Suppl. Table 1. SNP coding scheme of the inheritance modes

| SNP1	Additive[2]		Dominant[2]		Recessive[2]	
Maj/Min[1]=A/a	Original	Reverse	Original	Reverse	Original	Reverse
AA	0	2	0	1	0	1
Aa	1	1	1	0	0	1
aa	2	0	1	0	1	0
Data type	Continuous	Continuous	Binary	Binary	Binary	Binary

[1]Maj/Min= major/minor allele

[2]Original modes are based on a minor allele 'a'; Reverse coding is (1 - original coding) for the dominant and recessive mode, and (2 - original coding) for the additive mode

Suppl. Table 2. Descriptions of the 45 models of the SNP Interaction Pattern Identifier (SIPI)

| Model number & label		Model description[1]
1	DD_Full	Full interaction model, SNP1 with Dom coding and SNP2 with Dom coding
2	DD_M1_int_o_1	Model with main effect of SNP1 plus an interaction, SNP1 with original Dom coding and SNP2 with Dom coding
3	DD_M1_int_r_1	Model with main effect of SNP1 plus an interaction, SNP1 with reverse Dom coding and SNP2 with Dom coding
4	DD_M2_int_o_2	Model with main effect of SNP2 plus an interaction, SNP1 with Dom coding and SNP2 with original Dom coding
5	DD_M2_int_r_2	Model with main effect of SNP2 plus an interaction, SNP1 with Dom coding and SNP2 with reverse Dom coding
6	DD_int_oo	Interaction-only model, SNP1 with original Dom coding and SNP2 with original Dom coding
7	DD_int_or	Interaction-only model, SNP1 with original Dom coding and SNP2 with reverse Dom coding
8	DD_int_ro	Interaction-only model, SNP1 with reverse Dom coding and SNP2 with original Dom coding
9	DD_int_rr	Interaction-only model, SNP1 with reverse Dom coding and SNP2 with reverse Dom coding
10	DR_Full	Full interaction model, SNP1 with Dom coding and SNP2 with Rec coding
11	DR_M1_int_o_1	Model with main effect of SNP1 plus an interaction, SNP1 with original Dom coding and SNP2 with Rec coding
12	DR_M1_int_r_1	Model with main effect of SNP1 plus an interaction, SNP1 with reverse Dom coding and SNP2 with Rec coding
13	DR_M2_int_o_2	Model with main effect of SNP2 plus an interaction, SNP1 with Dom coding and SNP2 with original Rec coding
14	DR_M2_int_r_2	Model with main effect of SNP2 plus an interaction, SNP1 with Dom coding and SNP2 with reverse Rec coding
15	DR_int_oo	Interaction-only model, SNP1 with original Dom coding and SNP2 with original Rec coding
16	DR_int_or	Interaction-only model, SNP1 with original Dom coding and SNP2 with reverse Rec coding
17	DR_int_ro	Interaction-only model, SNP1 with reverse Dom coding and SNP2 with original Rec coding
18	DR_int_rr	Interaction-only model, SNP1 with reverse Dom coding and SNP2 with reverse Rec coding
19	RD_Full	Full interaction model, SNP1 with Rec coding and SNP2 with Dom coding
20	RD_M1_int_o_1	Model with main effect of SNP1 plus an interaction, SNP1 with original Rec coding and SNP2 with Dom coding
21	RD_M1_int_r_1	Model with main effect of SNP1 plus an interaction, SNP1 with reverse Rec coding and SNP2 with Dom coding
22	RD_M2_int_o_2	Model with main effect of SNP2 plus an interaction, SNP1 with Rec coding and SNP2 with original Dom coding
23	RD_M2_int_r_2	Model with main effect of SNP2 plus an interaction, SNP1 with Rec coding and SNP2 with reverse Dom coding
24	RD_int_oo	Interaction-only model, SNP1 with original Rec coding and SