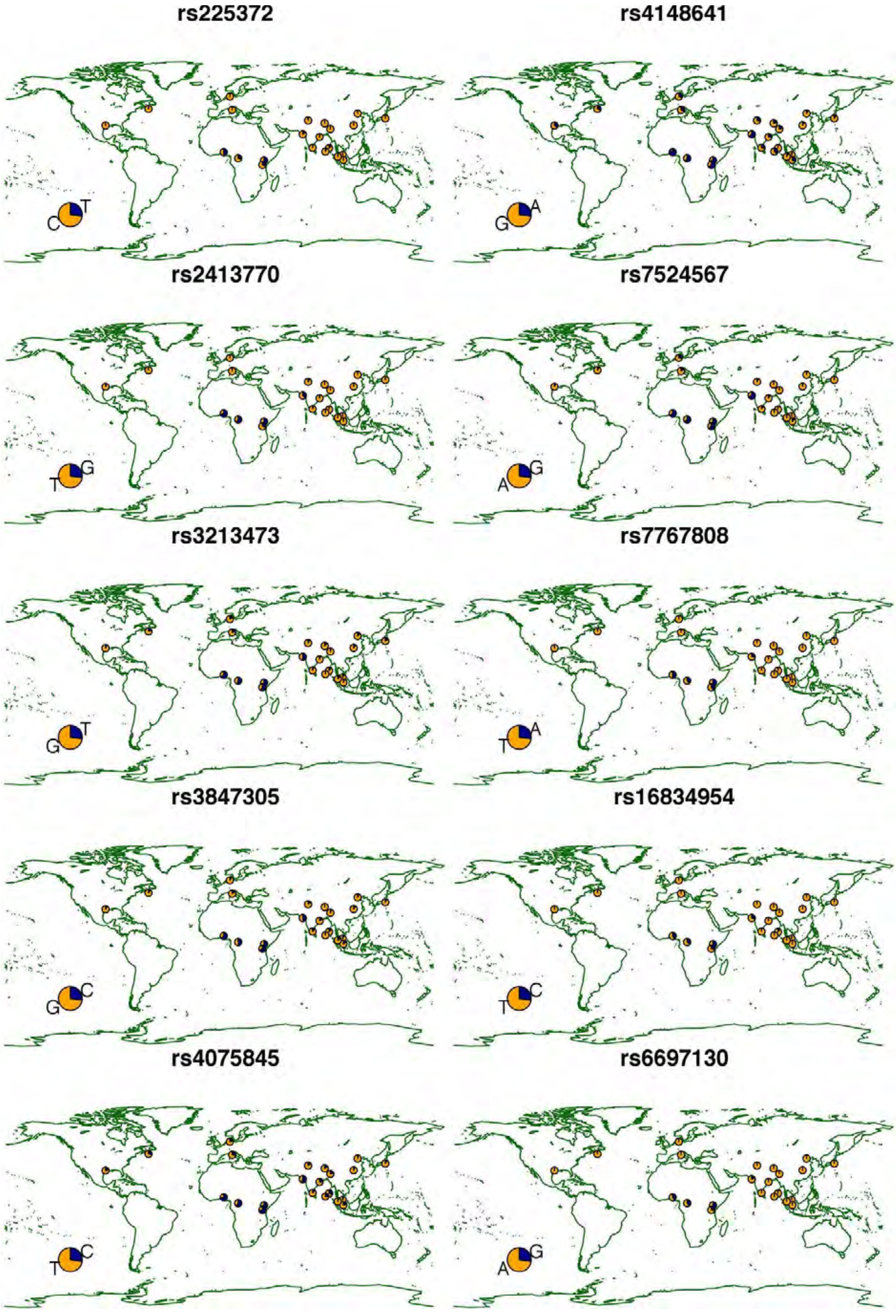

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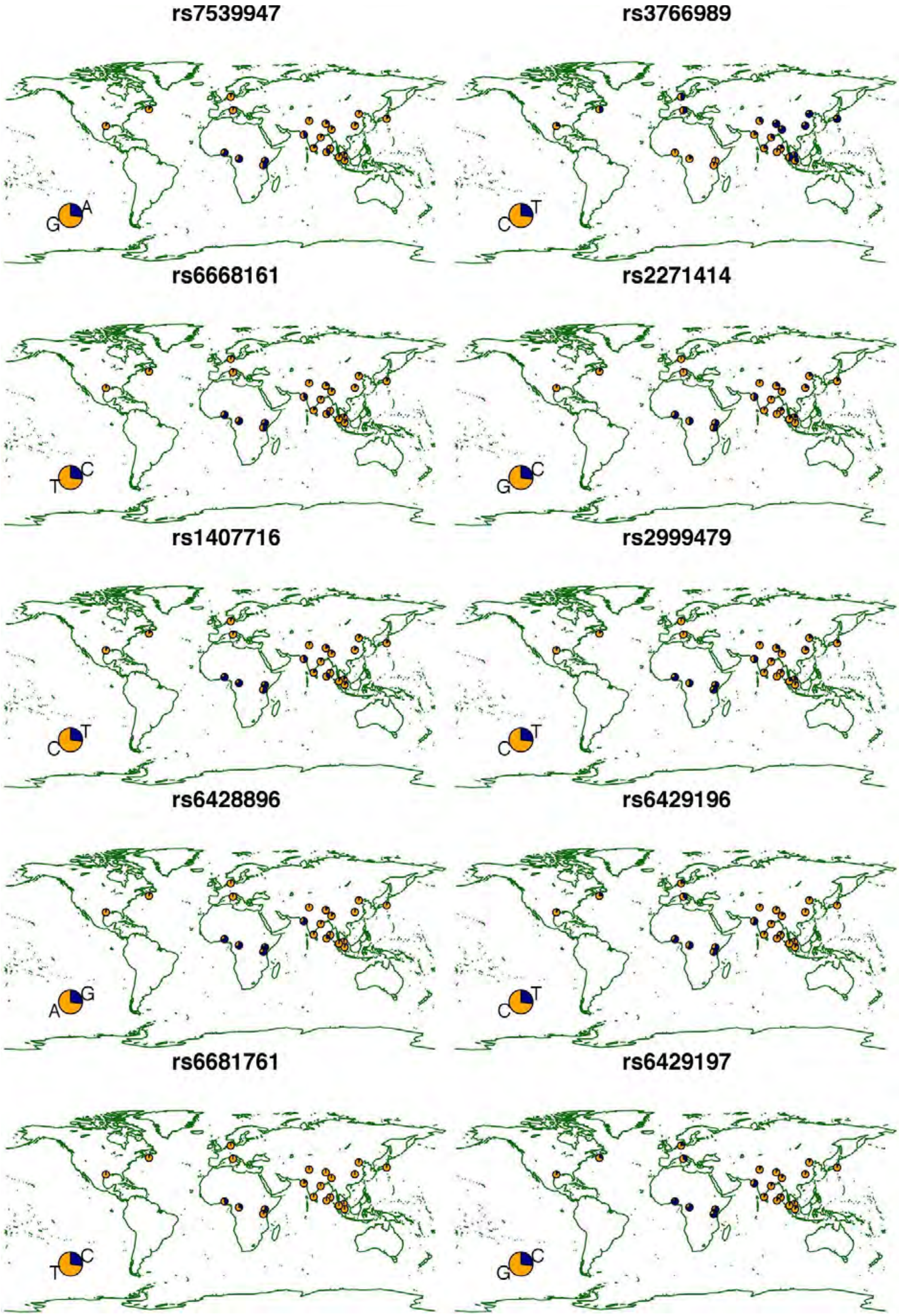
G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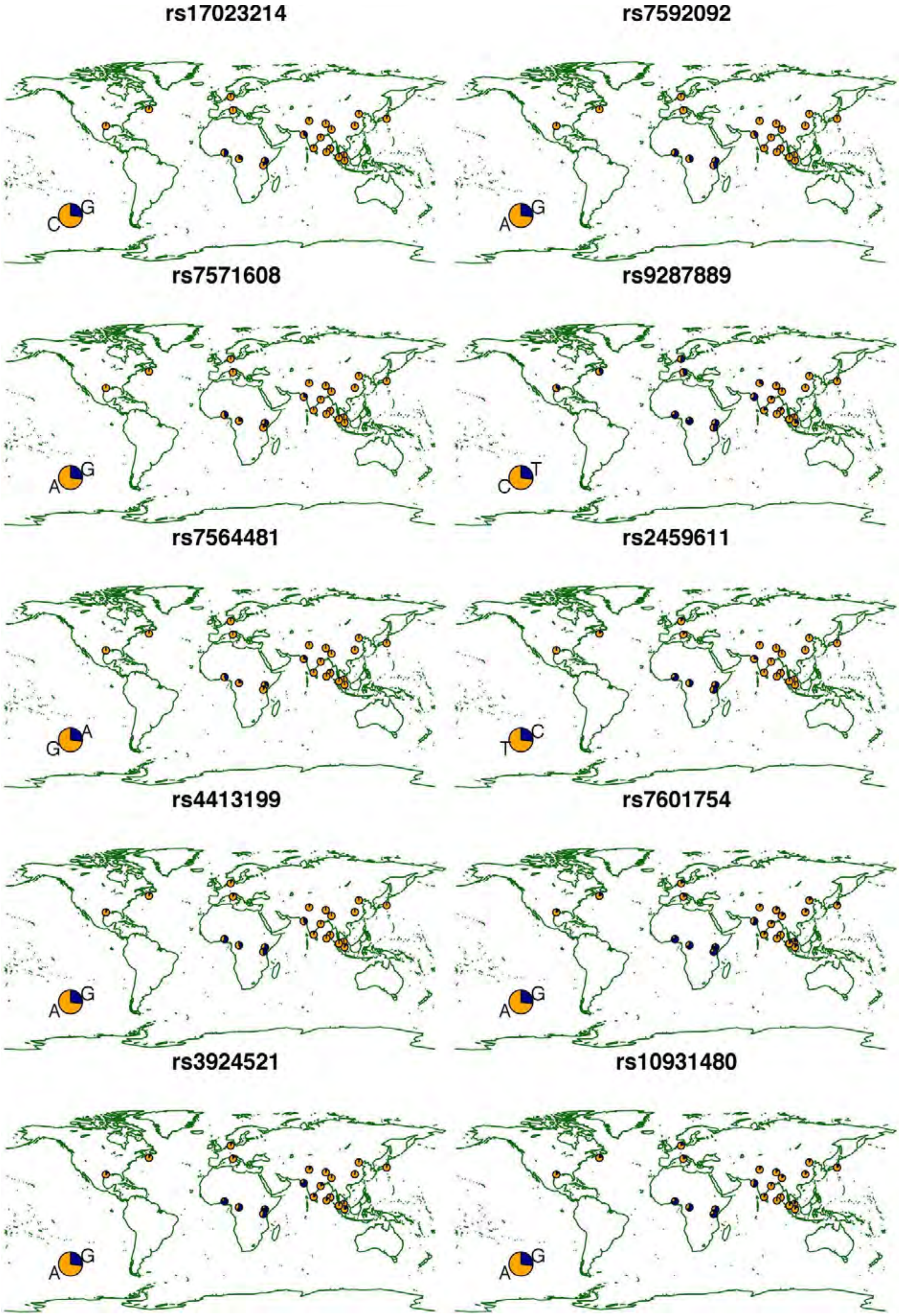

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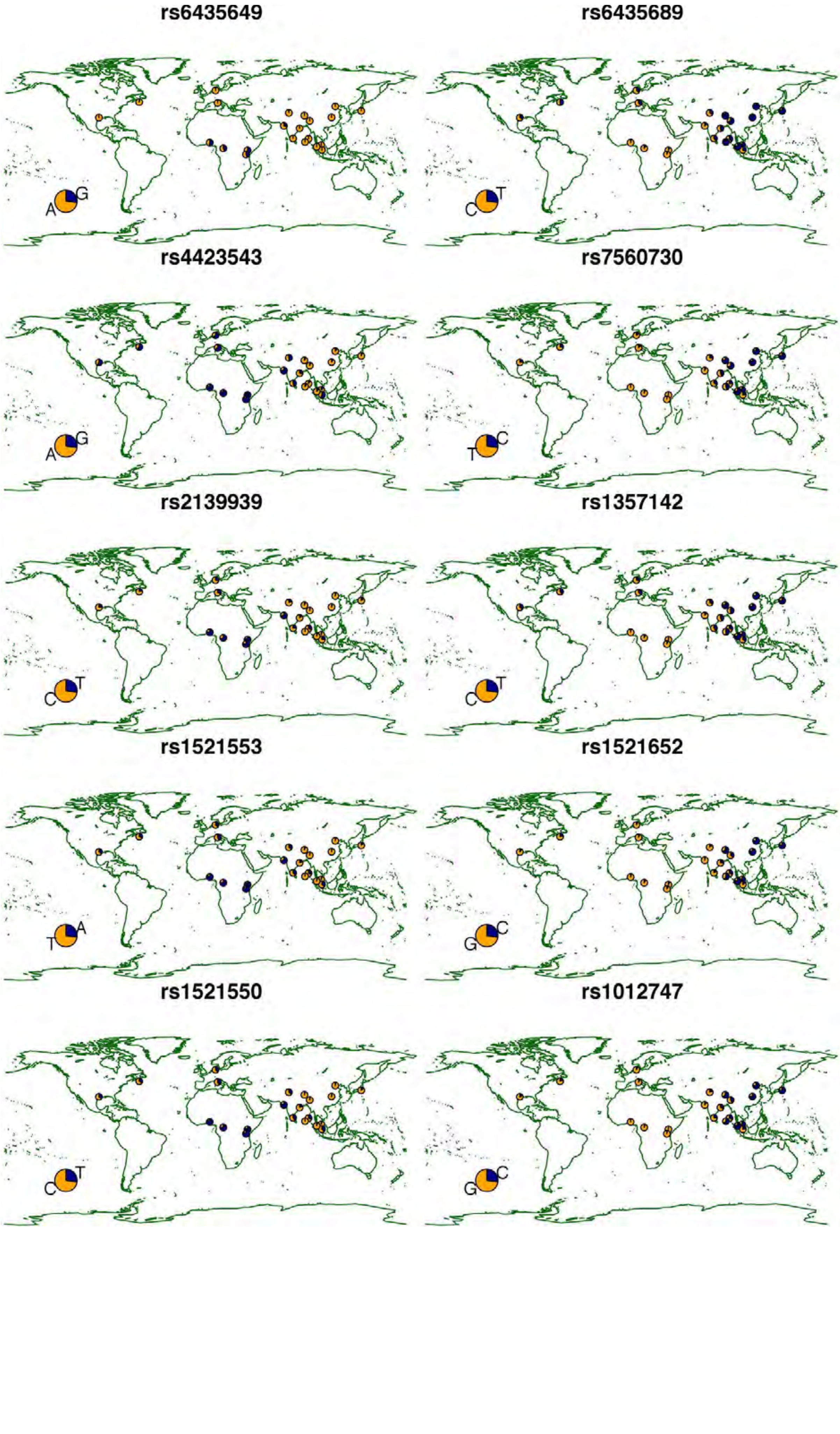
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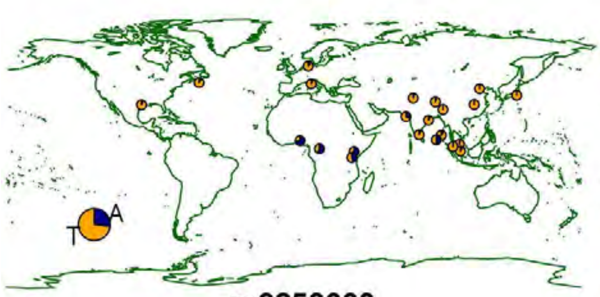

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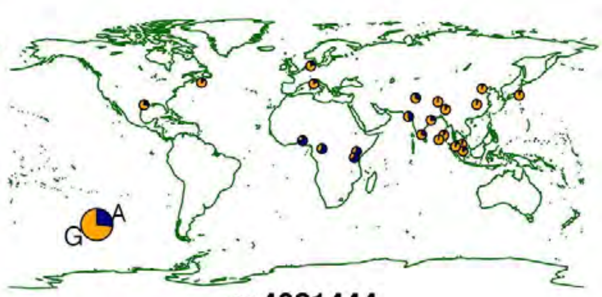

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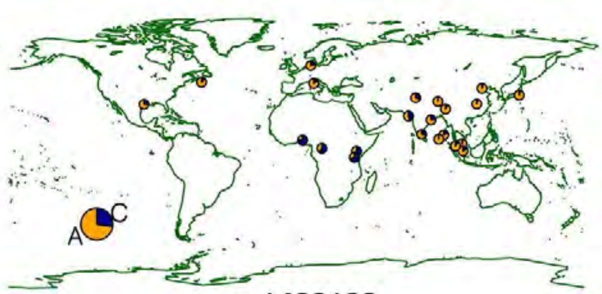

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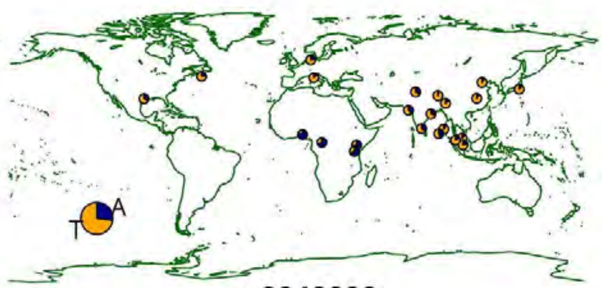

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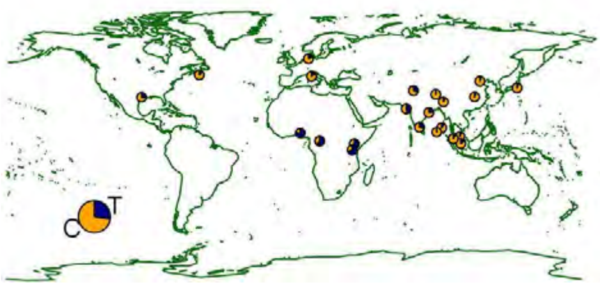

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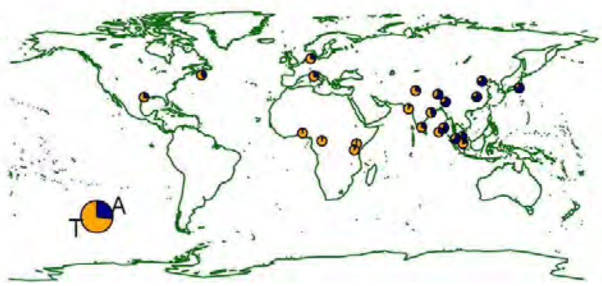

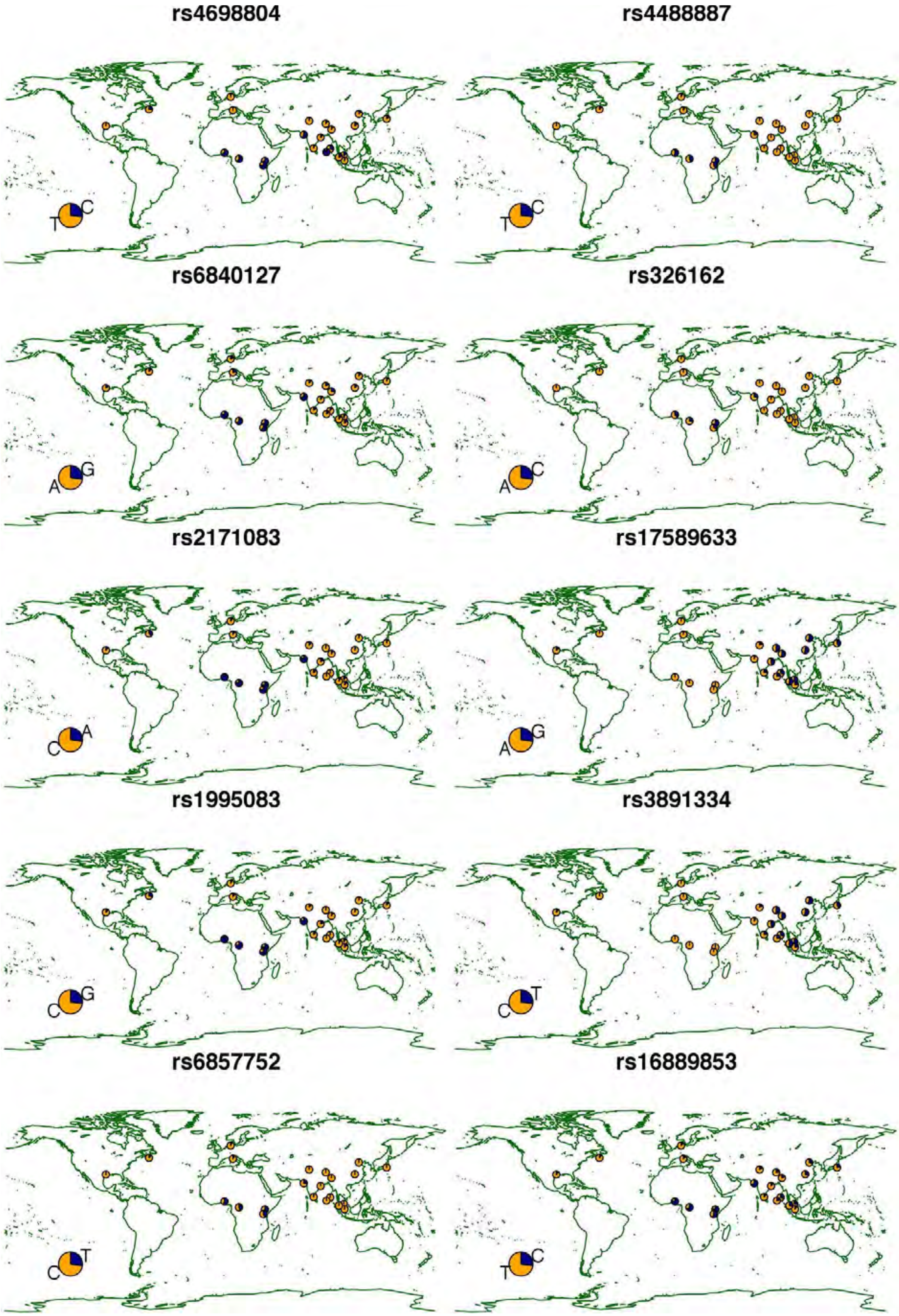
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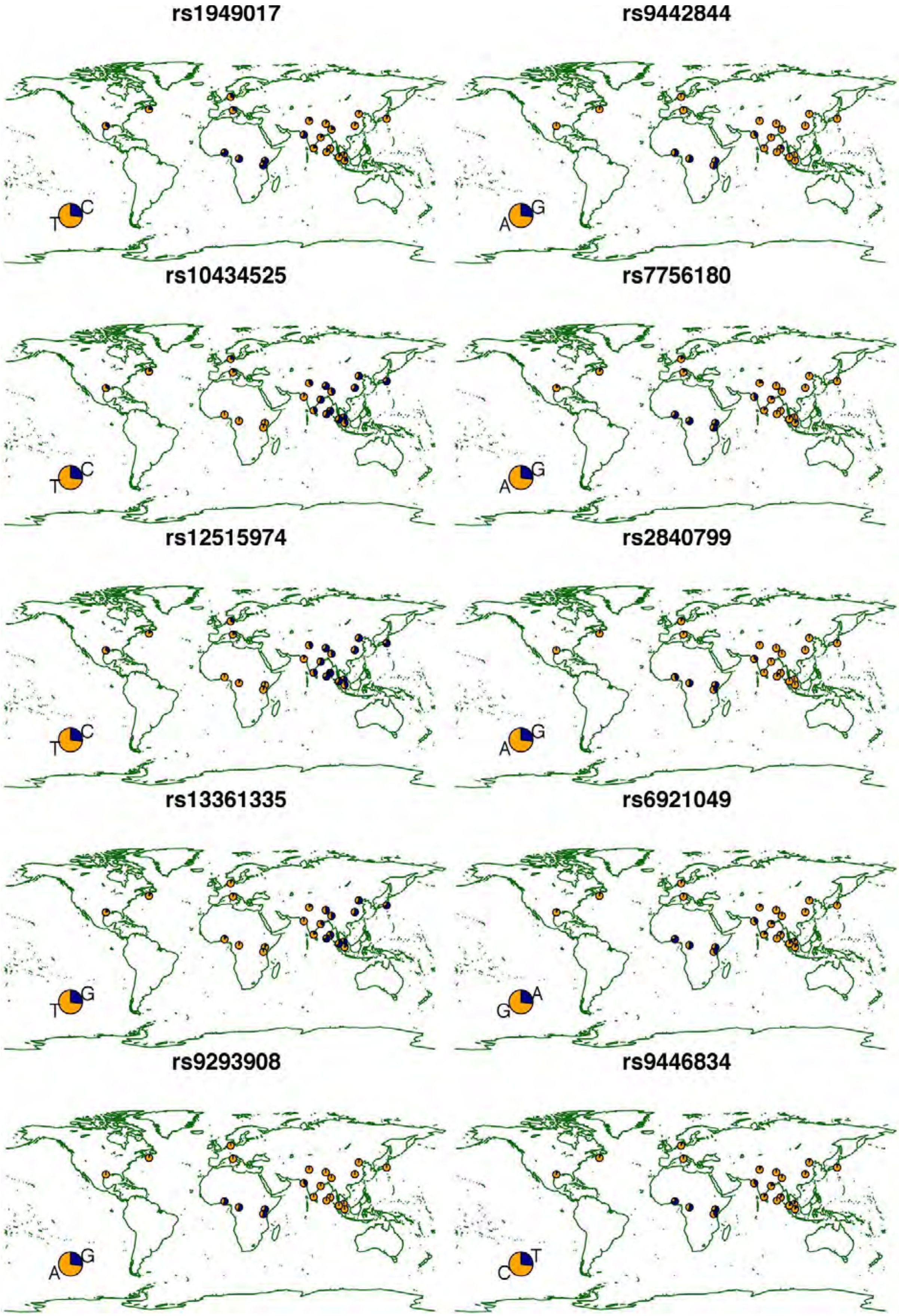
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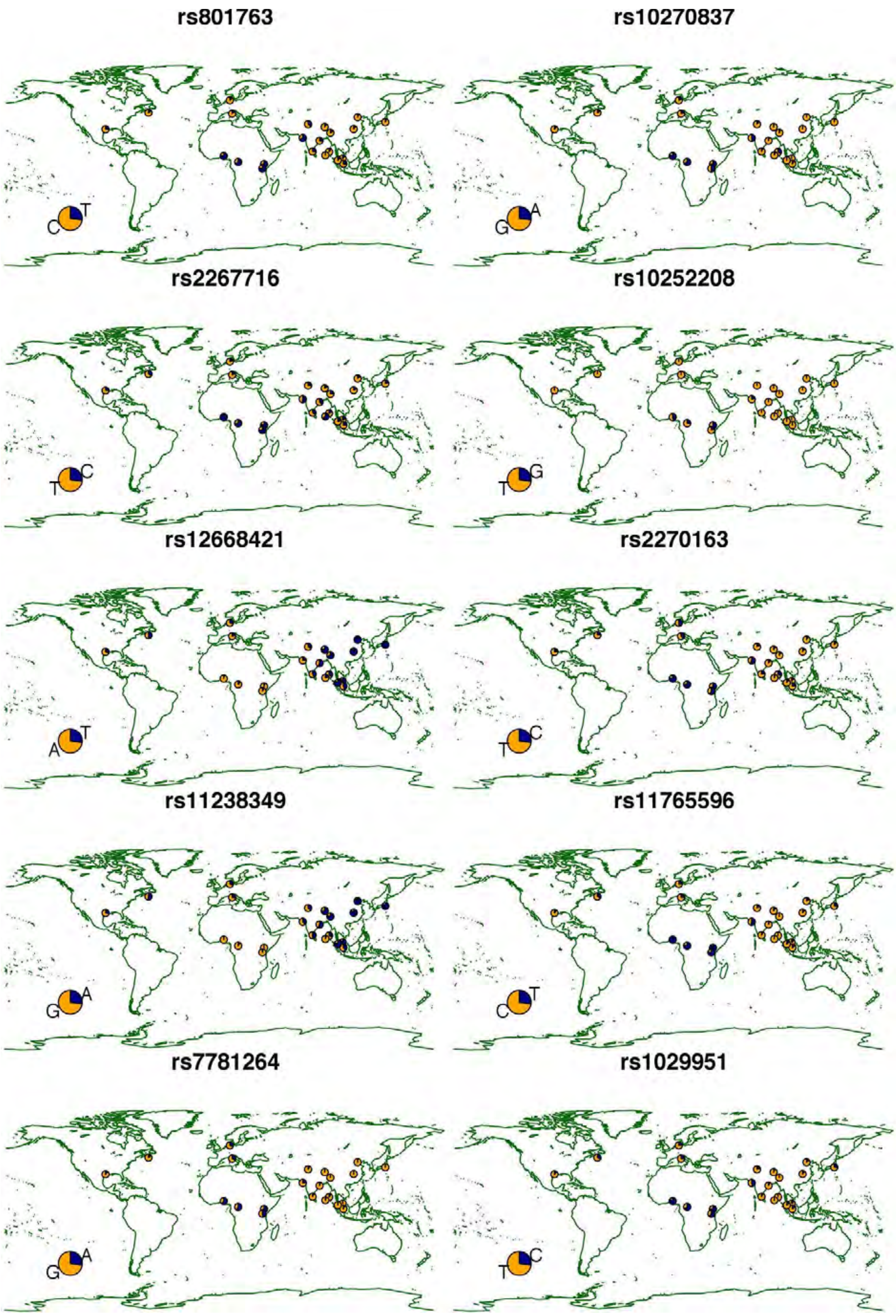
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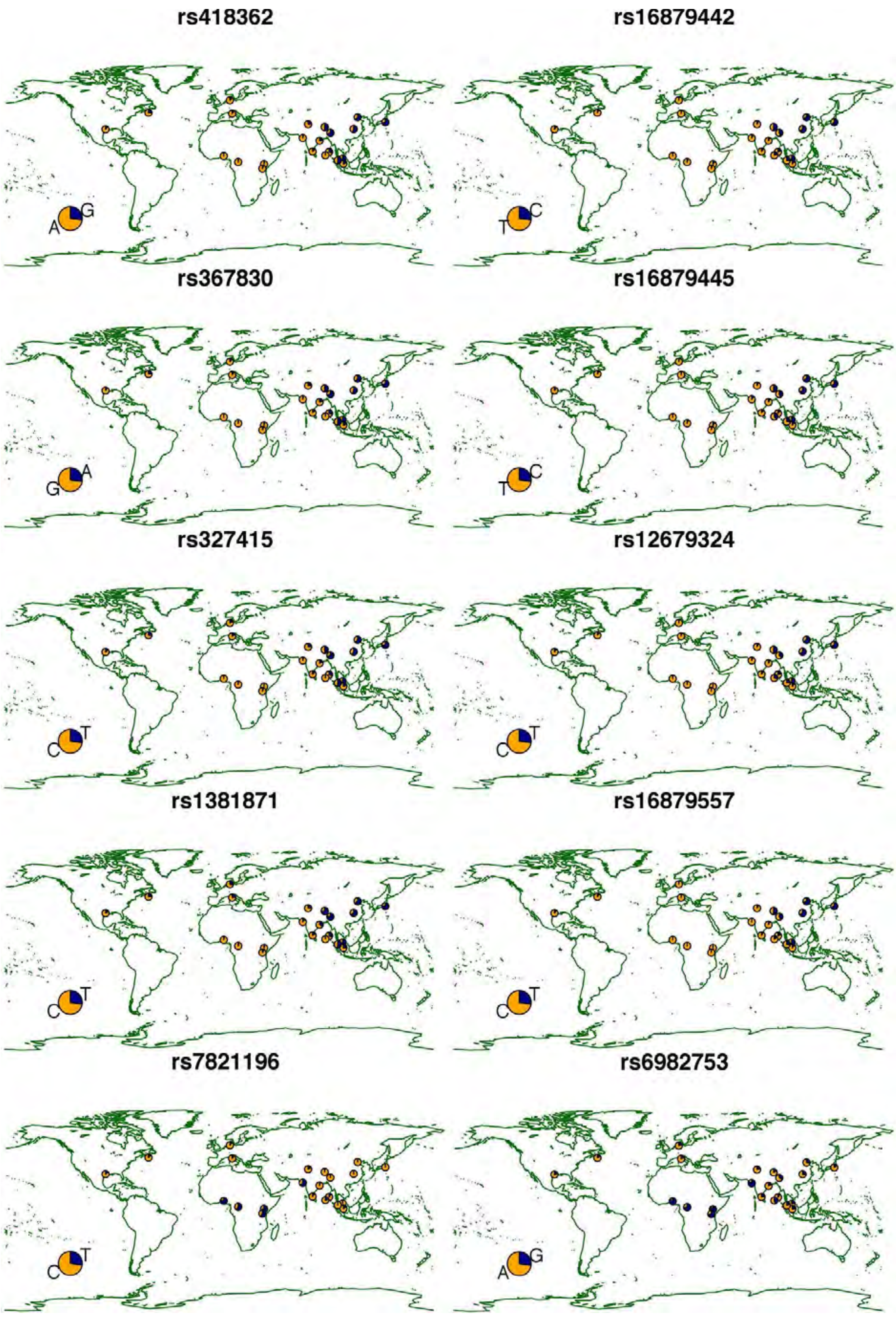
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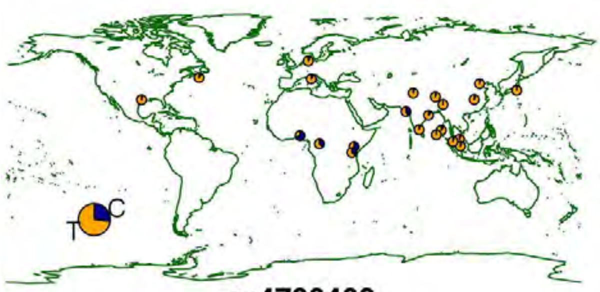

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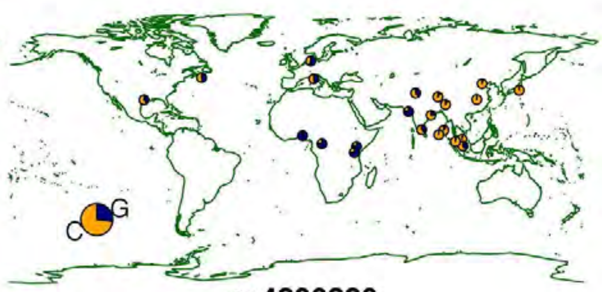

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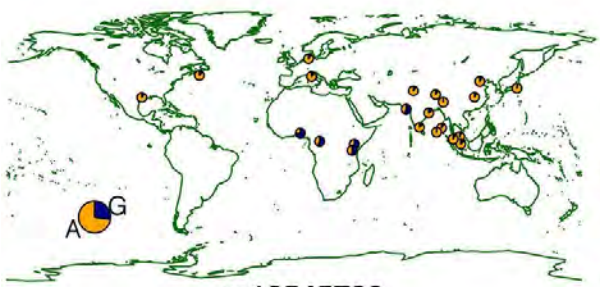

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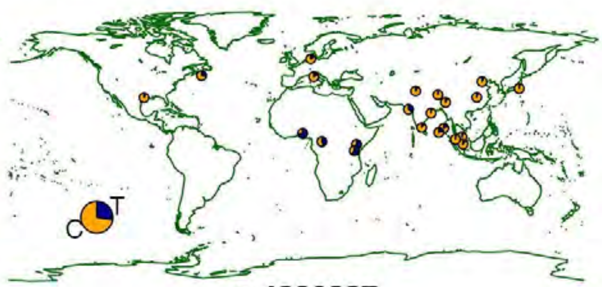

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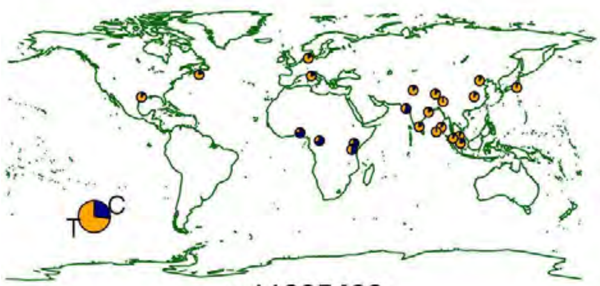

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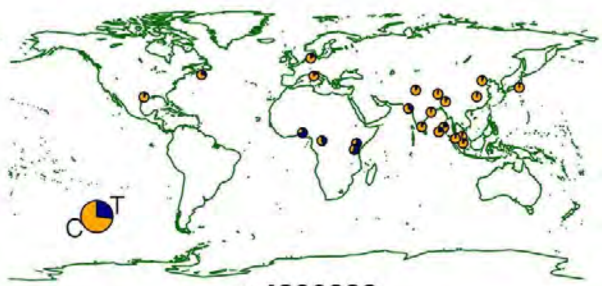

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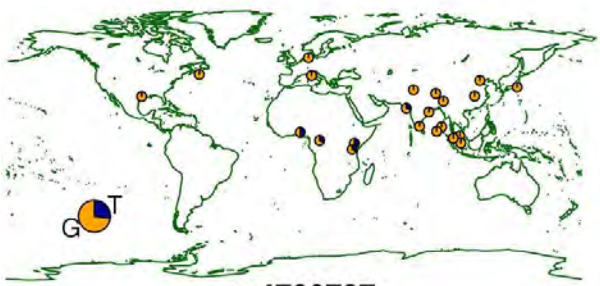

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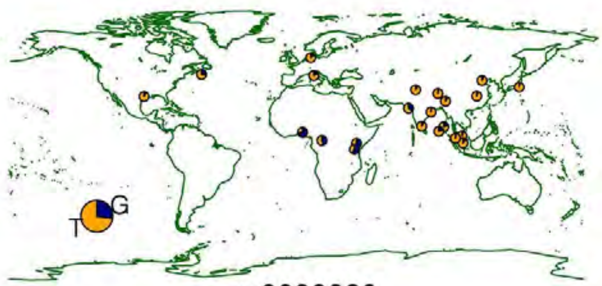

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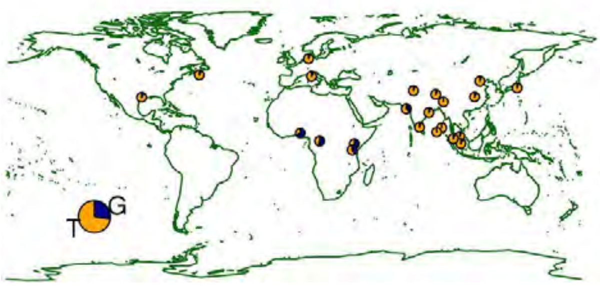

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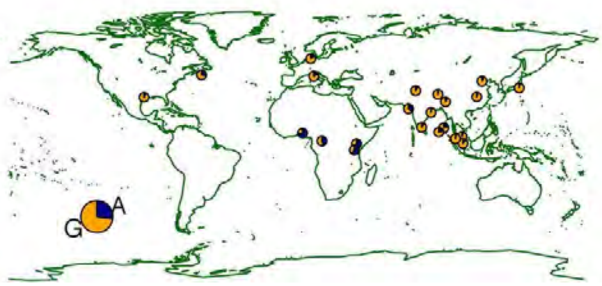

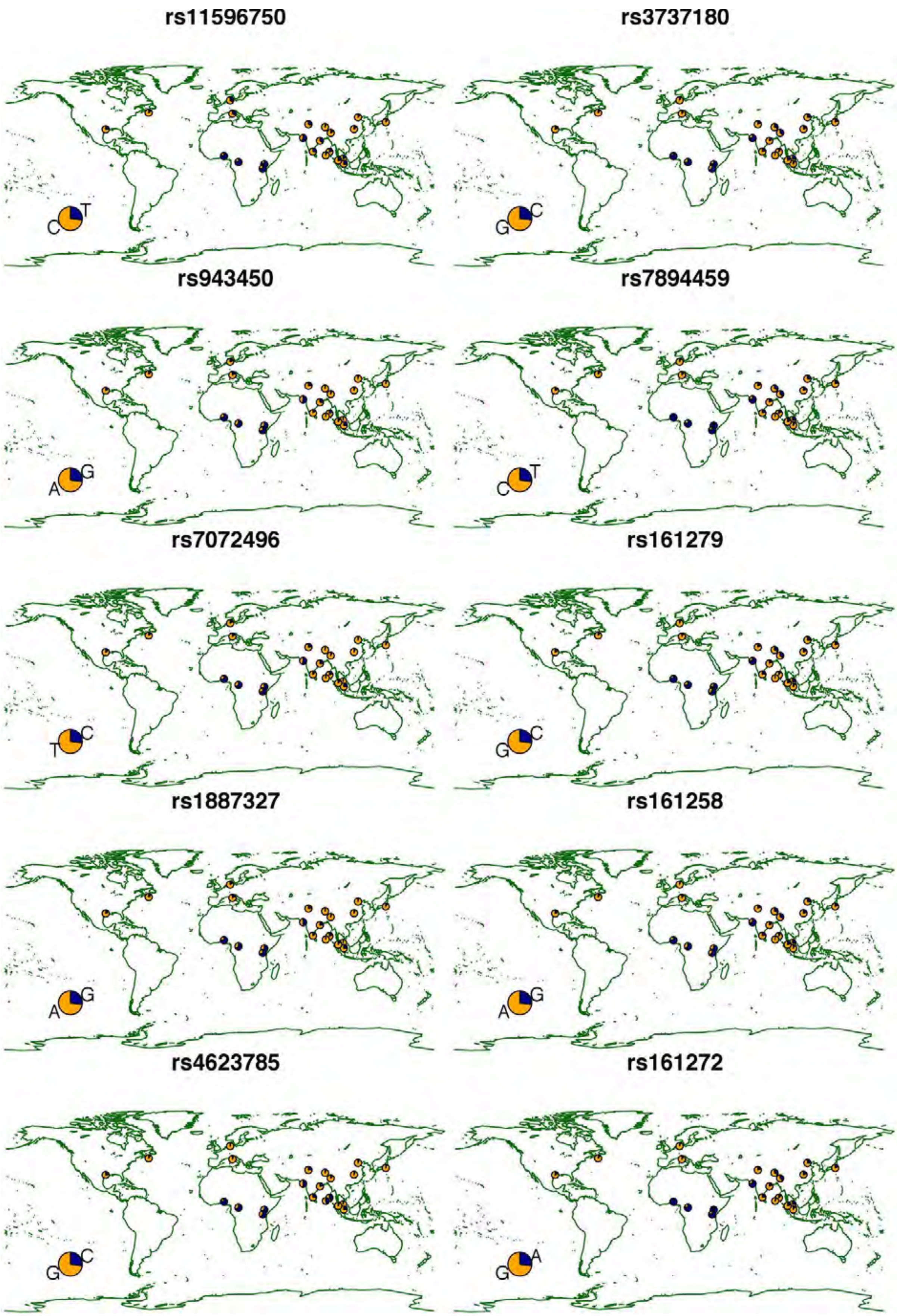
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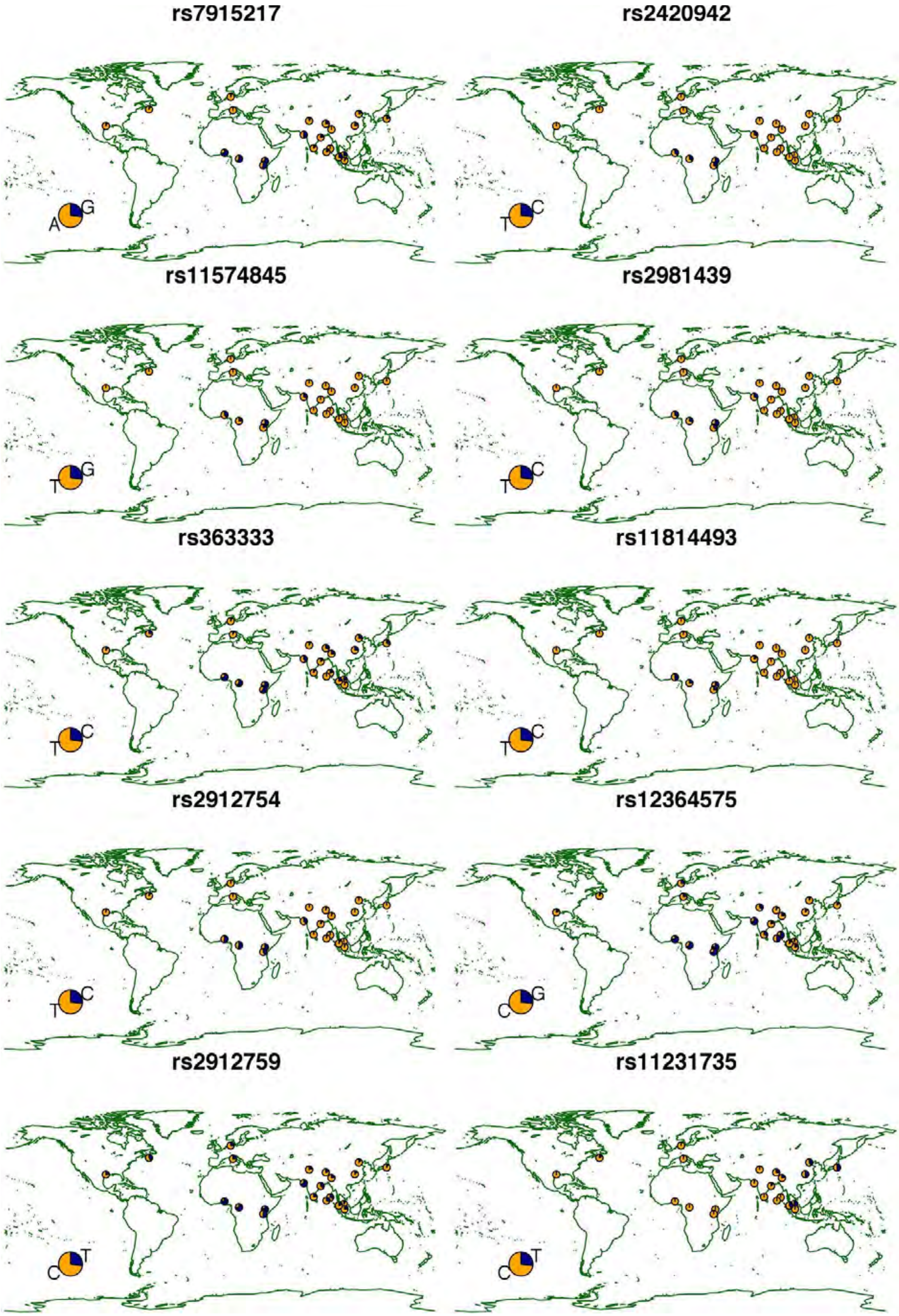
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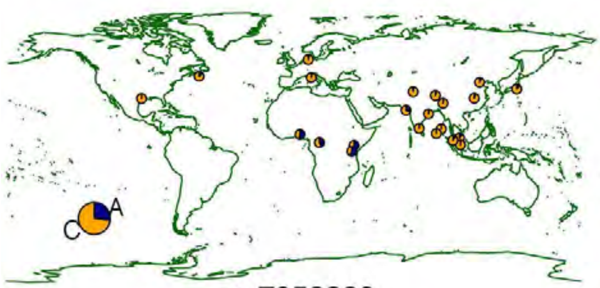

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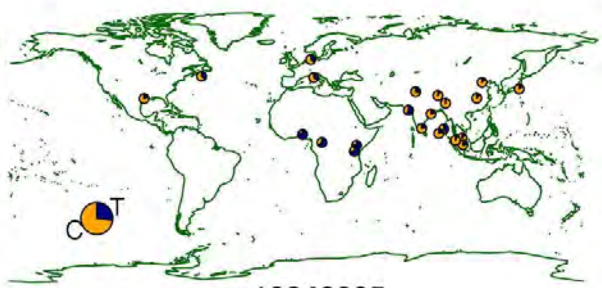

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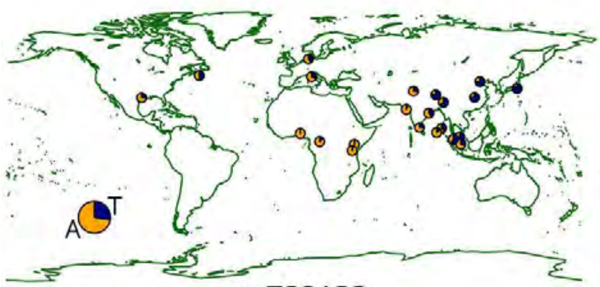

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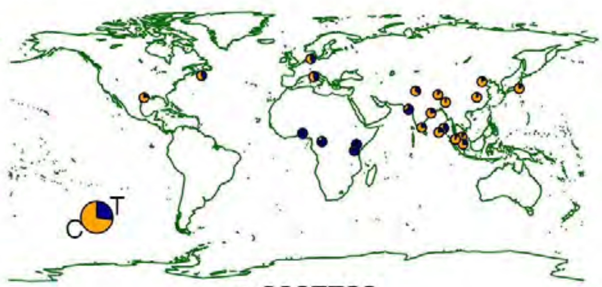

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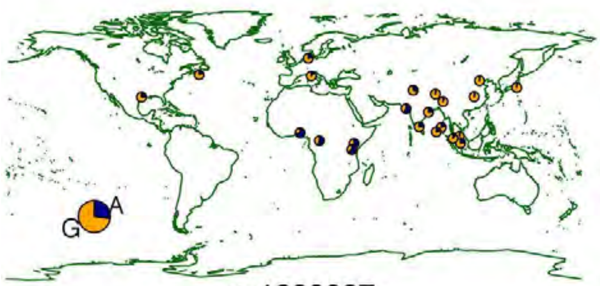

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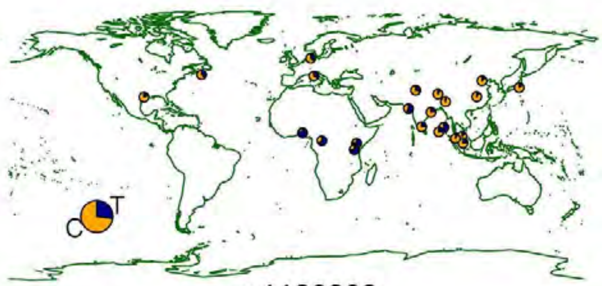

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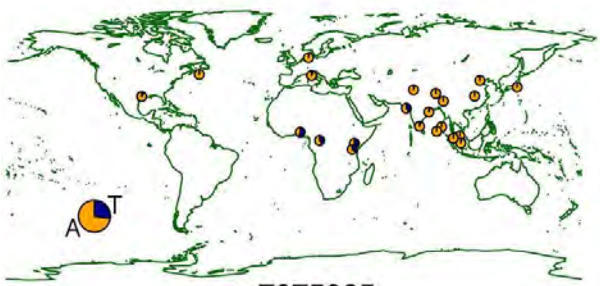

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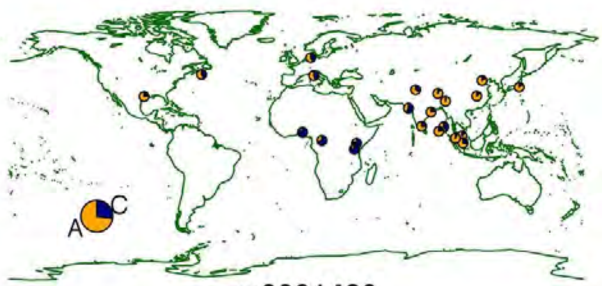

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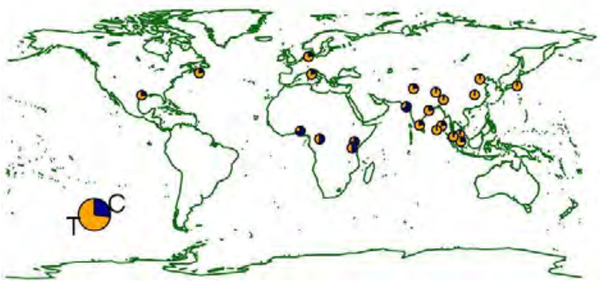

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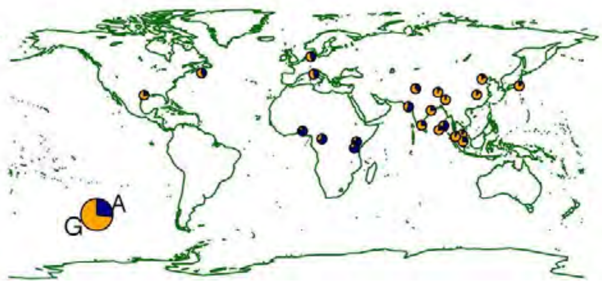

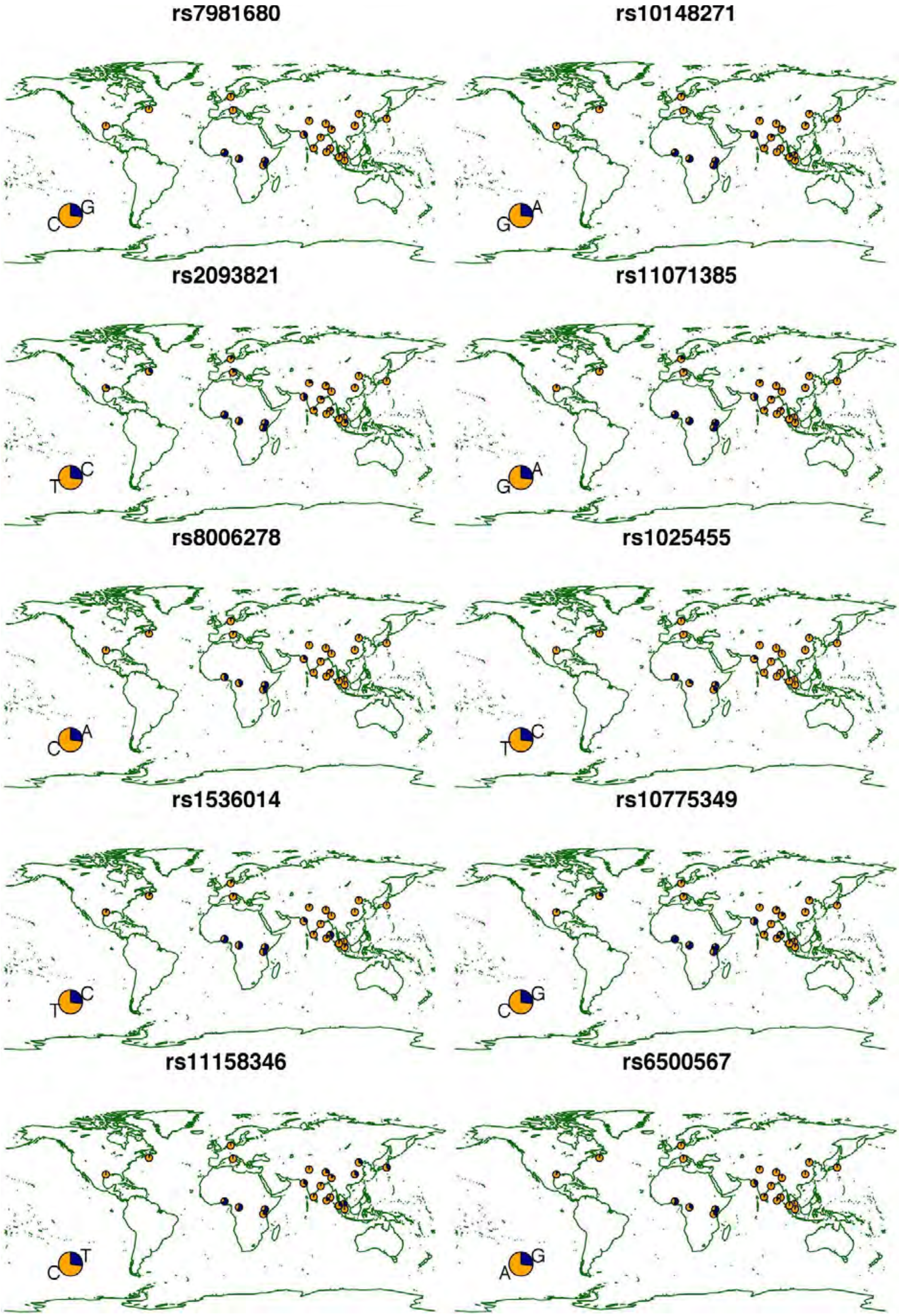
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C G
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C T
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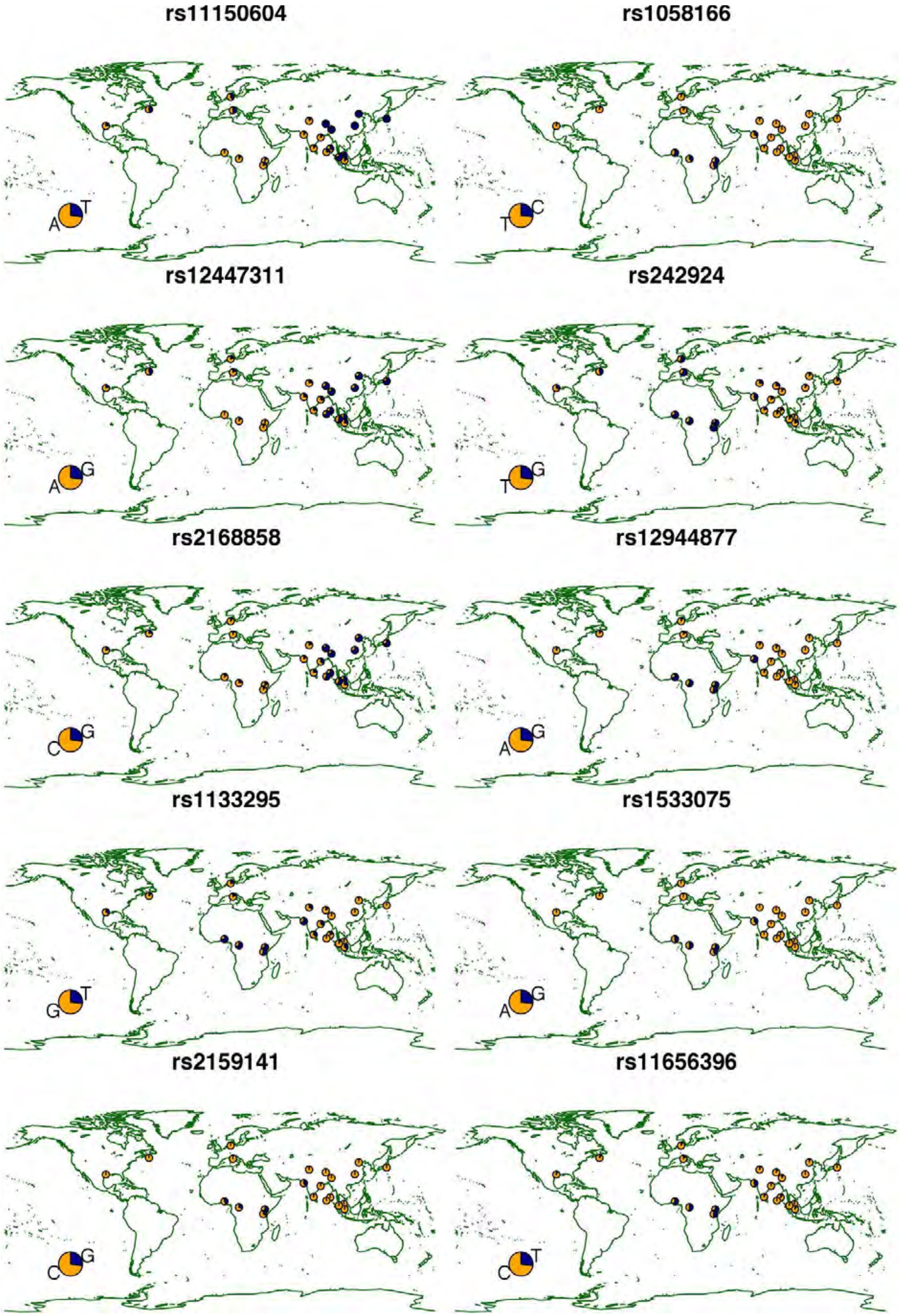
A G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A G
rs242924
T G
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rs12944877
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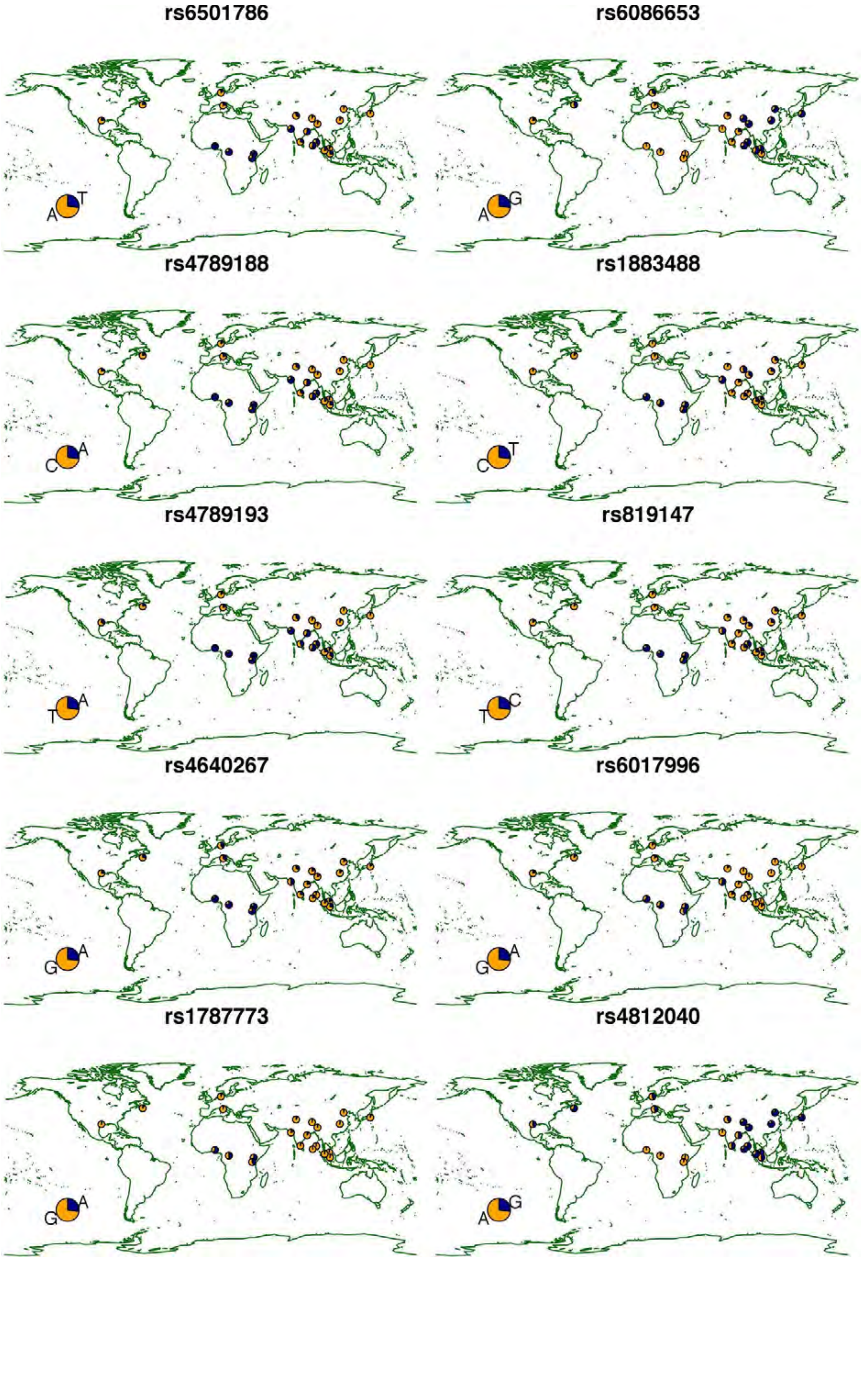
G T
rs1533075
A G
rs2159141
C G
rs11656396
C T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C
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G

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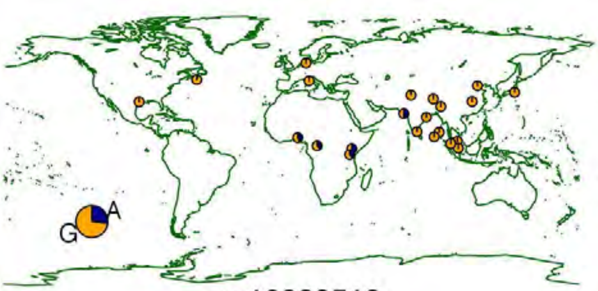

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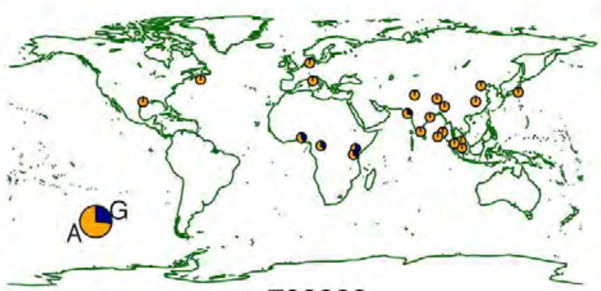

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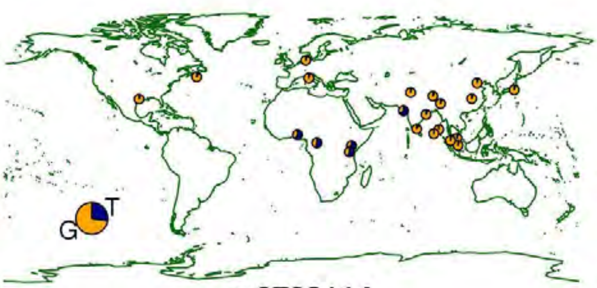

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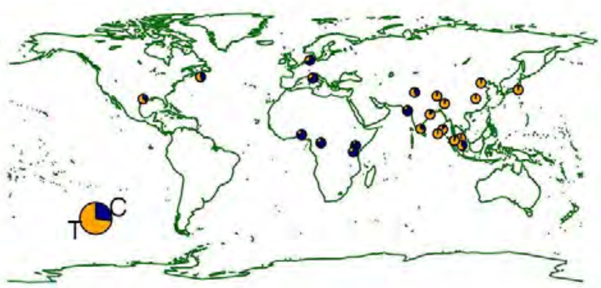

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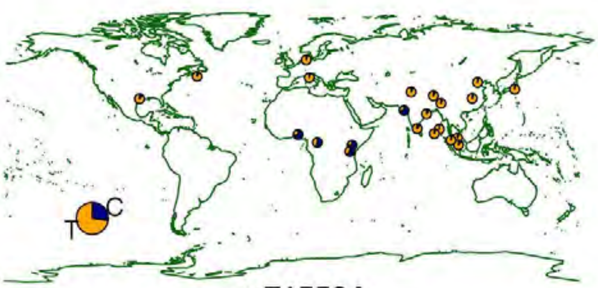

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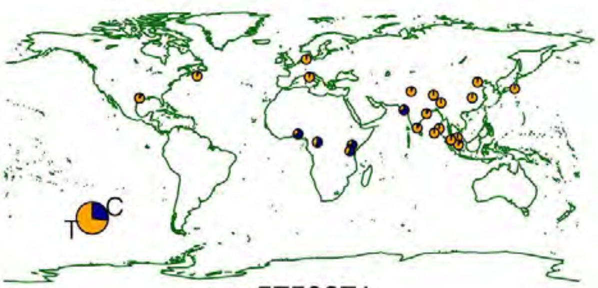

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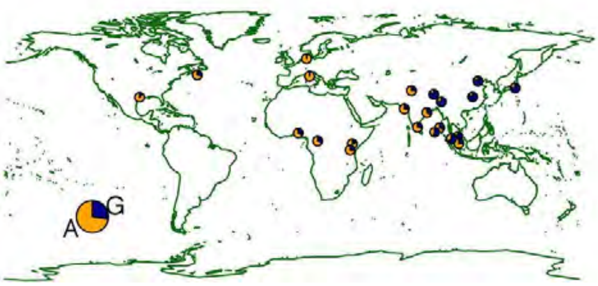
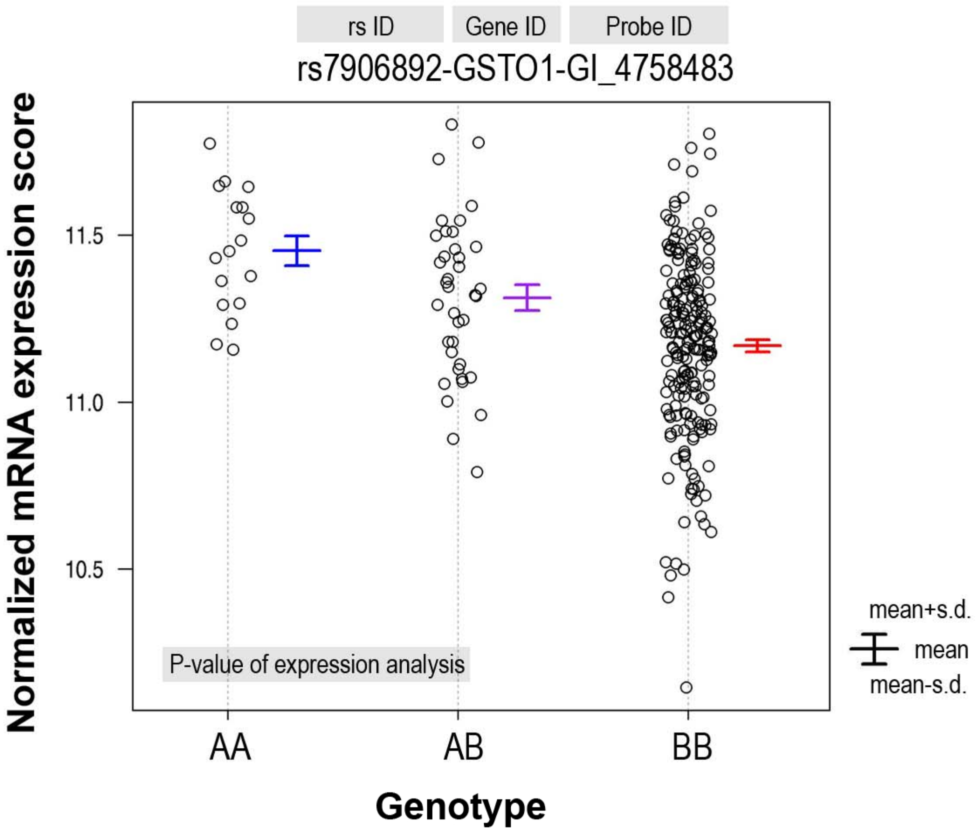
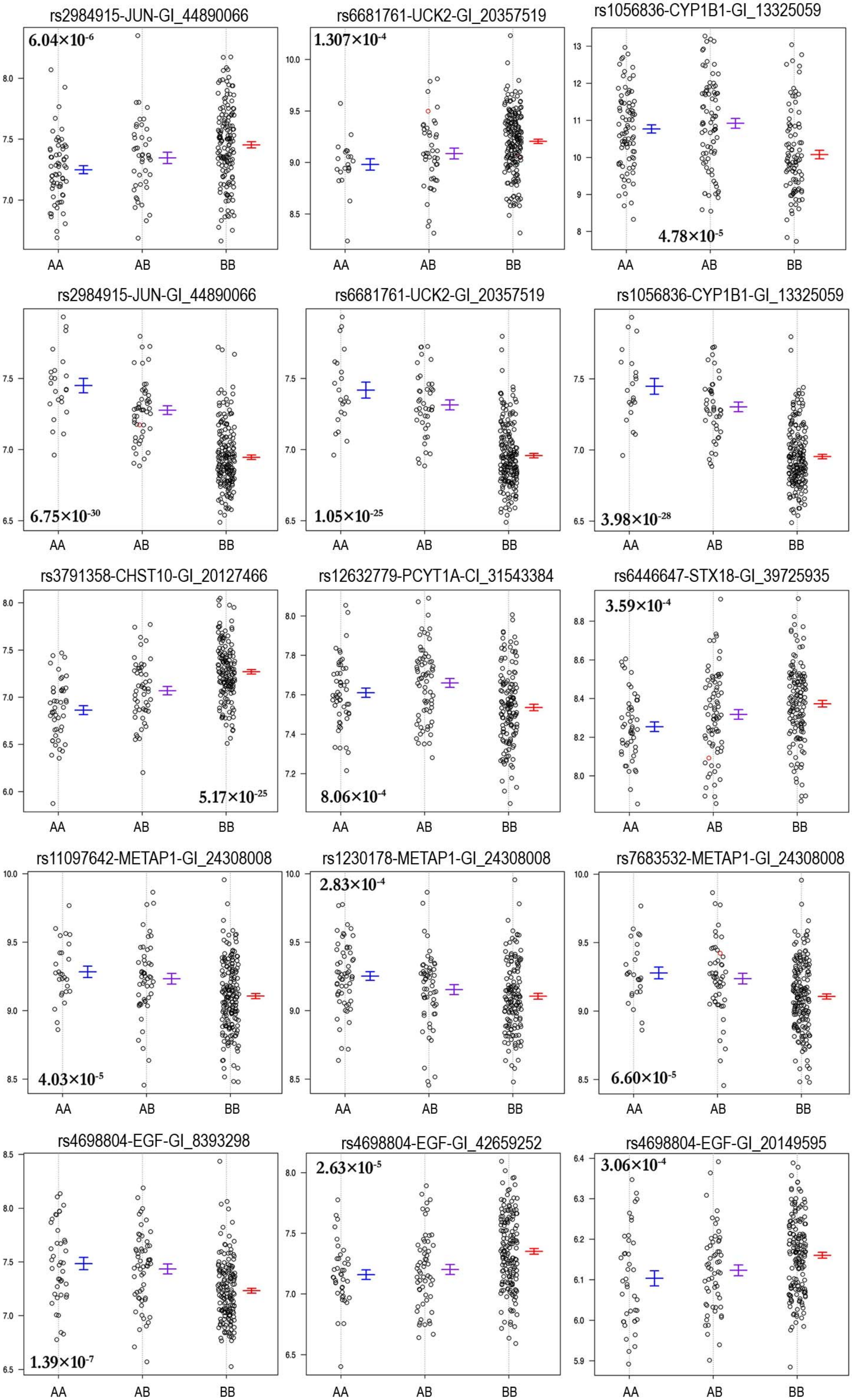


Figure S5: Quantitaive trait association analysis of Hard-sweep signals





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AA AB BB
rs6681761-UCK2-GI_20357519
1.307×10^-4
AA AB BB
rs1056836-CYP1B1-GI_13325059
4.78×10^-5
AA AB BB
rs2984915-JUN-GI_44890066
6.75×10^-30
AA AB BB
rs6681761-UCK2-GI_20357519
1.05×10^-25
AA AB BB
rs1056836-CYP1B1-GI_13325059
3.98×10^-28
AA AB BB
rs3791358-CHST10-GI_20127466
5.17×10^-25
AA AB BB
rs12632779-PCYT1A-GI_31543384
8.06×10^-4
AA AB BB
rs6446647-STX18-GI_39725935
3.59×10^-4
AA AB BB
rs11097642-METAP1-GI_24308008
4.03×10^-5
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rs1230178-METAP1-GI_24308008
2.83×10^-4
AA AB BB
rs7683532-METAP1-GI_24308008
6.60×10^-5
AA AB BB
rs4698804-EGF-GI_8393298
1.39×10^-7
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AA AB BB
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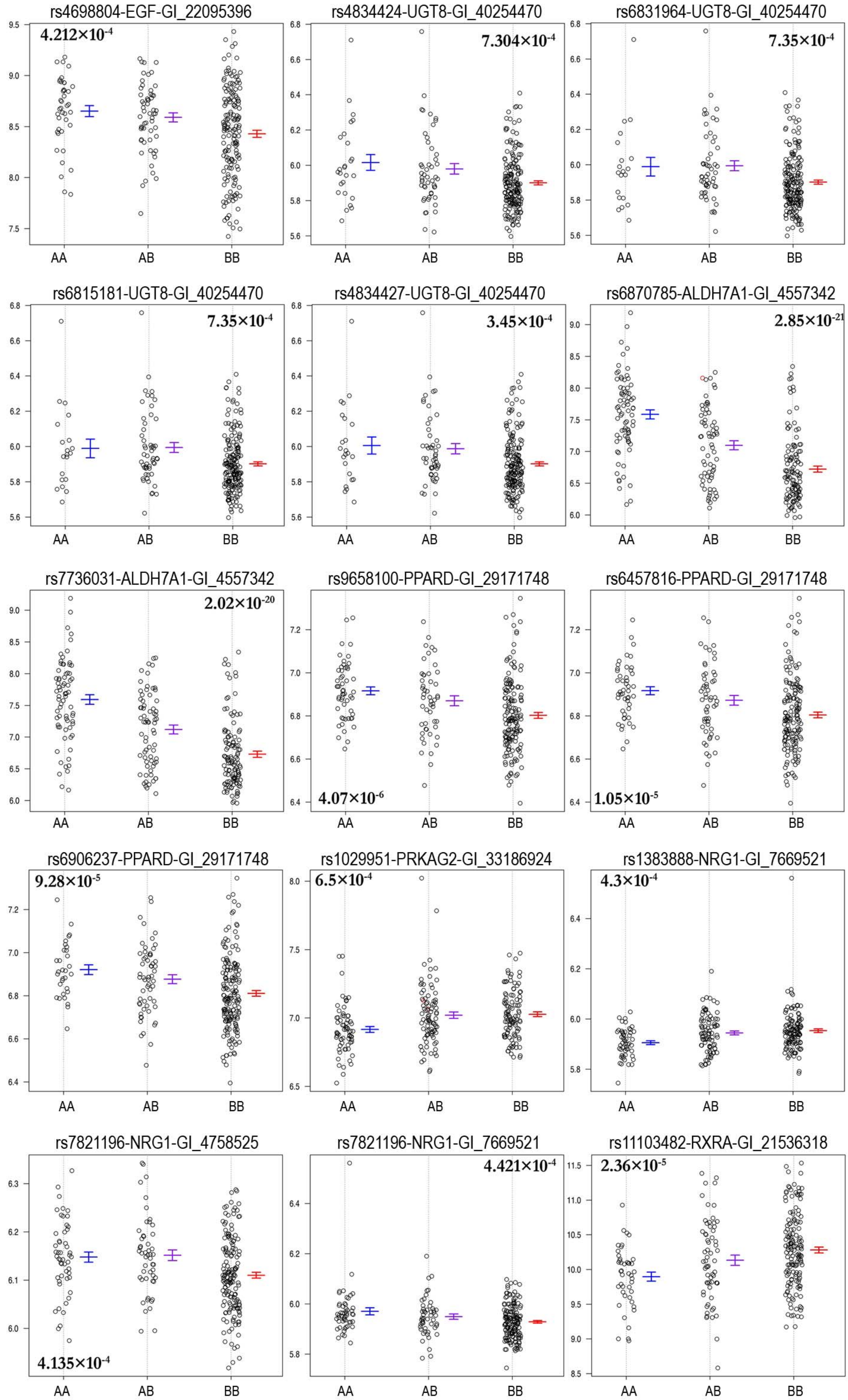
3.06×10^-4
AA AB BB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rs4834427-UGT8-GI_40254470
3.45×10^-4
rs6870785-ALDH7A1-GI_4557342
2.85×10^-21
rs7736031-ALDH7A1-GI_4557342
2.02×10^-20
rs9658100-PPARD-GI_29171748
4.07×10^-6
rs6457816-PPARD-GI_29171748
1.05×10^-5
rs6906237-PPARD-GI_29171748
9.28×10^-5
rs1029951-PRKAG2-GI_33186924
6.5×10^-4
rs1383888-NRG1-GI_7669521
4.3×10^-4
rs7821196-NRG1-GI_4758525
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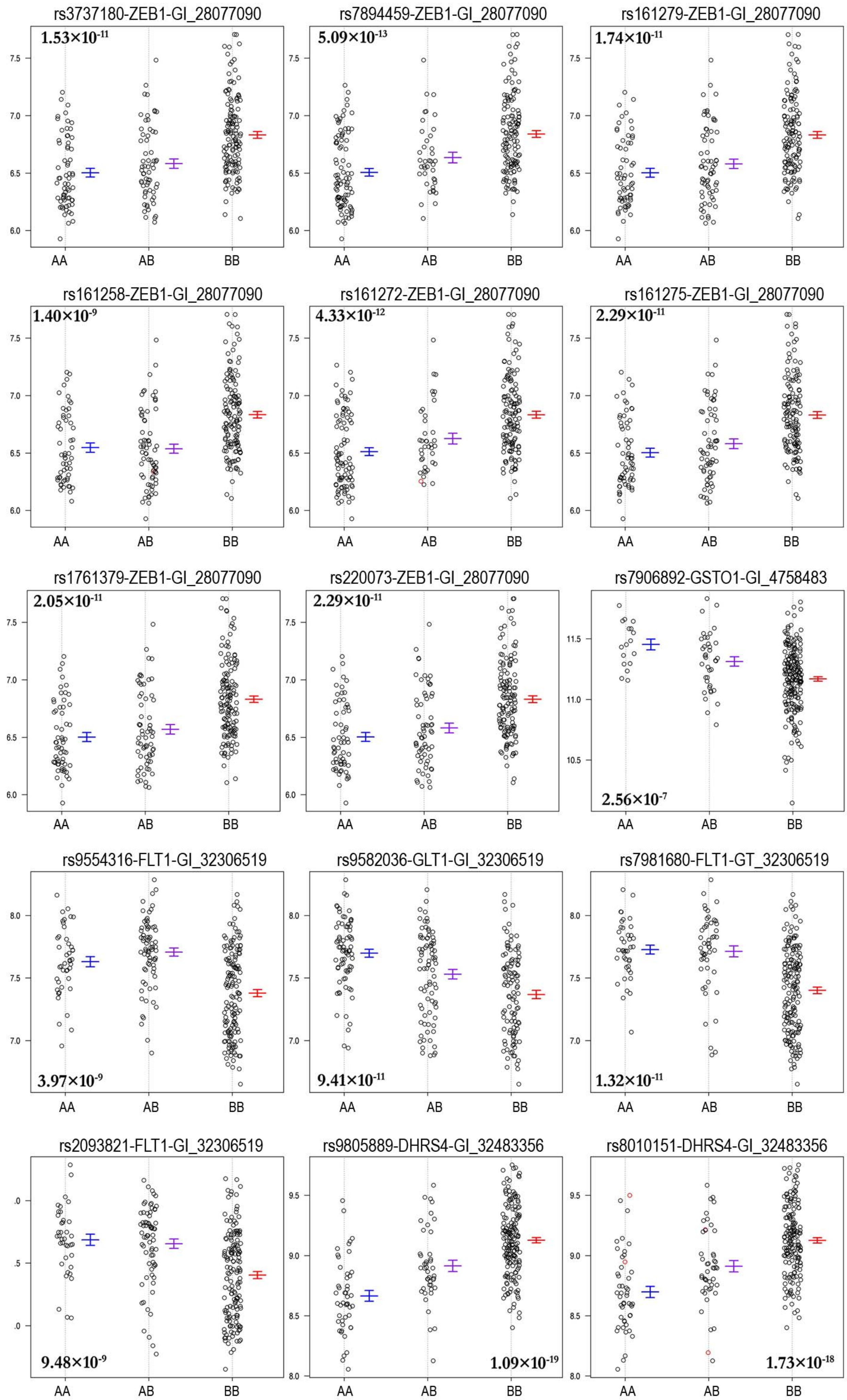
AA
AB
BB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rs161258-ZEB1-GI_28077090
1.40×10^{-9}
rs161272-ZEB1-GI_28077090
4.33×10^{-12}
rs161275-ZEB1-GI_28077090
2.29×10^{-11}
rs1761379-ZEB1-GI_28077090
2.05×10^{-11}
rs220073-ZEB1-GI_28077090
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rs7906892-GSTO1-GI_4758483
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rs9554316-FLT1-GI_32306519
3.97×10^{-9}
rs9582036-GLT1-GI_32306519
9.41×10^{-11}
rs7981680-FLT1-GT_32306519
1.32×10^{-11}
rs2093821-FLT1-GI_32306519
9.48×10^{-9}
rs9805889-DHRS4-GI_32483356
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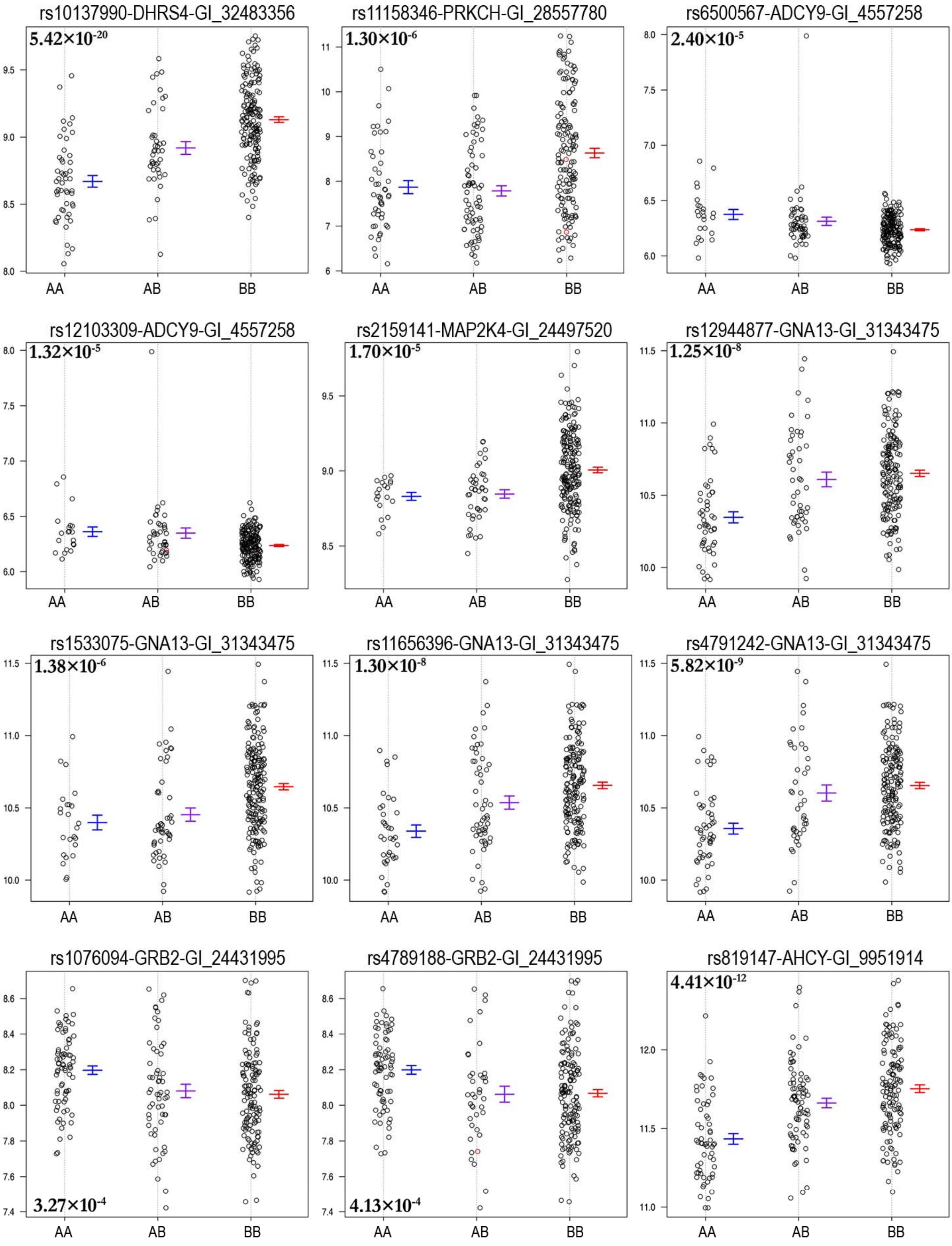
AA
AB
BB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1.30×10^{-6}
rs6500567-ADCY9-GI_4557258
2.40×10^{-5}
rs12103309-ADCY9-GI_4557258
1.32×10^{-5}
rs2159141-MAP2K4-GI_24497520
1.70×10^{-5}
rs12944877-GNA13-GI_31343475
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rs1533075-GNA13-GI_31343475
1.38×10^{-6}
rs11656396-GNA13-GI_31343475
1.30×10^{-8}
rs4791242-GNA13-GI_31343475
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rs1076094-GRB2-GI_24431995
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rs4789188-GRB2-GI_24431995
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AA
AB
BB

Figure S6: Age of the variants and their respective std-z score

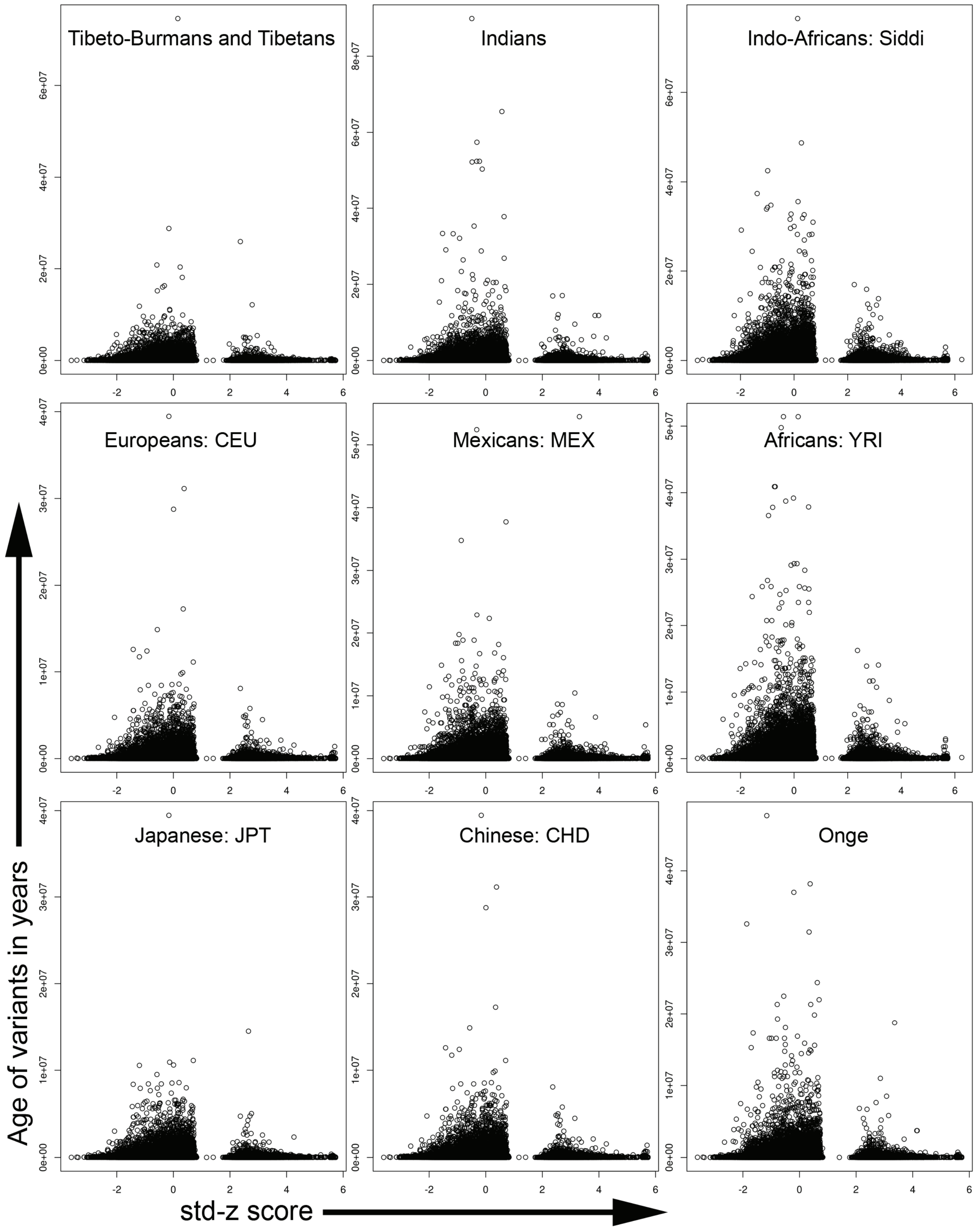

Table S1: Details of samples including source of data, number of individuals and their linguistic

#	Linguistic group	Caste	No. of individuals	Source of the data (Reference)
1	Austro-Asiatic	Kharia	5	1
2	Austro-Asiatic	Ho	5	2
3	Austro-Asiatic	Bhumij	5	2
4	Austro-Asiatic	Birhor	5	2
5	Austro-Asiatic	Korku	5	2
6	Austro-Asiatic	Munda	5	2
7	Austro-Asiatic	Gond_UP	5	2
8	Austro-Asiatic	Gond_chattisgarh	5	2
9	Austro-Asiatic	Gond_MP	5	2
10	Austro-Asiatic	Santhal	5	1
11	Dravidians	Paniyan	5	2
12	Dravidians	Paliyar	5	2
13	Dravidians	Kattunayakan	5	2
14	Dravidians	Irula	5	2
15	Dravidians	Chenchu	7	1
16	Dravidians	Madiga	13	1; 2
17	Dravidians	Adi-dravidian	5	2
18	Dravidians	Mala	12	1; 2
19	Dravidians	Kurumba	11	1
20	Dravidians	Kamsali	5	1
21	Dravidians	Mini	5	2
22	Dravidians	Kalliyar	5	2
23	Dravidians	Vysya	15	1; 2
24	Dravidians	Malaikuravara	5	2
25	Dravidians	Naidu	4	1
26	Dravidians	Malli	5	2
27	Dravidians	Hallaki	3	1
28	Dravidians	Velama	3	1
29	Dravidians	Gounder	5	2
30	Dravidians	Narikuravar	5	2
31	Dravidians	Jews	5	2
32	Dravidians	Jain	5	2
33	Indo-European	Sahariya	3	1
34	Indo-European	Satnami	2	1
35	Indo-European	Bhil_gujarat	11	1; 2
36	Indo-European	Tharu	4	1
37	Indo-European	Lodi	5	1
38	Indo-European	Bhil_MP	5	2
39	Indo-European	Meghawal	4	1
40	Indo-European	Vaish	2	1
41	Indo-European	Kshatriya-rajashthan	5	2
42	Indo-European	Kshatriya-UP	10	2
43	Indo-European	Brahmin	10	2
44	Indo-European	Kashmiri pandit	15	1; 2
45	Tibeto-Burmans	Aonaga	4	1
46	Tibeto-Burmans	Nyshi	3	1
47	Tibeto-Burmans	Sherpa	5	2
48	Tibeto-Burmans	Subba	5	2
49	Tibetans	Tibet refugees	5	2
50	Onge-Jarawas	Onge	10	1
51	Andamanese	Great-Andamanese	5	1
52	Indo-African	Siddi_gujarat	10	1; 2
53	Indo-African	Siddi_karnataka	4	2

54	Indian-II (Admix)	Singapore indians	83	http://www.statgen.nus.edu.sg/~SGVP/download.html
55	Malasians	Singapore malaysians	89	
56	East-Asians	Singapore chinese	96	
57	Indian-I (Admix)	HapMap-GIH	88	ftp://ftp.ncbi.nlm.nih.gov/hapmap/genotypes/2009-01_phaseIII/plink_format/
58	Africans	HapMap-ASW	83	
59	Africans	HapMap-LWK	90	
60	Africans	HapMap-MKK	171	
61	Africans	HapMap-YRI	167	
62	European	HapMap-CEU	165	
63	European	HapMap-TSI	88	
64	Mexicans	HapMap-MEX	77	
65	East-Asians	HapMap-CHB	84	
66	East-Asians	HapMap-CHD	85	
67	East-Asians	HapMap-JPT	86	
68	Tibetans	NCBI-GEO	31	GEO accession id: GSE21661

Table S2: Genome was divided into 20 bins (each 200,000 bps.) for standardization of z score. Corresponding number of SNPs, number of fragments and z-score distribution of bin were as given in the Table.

Bin No.	No. of SNPs in fragment	No. of fragments	Median	MAD/0.6745
1	1	766	-0.5187431	1.068024
2	2-15	744	-0.3738015	1.474672
3	16-21	758	-0.4474863	1.177962
4	22-25	659	-0.4181137	1.207891
5	26-28	630	-0.4671298	1.057244
6	29-31	644	-0.4697439	1.024041
7	32-34	702	-0.499824	1.05804
8	35-37	719	-0.4781689	1.046683
9	38-40	679	-0.5069641	1.060324
10	41-43	718	-0.490797	1.056721
11	44-46	713	-0.5020221	1.049941
12	47-49	647	-0.5120172	1.03602
13	50-52	642	-0.5120757	1.061145
14	53-55	609	-0.5017832	1.048398
15	56-59	745	-0.510556	1.048406
16	30-63	672	-0.5236802	1.069389
17	64-68	686	-0.5323148	1.053699
18	69-75	734	-0.5434064	1.061268
19	76-87	788	-0.5432452	1.082833
20	88-169	678	-0.5625902	1.089479

Table S3. Distribution of std-z score in genic and non-genic regions with variation in flanking region

All genomic markers (623462 SNPs)					
	Genic std-z score		Non-genic std-z score		Ratio of Genic/Non-genic
Flanking region (bps)	Median	MAD./0.6745	Median	MAD./0.6745	Median
0	0.0046	0.9996	-0.0031	0.9999	-1.4785
2000	0.0039	1.0004	-0.0028	0.9992	-1.3623
5000	0.0038	1.0002	-0.0031	0.9994	-1.2117
10000	0.0034	1	-0.0033	0.9997	-1.032
20000	0.0031	1.0005	-0.0037	0.9992	-0.8323
50000	0.0025	0.9992	-0.0046	1.0012	-0.54
100000	0.0018	0.9988	-0.0049	1.0028	-0.3702

Table S4. Central tendency and statistical dispersion of std-z score in different categories

Category	**Median**	**M.A.D./0.6745**
Transporter	-0.0859228	0.989056
Core	-0.0103867	0.9024186
Extended	-0.0184088	0.9981437
PhaseI	0.0066892	0.9578569
PhaseII	0.04865	1.005386
Modifier	0.0331328	0.9534738
All Pathway genes	0.0048129	0.9915011
Other Pathway genes	0.0036548	0.9985724
All Pharma genes	-0.0172291	0.9903678

Table S5. Number of SNPs having std-z score > 3 and their corresponding percentage in different categories

Category	Total genes	Total genes after filtering	Number of genes having std-z score >3 (percentage)
Core	32	26	3 (11.54)
Extended	257	236	44 (18.64)
Transporter	76	72	15 (20.83)
Phase-I	123	114	20 (17.54)
Phase-II	66	54	6 (11.11)
Modifier	**24**	**22**	**6 (27.27)**
Other pathway genes	688	611	100 (16.37)

Table S6. PharmGKB pathways, which are excluded due to less number of genes

Pathway	**# of genes**
Fluoropyrimidine Pathway Pharmacodynamic	1
Amodiaquine Pathway Pharmacokinetics	3
Anti diabetic Drug Nateglinide Pathway Pharmacokinetics	3
Anti diabetic Drug Repaglinide Pathway Pharmacokinetics	3
Aromatase Inhibitor Pathway Breast Cell Pharmacodynamics	3
Aromatase Inhibitor Pathway Multiple Tissues Pharmacodynamics	3
Citalopram Pathway Pharmacokinetics	3
Clomipramine Pathway Pharmacokinetics	3
Imipramine Desipramine Pathway Pharmacokinetics	3
Methylene Blue Pathway Pharmacodynamics	3
Proton Pump Inhibitor Pathway Pharmacokinetics	3
Rosiglitazone Pharmacokinetic Pathway	3
Tacrolimus Cyclosporine Pathway Pharmacokinetics	3
Uric Acid Lowering Drugs Pathway Pharmacodynamics	3
Celecoxib Pathway Pharmacokinetics	4
Doxepin Pathway Pharmacokinetics	4
Fluoxetine Pathway Pharmacokinetics	4
Nicotine Pathway Chromaffin Cell Pharmacodynamics	4
Pentose Phosphate Pathway Erythrocyte	4
Platinum Pathway Pharmacokinetics Pharmacodynamics	4
Rosuvastatin Pathway Pharmacokinetics	4
Theophylline Pathway Pharmacokinetics	4
Venlafaxine Pathway Pharmacokinetics	4
Artemisinin and Derivatives Pathway Pharmacokinetics	5
Glucocorticoid Pathway HPA Axis Pharmacodynamics	5
Losartan Pathway Pharmacokinetics	5
Nevirapine Pathway Pharmacokinetics	5
Oxidative Stress Regulatory Pathway Erythrocyte	5
Cyclophosphamide Pathway Pharmacokinetics	6
Ifosfamide Pathway Pharmacokinetics	6
Leukotriene modifiers pathway Pharmacodynamics	6
Metformin Pathway Pharmacokinetics	6
Sorafenib Pharmacokinetics	6
Tramadol Pharmacokinetics	6
Caffeine Pathway Pharmacokinetics	7
Gefitinib Pathway Pharmacokinetics	7
Methotrexate Pathway Brain Cell Pharmacokinetics	7
Codeine and Morphine Pathway Pharmacokinetics	8
Estrogen Metabolism Pathway	8
Nicotine Pathway Pharmacokinetics	8
TenofovirAdefovir Pathway Pharmacokinetics	8
Warfarin Pathway Pharmacokinetics	8
Benzodiazepine Pathway Pharmacokinetics	9
Erlotinib Pathway Pharmacokinetics	9
Pravastatin Pathway Pharmacokinetics	9

Table S7. Statistical significance of different pathways.

	Pathway	Total Genes	Hump1 (11399: 0.6869)	Hump2 (5031: 0.3032)	Hump3 (164: 0.0099)	chisq: p-value	q value
1	**Taxane Pathway Pharmacokinetics**	**10**	**3 (0.3)**	**5 (0.5)**	**2 (0.2)**	**2.53×10-09**	**1.28×10-07**
2	**Fluvastatin Pathway Pharmacokinetics**	**12**	**8 (0.666666667)**	**2 (0.166666667)**	**2 (0.166666667)**	**2.73×10-07**	**6.91×10-06**
3	**Atorvastatin-Lovastatin-Simvastatin Pathway Pharmacokinetics**	**13**	**9 (0.692307692)**	**2 (0.153846154)**	**2 (0.153846154)**	**8.79×10-07**	**1.48×10-05**
4	**Ibuprofen Pathway Pharmacokinetics**	**16**	**11 (0.6875)**	**3 (0.1875)**	**2 (0.125)**	**1.76×10-05**	**0.000222609**
5	**Statin Pathway Generalized Pharmacokinetics**	**19**	**10 (0.526315789)**	**7 (0.368421053)**	**2 (0.105263158)**	**0.0001085**	**0.001097864**
6	**β-agonist/β-blocker Pathway Pharmacodynamics**	**58**	**26 (0.448275862)**	**31 (0.534482759)**	**1 (0.017241379)**	**0.0004794**	**0.004042367**
7	**Zidovudine Pathway Pharmacokinetics & Pharmacodynamics**	**17**	**5 (0.294117647)**	**11 (0.647058824)**	**1 (0.058823529)**	**0.0007003**	**0.005061452**
8	Sympathetic-Nerve Pathway Pre & Post Ganglionic Junction	10	2 (0.2)	8 (0.8)	0 (0)	0.002911	0.01840947
9	Proton Pump Inhibitor Pathway Pharmacodynamics	45	21 (0.466666667)	24 (0.533333333)	0 (0)	0.003276	0.01841579
10	Celecoxib Pathway Pharmacodynamics	54	27 (0.5)	27 (0.5)	0 (0)	0.006292	0.03183301
11	EGFR Inhibitor Pathway Pharmacodynamics	62	32 (0.52)	30 (0.48)	0 (0)	0.007171	0.03298031
12	Imatinib Pathway Pharmacokinetics Pharmacodynamics	10	5 (0.5)	4 (0.4)	1 (0.1)	0.01119	0.05146671
13	Vinka Alkaloid Pathway Pharmacokinetics	10	6 (0.6)	3 (0.3)	1 (0.1)	0.01594	0.0620346
14	Clopidogrel Pathway Pharmacokinetics	10	6 (0.6)	3 (0.3)	1 (0.1)	0.01594	0.0620346
15	Mycophenolicacid Pathway PharmacokineticsP harmacodynamics	12	9 (0.75)	2 (0.166666667)	1 (0.083333333)	0.02576	0.09309081
16	Irinotecan Pathway Pharmacokinetics	13	7 (0.538461538)	5 (0.384615385)	1 (0.076923077)	0.03731	0.1228141
17	Tamoxifen Pathway Pharmacokinetics	16	13 (0.8125)	2 (0.125)	1 (0.0625)	0.03884	0.1228141
18	Methotrexate Pathway Pharmacokinetics	13	8 (0.615384615)	4 (0.307692308)	1 (0.076923077)	0.05045	0.1501417
19	Etoposide Pathway Pharmacokinetics Pharmacodynamics	14	8 (0.571428571)	5 (0.357142857)	1 (0.071428571)	0.05672	0.1594236
20	Phenytoin Pathway Pharmacokinetics	16	12 (0.75)	3 (0.1875)	1 (0.0625)	0.07232	0.1925723
21	Carbamazepine Pathway Pharmacokinetics	16	9 (0.5625)	6 (0.375)	1 (0.0625)	0.07859	0.1988045
22	Valproic Acid Pathway Pharmacodynamics	14	6 (0.428571429)	8 (0.571428571)	0 (0)	0.09002	0.2168746
23	Vemurafenib Pathway Pharmacodynamics	22	11 (0.5)	11 (0.5)	0 (0)	0.1262	0.2902189
24	Sorafenib Pharmacodynamics	25	13 (0.52)	12 (0.48)	0 (0)	0.1472	0.3237941
25	Acetaminophen Pathway Pharmacokinetics	19	12 (0.631578947)	6 (0.315789474)	1 (0.052631579)	0.1664	0.3397815
26	VEGFSignaling Pathway	56	32 (0.571428571)	23 (0.410714286)	1 (0.017857143)	0.1679	0.3397815
27	Lamivudine Pathway Pharmacokinetics/Pharmacodynamics	16	8 (0.5)	8 (0.5)	0 (0)	0.2217	0.4314012
28	Cyclophosphamide Pathway Pharmacodynamics	14	7 (0.5)	7 (0.5)	0 (0)	0.2676	0.5014312
29	Diuretics Pathway Pharmacodynamics	26	16 (0.615384615)	9 (0.346153846)	1 (0.038461538)	0.2883	0.5209255
30	Selective Serotonin Reuptake Inhibitor Pathway Pharmacodynamics	25	14 (0.56)	11 (0.44)	0 (0)	0.3053	0.5326204
31	Uricosurics Pathway Pharmacodynamics	12	6 (0.5)	6 (0.5)	0 (0)	0.323	0.536284
32	Metformin Pathway Pharmacodynamic	27	19 (0.703703704)	7 (0.259259259)	1 (0.037037037)	0.3354	0.536284

33	Thiopurine Pathway Pharmacokinetics Pharmacodynamics	20	11 (0.55)	9 (0.45)	0 (0)	0.3392	0.536284
34	Platelet Aggregation Inhibitor Pathway Pharmacodynamics	48	29 (0.604166667)	18 (0.375)	1 (0.020833333)	0.3926	0.6019014
35	Doxorubicin athway Pharmacokinetics	21	12 (0.571428571)	9 (0.428571429)	0 (0)	0.427	0.6353865
36	Ifosfamide Pathway Pharmacodynamics	13	7 (0.538461538)	6 (0.461538462)	0 (0)	0.445	0.6432517
37	Antidiabetic Drug Potassium Channe lInhibitors Pathway Pharmacodynamics	26	16 (0.615384615)	10 (0.384615385)	0 (0)	0.6011	0.8033018
38	Methotrexate Pathway Cancer Cell Pharmacodynamics	15	12 (0.8)	3 (0.2)	0 (0)	0.6208	0.8033018
39	Tacrolimus Cyclosporine Pathway Pharmacodynamics	39	25 (0.641025641)	14 (0.358974359)	0 (0)	0.6363	0.8033018
40	Doxorubicin Pathway Cancer Cell Pharmacodynamics	12	7 (0.583333333)	5 (0.416666667)	0 (0)	0.6652	0.8033018
41	Gemcitabine Pathway	12	7 (0.583333333)	5 (0.416666667)	0 (0)	0.6652	0.8033018
42	Valproic Acid Pathway Pharmacokinetics	18	14 (0.777777778)	4 (0.222222222)	0 (0)	0.6761	0.8033018
43	Fluoropyrimidine Pathway Pharmacokinetics	21	13 (0.619047619)	8 (0.380952381)	0 (0)	0.6816	0.8033018
44	Busulfan Pathway Pharmacodynamics	14	11 (0.785714286)	3 (0.214285714)	0 (0)	0.7041	0.8033018
45	Benzodiazepine Pathway Pharmacodynamics	14	11 (0.785714286)	3 (0.214285714)	0 (0)	0.7041	0.8033018
46	Doxorubicin Pathway Cardiomyocyte Cell Pharmacodynamics	21	16 (0.761904762)	5 (0.238095238)	0 (0)	0.7145	0.8033018
47	Bisphosphonate Pathway Pharmacodynamics	16	10 (0.625)	6 (0.375)	0 (0)	0.7713	0.846192
48	Antimetabolite Pathway Folate Cycle Pharmacodynamics	13	10 (0.769230769)	3 (0.230769231)	0 (0)	0.7861	0.846192
49	Nicotine Pathway Dopaminergic Neuron Pharmacodynamics	43	30 (0.697674419)	13 (0.302325581)	0 (0)	0.8056	0.8466169
50	Irinotecan Pathway Pharmacodynamics	14	9 (0.642857143)	5 (0.357142857)	0 (0)	0.8555	0.8466169
51	Sympathetic Nerve Pathway Neuroeffector Junction	21	15 (0.714285714)	6 (0.285714286)	0 (0)	0.8818	0.8466169
52	Statin Pathway Pharmacodynamics	22	15 (0.681818182)	7 (0.318181818)	0 (0)	0.8893	0.8466169
53	Abacavir Pathway Pharmacokinetics Pharmacodynamics	11	8 (0.727272727)	3 (0.272727273)	0 (0)	0.9193	0.8466169
54	Gemtuzumabozogamicin Pathway Pharmacokinetics Pharmacodynamics	16	11 (0.6875)	5 (0.3125)	0 (0)	0.9219	0.8466169
55	ACEInhibitor Pathway Pharmacodynamics	16	11 (0.6875)	5 (0.3125)	0 (0)	0.9219	0.8466169
56	Agents Acting on the Renin Angiotensin System Pathway Pharmacodynamics	16	11 (0.6875)	5 (0.3125)	0 (0)	0.9219	0.8466169
57	Warfarin Pathway Pharmacodynamics	13	9 (0.692307692)	4 (0.307692308)	0 (0)	0.9371	0.8466169

Table S8. Std-z score of representative SNP (with highest std-z score) of genes in the pathways which are under natural selection.

Pathway	SNP-ID	Gene	Std-z score
Taxane pathways: Pharmacokinetics	rs7909236	*CYP2C8*	0.648219785
	rs17216177	*ABCC2*	0.698375272
	rs3784863	*ABCC1*	0.715639496
	rs1202184	*ABCB1*	2.337419052
	rs10242455	*CYP3A5*	2.96776873
	rs1056836	*CYP1B1*	3.136306384
	rs1403527	*NR1I2*	3.361005362
	rs2622610	*ABCG2*	3.662585022
	rs2196019	*SLCO1B3*	5.578785151
	rs1851426	*CYP3A4*	5.60910014
Fluvastatin pathways: pharmacokinetics	rs6742078	*UGT1A1*	0.455625814
	rs1054804	*UGT1A3*	0.592583812
	rs4641393	*CYP2C19*	0.601325053
	rs7909236	*CYP2C8*	0.648219785
	rs6600884	*UGT2B7*	0.674197776
	rs11045821	*SLCO1B1*	0.680895057
	rs12361540	*SLCO2B1*	0.687367222
	rs9332242	*CYP2C9*	0.711510074
	rs4772126	*SLC15A1*	2.723151041
	rs10242455	*CYP3A5*	2.96776873
	rs2196019	*SLCO1B3*	5.578785151
	rs1851426	*CYP3A4*	5.60910014
Atorvastatin, Lovastatin, Simvastatin pathways: pharmacokinetics	rs6742078	*UGT1A1*	0.455625814
	rs1054804	*UGT1A3*	0.592583812
	rs4641393	*CYP2C19*	0.601325053
	rs7909236	*CYP2C8*	0.648219785
	rs6600884	*UGT2B7*	0.674197776
	rs11045821	*SLCO1B1*	0.680895057
	rs12361540	*SLCO2B1*	0.687367222
	rs17216177	*ABCC2*	0.698375272
	rs9332242	*CYP2C9*	0.711510074
	rs1202184	*ABCB1*	2.337419052
	rs10242455	*CYP3A5*	2.96776873

Pathway	SNP-ID	Gene	Std-z score
Ibuprofen pathway: pharmacokinetics	rs11231294	*SLC22A6*	0.547420194
	rs1054804	*UGT1A3*	0.592583812
	rs4641393	*CYP2C19*	0.601325053
	rs7909236	*CYP2C8*	0.648219785
	rs34687	*AMACR*	0.65929798
	rs6600884	*UGT2B7*	0.674197776
	rs1080755	*UGT2B4*	0.676123319
	rs11045821	*SLCO1B1*	0.680895057
	rs17216177	*ABCC2*	0.698375272
	rs9332242	*CYP2C9*	0.711510074
	rs2602381	*UGT1A9*	0.717774468
	rs2766481	*ABCC4*	2.20317462
	rs631157	*SLC22A9*	2.522943189
	rs11231300	*SLC22A8*	3.215994776
	rs2196019	*SLCO1B3*	5.578785151
	rs1851426	*CYP3A4*	5.60910014
Statin pathways generalized: pharmacokinetics	rs12718462	*APOA1*	-0.083483207
	rs1736493	*PLTP*	0.232349371
	rs12709889	*APOC2*	0.282473096
	rs1466535	*LRP1*	0.369319416
	rs3757973	*DGAT1*	0.409931782
	rs7396835	*APOA4*	0.475858712
	rs6709904	*ABCG8*	0.490564557
	rs2071521	*APOC3*	0.57671236
	rs13251066	*CYP7A1*	0.609493833
	rs3846663	*HMGCR*	0.614390253
	rs11600380	*APOA5*	0.625697665
	rs253	*LPL*	0.661892621
	rs5929	*LDLR*	0.672221282
	rs16853894	*SOAT1*	0.699737304
	rs17029189	*MTTP*	0.703654573
	rs1202184	*ABCB1*	2.337419052
	rs10093770	*SQLE*	2.604816557

Pathway	SNP-ID	Gene	Std-z score
Beta agonist beta blocker pathway: pharmacodynamic	rs3804984	*ITPR1*	7.52×10-05
	rs1051738	*PDE4A*	-0.90554537
	rs2089480	*ARRB2*	-0.095643647
	rs312397	*GNG5*	0.018316974
	rs12791853	*ADRBK1*	0.051846493
	rs12742323	*GNB1*	0.114144883
	rs4981504	*ADCY4*	0.342919923
	rs4631721	*SLC9A1*	0.374422602
	rs2305648	*PLCB2*	0.39195199
	rs307952	*PRKCG*	0.414992685
	rs2292857	*PRKCZ*	0.523994043
	rs1359062	*RGS1*	0.530863755
	rs9904111	*SLC9A3R1*	0.567320755
	rs17799872	*ADCY3*	0.570214878
	rs2434389	*SLC9A3*	0.59265757
	rs1601770	*ELF2*	0.639562083
	rs9936021	*ADCY7*	0.670809301
	rs5755074	*MAPK1*	0.67579971
	rs10937003	*GNB4*	0.687884723
	rs11982719	*ADCY1*	0.690640633
	rs12403523	*CACNA1S*	0.692805313
	rs10268519	*GNAI1*	0.693272348
	rs7546625	*PRKACB*	0.709334077
	rs11144780	*PRKACG*	0.719185903
	rs1016160	*SLC9A2*	0.720624374
	rs17133858	*ARRB1*	0.72130222
	rs11803546	*GNAI3*	2.426151765
	rs2116715	*ADRB2*	2.447988511
	rs2238646	*PDE4C*	2.583139195
	rs4758096	*PRKCDBP*	2.634769205
	rs13084863	*PRKCD*	2.660396068
	rs2075193	*SLC9A4*	2.717058085
	rs7257500	*GNG7*	2.72587841

Pathway	SNP-ID	Gene	Std-z score
Beta agonist beta blocker pathway: pharmacodynamic	rs6017996	*SRC*	3.064644451
	rs326162	*ADCY2*	3.112587554
	rs8006278	*GNG2*	3.1420801
	rs1536014	*PRKCH*	3.181269651
	rs7975385	*ADCY6*	3.183066335
	rs12230535	*CACNA1C*	3.192157951
	rs6086653	*PLCB1*	3.225401467
	rs6986535	*ADCY8*	3.28680649
	rs6504438	*PRKCA*	3.288267362
	rs1883488	*PLCB4*	3.320398244
	rs12106549	*GNB1L*	3.387111554
	rs9923820	*PRKCB*	3.391422579
	rs943450	*PRKCQ*	3.41717054
	rs6766988	*CACNA1D*	3.503937932
	rs11137364	*CACNA1B*	3.823808258
	rs10775349	*ADCY9*	3.87143019
	rs7592092	*PRKCE*	4.28321397
	rs715534	*ADRBK2*	4.66641134
	rs6429197	*GNG4*	4.815476342
	rs10059859	*PDE4D*	5.598378276
Zidovudin pathways: pharmacokinetics and dynamics	rs2159359	*NME1*	0.252374101
	rs2661679	*TK1*	0.486153636
	rs11231294	*SLC22A6*	0.547420194
	rs6600884	*UGT2B7*	0.674197776
	rs9332242	*CYP2C9*	0.711510074
	rs2766481	*ABCC4*	2.20317462
	rs1202184	*ABCB1*	2.337419052
	rs12438877	*SLC28A1*	2.432255969
	rs2070676	*CYP2E1*	2.665623581
	rs3898649	*POR*	2.695696283
	rs7124676	*SLC22A11*	2.754998151
	rs7613247	*ABCC5*	2.93621938
	rs4605213	*NME2*	2.990114016

	rs2196019	*SLCO1B3*	5.578785151		rs520354	*APOB*	2.732249088		rs3211995	*SLC9A3R2*	2.800438252		rs11231300	*SLC22A8*	3.215994776
	rs1851426	*CYP3A4*	5.60910014		rs4148189	*ABCG5*	2.832264577		rs2236944	*GNAI2*	2.83215761		rs12347156	*SLC28A3*	3.392861021
					rs11057825	*SCARB1*	2.969047374		rs519712	*PDE4B*	2.862251109		rs2622610	*ABCG2*	3.662585022
	-				rs1123140	*FDFT1*	3.240649696		rs10934643	*ADCY5*	2.960810042		rs1851426	*CYP3A4*	5.60910014
					rs11071385	*LIPC*	3.707064276		rs6100260	*GNAS*	3.031807924		-		

Table S9. **“**Hard sweeps” signals of selection in all categories

Category		SNP-id	Gene	std-z scrore	Category	SNP-id	Gene	std-z scrore	Category	SNP-id	Gene	std-z scrore	Category	SNP-id	Gene	std-z scrore
PI	Core	rs1851426	*CYP3A4*	5.60910014	Other pathways genes	rs16834954	*HDAC1*	3.1834568	Other pathways genes	rs10434525	*PDE4D*	3.42598003	Other pathways genes	rs11231735	*BAD*	3.3094922
Transporter	Core	rs11723264	*ABCG2*	3.296256731		rs6697130	*HDAC1*	3.2622479		rs12515974	*PDE4D*	3.22770667		rs10896065	*FOSL1*	3.2050935
Transporter	Core	rs2196019	*SLCO1B3*	5.578785151		rs2984915	*JUN*	3.4680616		rs13361335	*HTR1A*	3.10210784		rs12230535	*CACNA1C*	3.192158
Transporter	Core	rs2622610	*ABCG2*	3.662585022		rs4372299	*AK4*	3.1702437		rs9293908	*KCNQ5*	4.03315031		rs758563	*CACNA1C*	3.0950105
Transporter	Core	rs2725267	*ABCG2*	3.429827945		rs6699614	*AK4*	3.3206238		rs9442844	*KCNQ5*	3.90392314		rs7295775	*CACNA1C*	3.0535714
Transporter	Core	rs919840	*SLCO1B3*	3.54271229		rs10889906	*PTGER3*	3.620197		rs7756180	*KCNQ5*	3.56324104		rs10466907	*CACNA1C*	3.1689571
Modifier	Extended	rs10281281	*CFTR*	3.655771963		rs2878575	*ATP1A1*	3.1414203		rs2840799	*KCNQ5*	3.01631337		rs7957163	*CACNA1C*	3.1325578
Modifier	Extended	rs11103482	*RXRA*	3.300724399		rs7539947	*ATP1A1*	3.1520018		rs6921049	*KCNQ5*	3.32042411		rs7958883	*VWF*	3.5174097
Modifier	Extended	rs11712211	*NR1I2*	3.33778217		rs6668161	*ATP1A1*	3.1942228		rs9446834	*KCNQ5*	3.38923352		rs723188	*VWF*	3.1914828
Modifier	Extended	rs1403527	*NR1I2*	3.361005362		rs1407716	*ATP1A1*	3.6254824		rs6453633	*KCNQ5*	3.40676011		rs1800387	*VWF*	3.1508135
Modifier	Extended	rs17139943	*CFTR*	3.307159918		rs6428896	*ATP1A1*	5.6148511		rs9293920	*KCNQ5*	3.73059716		rs7975385	*ADCY6*	3.1830663
Modifier	Extended	rs1899951	*PPARG*	3.288482285		rs6681761	*UCK2*	3.2051442		rs9442895	*KCNQ5*	3.07857291		rs1554807	*STX2*	3.3137344
Modifier	Extended	rs2472670	*NR1I2*	3.326126581		rs3766989	*CACNA1E*	3.023893		rs6929988	*KCNQ5*	3.09482401		rs10848205	*STX2*	3.6903334
Modifier	Extended	rs2472671	*NR1I2*	3.329980657		rs2271414	*PIK3C2B*	3.0231949		rs220729	*MAS1*	3.02961571		rs2037789	*STX2*	3.3264812
Modifier	Extended	rs4684104	*PPARG*	3.631348439		rs2999479	*PIK3C2B*	3.4397911		rs801763	*HDAC9*	3.548346		rs1106369	*STX2*	3.3246944
Modifier	Extended	rs6008197	*PPARA*	4.125983761		rs6429196	*GNG4*	3.0029958		rs2267716	*CRHR2*	3.19703094		rs2001483	*STX2*	3.1461612
Modifier	Extended	rs6457816	*PPARD*	4.002995311		rs6429197	*GNG4*	4.8154763		rs12668421	*EGFR*	3.89814181		rs1609985	*STX2*	3.6234698
Modifier	Extended	rs6906237	*PPARD*	3.17958232		rs636167	*RYR2*	3.2210013		rs11238349	*EGFR*	4.12106097		rs10848212	*STX2*	3.7199074
Modifier	Extended	rs7627605	*PPARG*	4.345238795		rs581645	*RYR2*	3.1273389		rs7781264	*EGFR*	3.2922844		rs2387355	*FLT3*	3.2116102
Modifier	Extended	rs9658100	*PPARD*	4.604327323		rs2790326	*CHRM3*	3.3806781		rs10270837	*CACNA2D1*	3.68992448		rs9554316	*FLT1*	4.0877333
PhaseI	Extended	rs10047560	*PDE3A*	3.199794334		rs7527677	*CHRM3*	3.2028451		rs10252208	*TBXAS1*	3.59932497		rs9582036	*FLT1*	3.8837962
PhaseI	Extended	rs10137990	*DHRS4*	3.523457569		rs7567003	*KCNK3*	3.6726867		rs2270163	*TBXAS1*	3.04092423		rs7981680	*FLT1*	4.0565268
PhaseI	Extended	rs1042026	*ADH1B*	3.138823993		rs17023214	*SOS1*	3.1178133		rs11765596	*PRKAG2*	4.62751788		rs2093821	*FLT1*	3.048008
PhaseI	Extended	rs10438016	*DHRS2*	3.046906403		rs7571608	*SOS1*	3.0668693		rs1029951	*PRKAG2*	3.17667474		rs8006278	*GNG2*	3.1420801
PhaseI	Extended	rs1056836	*CYP1B1*	3.136306384		rs7564481	*SOS1*	3.1706149		rs13235920	*PRKAG2*	4.43864589		rs1536014	*PRKCH*	3.1812697
PhaseI	Extended	rs10744777	*ALDH2*	3.311478082		rs4413199	*PRKCE*	3.1671269		rs7796138	*PRKAG2*	3.9234133		rs11158346	*PRKCH*	3.0025389
PhaseI	Extended	rs11066032	*ALDH2*	3.395362679		rs3924521	*PRKCE*	3.6569236		rs1123140	*FDFT1*	3.2406497		rs10148271	*JDP2*	3.5532691
PhaseI	Extended	rs11097642	*METAP1*	3.103200082		rs7592092	*PRKCE*	4.283214		rs1383888	*NRG1*	3.10383996		rs11071385	*LIPC*	3.7070643
PhaseI	Extended	rs11900892	*XDH*	3.072459543		rs9287889	*STK39*	3.1349941		rs369828	*NRG1*	3.05400976		rs1025455	*MAP2K1*	3.4595674
PhaseI	Extended	rs11981167	*CYP3A43*	3.102703154		rs2459611	*STAT4*	3.5582981		rs418362	*NRG1*	3.06237771		rs10775349	*ADCY9*	3.8714302
PhaseI	Extended	rs12027066	*ALDH9A1*	3.254954944		rs7601754	*STAT4*	3.6123645		rs367830	*NRG1*	3.06083393		rs6500567	*ADCY9*	3.0060239

	rs1230178	*METAP1*	3.704828454	rs10931480	*STAT4*	3.3770061	rs327415	*NRG1*	3.03061853	rs2601831	*ADCY9*	3.7069969
	rs12334538	*EPHX2*	3.795110639	rs4672912	*AOX2P*	3.0225177	rs1381871	*NRG1*	3.01190626	rs12103309	*ADCY9*	3.0758123
	rs12909230	*ALDH1A3*	4.290975829	rs13392814	*ERBB4*	3.250341	rs7821196	*NRG1*	4.02468353	rs2532001	*ADCY9*	3.0255134
	rs1441817	*ALDH1A2*	3.109072914	rs10208487	*ERBB4*	3.0436439	rs16879442	*NRG1*	3.29162099	rs9923820	*PRKCB*	3.3914226
	rs2161850	*GSR*	3.138350083	rs11887436	*ERBB4*	3.2561907	rs16879445	*NRG1*	3.26318229	rs9788865	*STX1B*	3.0958526
	rs2339840	*ALDH2*	3.800667016	rs6706854	*ERBB4*	3.8393287	rs12679324	*NRG1*	3.63939058	rs11150604	*STX4*	4.7854538
	rs2671272	*EPHX1*	3.057048258	rs6435649	*ERBB4*	3.6379111	rs16879557	*NRG1*	3.76712315	rs12447311	*PLCG2*	3.2163034
	rs2854450	*EPHX1*	3.070424274	rs4423543	*ERBB4*	3.0384791	rs6982753	*CHRNA6*	3.11566611	rs2168858	*STX8*	3.0070663
	rs3805322	*ADH4*	4.498988724	rs2139939	*ERBB4*	3.6757588	rs892413	*CHRNA6*	3.04743671	rs1133295	*STX8*	3.0471714
	rs472660	*CYP3A43*	4.320766471	rs1521553	*ERBB4*	3.4965248	rs1231201	*PRKDC*	3.08578715	rs2159141	*MAP2K4*	3.1247165
	rs4737681	*CYP7B1*	3.524094358	rs1521550	*ERBB4*	3.4222104	rs6984398	*CRH*	3.00073884	rs1058166	*HNF1B*	3.1208057
	rs4767944	*ALDH2*	3.634776642	rs6435689	*ERBB4*	3.5795805	rs7013524	*CRH*	3.81983846	rs242924	*CRHR1*	3.0527085
	rs501275	*CYP3A43*	3.624484208	rs7560730	*ERBB4*	4.7659535	rs6986535	*ADCY8*	3.28680649	rs12944877	*GNA13*	3.6272293
	rs642761	*CYP3A43*	4.392995902	rs1357142	*ERBB4*	3.3780847	rs7815277	*ADCY8*	3.23977508	rs1533075	*GNA13*	3.5154491
	rs6558002	*EPHX2*	3.082187715	rs1521652	*ERBB4*	3.9008694	rs4736462	*ADCY8*	3.11429427	rs11656396	*GNA13*	3.052676
	rs6870785	*ALDH7A1*	3.33501115	rs1012747	*ERBB4*	3.9082823	rs12545796	*ADCY8*	3.203146	rs4791242	*GNA13*	3.6692325
	rs7015380	*SULF1*	3.176102046	rs4672645	*ERBB4*	3.1209626	rs11995439	*ADCY8*	3.18606742	rs6504438	*PRKCA*	3.2882674
	rs7683532	*METAP1*	3.107445521	rs7586969	*ATIC*	3.4653924	rs4736727	*ADCY8*	3.13464996	rs9904728	*ATP5H*	3.097687
	rs7736031	*ALDH7A1*	3.244859299	rs16859382	*PRKAG3*	4.4147381	rs944481	*SHC3*	3.37665969	rs4789143	*NT5C*	3.3238132
	rs7829823	*SULF1*	3.113818052	rs3729931	*RAF1*	3.1669237	rs4836886	*PTGS1*	3.39277132	rs1076094	*GRB2*	3.0621962
	rs8010151	*DHRS4*	3.410793528	rs2442809	*RAF1*	3.096281	rs4836887	*PTGS1*	3.39499353	rs6501786	*GRB2*	3.8872775
	rs9805889	*DHRS4*	3.452804966	rs6766988	*CACNA1D*	3.5039379	rs4836888	*PTGS1*	3.39528943	rs4789188	*GRB2*	4.1817875
PhaseII	rs11934139	*GSTCD*	5.634440892	rs9853660	*CACNA2D3*	3.2520616	rs9299280	*PTGS1*	3.40408562	rs4789193	*GRB2*	3.501816
	rs13148869	*GSTCD*	5.634440892	rs9810700	*CACNA2D3*	3.2453474	rs10306187	*PTGS1*	3.60365601	rs4640267	*NEDD4L*	3.0389225
	rs13152031	*UGT8*	3.127875584	rs9847961	*CACNA2D3*	3.4137661	rs11244164	*ABL1*	3.53371261	rs1787773	*NEDD4L*	3.0680754
	rs3791358	*CHST10*	3.078068634	rs4681440	*AGTR1*	3.4648586	rs4740377	*ABL1*	3.28785998	rs6086653	*PLCB1*	3.2254015
	rs4521362	*UGT8*	3.246129948	rs4681443	*AGTR1*	3.4648872	rs11137364	*CACNA1B*	3.82380826	rs1883488	*PLCB4*	3.3203982
	rs4698951	*GSTCD*	3.192096298	rs4681444	*AGTR1*	3.4713733	rs2236380	*PRKCQ*	3.13344038	rs819147	*AHCY*	3.0766003
	rs4805930	*CHST8*	3.741709262	rs1492100	*AGTR1*	3.0622976	rs11596750	*PRKCQ*	3.09581902	rs6017996	*SRC*	3.0646445
	rs4834424	*UGT8*	3.388034316	rs2342309	*PCYT1A*	3.2633019	rs943450	*PRKCQ*	3.41717054	rs4812040	*GNAS*	3.0284452
	rs4834426	*UGT8*	3.26907265	rs12632779	*PCYT1A*	3.5206544	rs7072496	*PRKCQ*	3.38226811	rs6100260	*GNAS*	3.0318079
	rs4834427	*UGT8*	3.180948098	rs6446647	*STX18*	3.6628182	rs1887327	*PRKCQ*	3.37646266	rs3895449	*KCNQ2*	3.2817205
	rs6533218	*GSTCD*	5.60910014	rs6841963	*STX18*	3.632184	rs4623785	*CAMK1D*	3.7229142	rs1052978	*GNB1L*	3.1727304
	rs6815181	*UGT8*	3.207004849	rs10805074	*DCK*	3.6219414	rs3737180	*ZEB1*	3.75270214	rs12106549	*GNB1L*	3.3871116
	rs6831964	*UGT8*	3.188523115	rs7684954	*DCK*	3.6178725	rs7894459	*ZEB1*	3.83044223	rs6518585	*GNB1L*	3.3837038
	rs7686242	*UGT8*	3.203322365	rs2851060	*PPP3CA*	3.5803671	rs161279	*ZEB1*	3.5887484	rs16980239	*ADRBK2*	3.1961178
	rs7906892	*GSTO1*	3.073267976	rs4698804	*EGF*	3.5641027	rs161258	*ZEB1*	3.10648723	rs16980512	*ADRBK2*	3.6086105

		rs835316	*UGT2B10*	3.013089445		rs6840127	*NR3C2*	3.4465294		rs161272	*ZEB1*	3.7803372		rs3730114	*ADRBK2*	3.8414209
Transporter		rs11231300	*SLC22A8*	3.215994776		rs2171083	*VEGFC*	5.6257595		rs161275	*ZEB1*	3.48646289		rs715534	*ADRBK2*	4.6664113
		rs1158335	*SLC22A15*	3.220116581		rs1995083	*VEGFC*	4.5569004		rs1761379	*ZEB1*	3.39061409		rs5750871	*CACNA1I*	3.2714076
		rs12347156	*SLC28A3*	3.392861021		rs6857752	*VEGFC*	3.0183113		rs220073	*ZEB1*	3.54653944		rs6001649	*CACNA1I*	3.1781263
		rs1275526	*SLC5A6*	3.204560401		rs4488887	*VEGFC*	3.0071001		rs2289805	*MAPK8*	3.49869537		rs739092	*TSPO*	3.1708662
		rs1515777	*SLCO1C1*	3.964060639		rs326162	*ADCY2*	3.1125876		rs10762276	*HK1*	3.85724534				
		rs2077654	*ABCC8*	3.760092969		rs17589633	*PDE4D*	3.0881071		rs7915217	*NRG3*	3.21906469				
		rs225372	*ABCG1*	3.264884794		rs3891334	*PDE4D*	3.1279141		rs11574845	*NFKB2*	3.08398527				
		rs2413770	*SLC28A2*	3.9932371		rs16889853	*PDE4D*	3.2579803		rs363333	*SLC18A2*	3.1552855				
		rs3213473	*ABCC6*	3.090094809		rs173945	*PDE4D*	3.6965117		rs2912754	*FGFR2*	3.36832868				
		rs3847305	*ABCA1*	3.079380777		rs16890314	*PDE4D*	3.0822322		rs2912759	*FGFR2*	3.04844918				
		rs4075845	*SLCO3A1*	3.338766023		rs159622	*PDE4D*	3.1700629		rs2420942	*FGFR2*	3.21067791				
		rs4148641	*ABCC8*	3.065567524		rs159608	*PDE4D*	3.4688445		rs2981439	*FGFR2*	3.05806992				
		rs7524567	*SLC16A1*	3.445812278		rs10059859	*PDE4D*	5.5983783		rs11814493	*FGFR2*	3.29946245				
		rs7767808	*SLC22A16*	3.633462281		rs1949017	*PDE4D*	3.4173394		rs12364575	*CCKBR*	3.44438592				

Table S10. EnsEMBL-BioMart mining for "Hard sweep" signals

Gene	rsID	Title of article	References
ADME genes			
ADH1B	rs1042026	ADH single nucleotide polymorphism associations with alcohol metabolism in vivo.	3
ADH1B	rs1042026	ADH1A variation predisposes to personality traits and substance dependence.	4
ADH1B	rs1042026	Associations and interactions between SNPs in the alcohol metabolizing genes and alcoholism phenotypes in European Americans.	5
ADH1B	rs1042026	Associations of ADH and ALDH2 gene variation with self report alcohol reactions, consumption and dependence: an integrated analysis.	6
ADH1B	rs1042026	Diplotype trend regression analysis of the ADH gene cluster and the ALDH2 gene: multiple significant associations with alcohol dependence.	7
ADH1B	rs1042026	Evidence of positive selection on a class I ADH locus.	8
ADH1B	rs1042026	Multiple ADH genes modulate risk for drug dependence in both African- and European-Americans.	9
ADH1B	rs1042026	The ADH1B Arg47His polymorphism in east Asian populations and expansion of rice domestication in history.	10
CYP1B1	rs1056836	Assessment of interactions between PAH exposure and genetic polymorphisms on PAH-DNA adducts in African American, Dominican, and Caucasian mothers and newborns.	11
CYP1B1	rs1056836	Associations between smoking, polymorphisms in polycyclic aromatic hydrocarbon (PAH) metabolism and conjugation genes and PAH-DNA adducts in prostate tumors differ by race.	12
CYP1B1	rs1056836	Associations of common variants in genes involved in metabolism and response to exogenous chemicals with risk of multiple myeloma.	13
CYP1B1	rs1056836	CYP1A1 and CYP1B1 polymorphisms and their association with estradiol and estrogen metabolites in women who are premenopausal and perimenopausal.	14
CYP1B1	rs1056836	Carcinogen metabolism, cigarette smoking, and breast cancer risk: a Bayes model averaging approach.	15
CYP1B1	rs1056836	Chromosomal aberrations in tire plant workers and interaction with polymorphisms of biotransformation and DNA repair genes.	16
CYP1B1	rs1056836	Cytochrome 450 1B1 (CYP1B1) polymorphisms associated with response to docetaxel in Castration-Resistant Prostate Cancer (CRPC) patients.	17
CYP1B1	rs1056836	Cytochrome P450 1B1 gene polymorphisms as predictors of anticancer drug activity: studies with in vitro models.	18
CYP1B1	rs1056836	Dietary phytoestrogen intake is associated with reduced colorectal cancer risk.	19
CYP1B1	rs1056836	Effect of cytochrome P450 polymorphism on arachidonic acid metabolism and their impact on cardiovascular diseases.	20
CYP1B1	rs1056836	Estrogen metabolism genotypes, use of long-term hormone replacement therapy and risk of postmenopausal breast cancer.	21
CYP1B1	rs1056836	Genetic association of aromatic hydrocarbon receptor (AHR) and cytochrome P450, family 1, subfamily A, polypeptide 1 (CYP1A1) polymorphisms with dioxin blood concentrations among pregnant Japanese women.	22
CYP1B1	rs1056836	Genetic variation in the bioactivation pathway for polycyclic hydrocarbons and heterocyclic amines in relation to risk of colorectal neoplasia.	23
CYP1B1	rs1056836	Joint effects of smoking and gene variants involved in sex steroid metabolism on hot flashes in late reproductive-age women.	24
CYP1B1	rs1056836	Red meat intake, doneness, polymorphisms in genes that encode carcinogen-metabolizing enzymes, and colorectal cancer risk.	25

CYP1B1	rs1056836	The influence of metabolic gene polymorphisms on urinary 1-hydroxypyrene concentrations in Chinese coke oven workers.	26
CYP1B1	rs1056836	Tobacco and estrogen metabolic polymorphisms and risk of non-small cell lung cancer in women.	27
CYP1B1	rs1056836	Variation in PAH-related DNA adduct levels among non-smokers: the role of multiple genetic polymorphisms and nucleotide excision repair phenotype.	28
RXRA	rs11103482	Effects of vitamin A and D receptor gene polymorphisms/haplotypes on immune responses to measles vaccine.	29
NR1I2	rs1403527	Human loci involved in drug biotransformation: worldwide genetic variation, population structure, and pharmacogenetic implications.	30
CYP3A4	rs1851426	Phenotype-genotype variability in the human CYP3A locus as assessed by the probe drug quinine and analyses of variant CYP3A4 alleles.	31
EPHX1	rs2854450	Genetic variants in antioxidant genes are associated with diisocyanate-induced asthma.	32
CYP3A43	rs472660	Genetic variation in CYP3A43 explains racial difference in olanzapine clearance.	33
PPARD	rs6457816	Mechanisms of peripheral neuropathy associated with bortezomib and vincristine in patients with newly diagnosed multiple myeloma: a prospective analysis of data from the HOVON-65/GMMG-HD4 trial	34
Other pathway genes			
PDE4D	rs10059859	Effect of Single Doses of Capromorelin and Ghrelin On Esophageal Reflux Parameters and Esophageal Function: A Randomized, Double-Blind, Placebo-Controlled Study	-
STX4	rs11150604	Dependency of phenprocoumon dosage on polymorphisms in the VKORC1, CYP2C9, and CYP4F2 genes	35
CRHR1	rs242924	Genetic association of FKBP5 and CRHR1 with cortisol response to acute psychosocial stress in healthy adults.	36
CRHR1	rs242924	Interaction of childhood maltreatment with the corticotropin-releasing hormone receptor gene: effects on hypothalamic-pituitary-adrenal axis reactivity.	37
CRHR1	rs242924	Personalized medicine in psychiatry: problems and promises.	38
JUN	rs2984915	The role of polymorphisms in Toll-like receptors and their associated intracellular signaling genes in measles vaccine immunity.	39
SLC18A2	rs363333	Association of DNA polymorphisms in the synaptic vesicular amine transporter gene (SLC18A2) with alcohol and nicotine dependence.	40
SRC	rs6017996	Impact of genetic polymorphisms on adenoma recurrence and toxicity in a COX2 inhibitor (celecoxib) trial: results from a pilot study.	41
CHRNA6	rs892413	A candidate gene approach identifies the CHRNA5-A3-B4 region as a risk factor for age-dependent nicotine addiction.	42
CHRNA6	rs892413	Genetic association of the CHRNA6 and CHRNB3 genes with tobacco dependence in a nationally representative sample.	43
CHRNA6	rs892413	SNPs in CHRNA6 and CHRNB3 are associated with alcohol consumption in a nationally representative sample.	44
FLT1	rs9554316	VEGFR1 single nucleotide polymorphisms associated with outcome in patients with metastatic renal cell carcinoma treated with sunitinib - a multicentric retrospective analysis.	45
FLT1	rs9582036	14LBA Randomized phase 3 study of panitumumab with FOLFIRI vs FOLFIRI alone as second-line treatment (tx) in patients (pts) with metastatic colorectal cancer (mCRC)	-
FLT1	rs9582036	15LBA Intermittent versus continuous oxaliplatin-based combination chemotherapy in patients with advanced colorectal cancer: a randomised non-inferiority trial (MRC COIN)	-
FLT1	rs9582036	16LBA VEGFR-1 polymorphisms as potential predictors of clinical outcome in bevacizumab-treated patients with metastatic pancreatic cancer	-
FLT1	rs9582036	Biomarker results from the AVADO phase 3 trial of first-line	46

		bevacizumab plus docetaxel for HER2-negative metastatic breast cancer.	
FLT1	rs9582036	Pharmacogenetic biomarkers for the prediction of response to antiangiogenic treatment.	47
FLT1	rs9582036	Understanding and targeting resistance to anti-angiogenic therapies.	48
FLT1	rs9582036	VEGF pathway genetic variants as biomarkers of treatment outcome with bevacizumab: an analysis of data from the AViTA and AVOREN randomised trials.	49
FLT1	rs9582036	VEGFR1 single nucleotide polymorphisms associated with outcome in patients with metastatic renal cell carcinoma treated with sunitinib - a multicentric retrospective analysis.	45

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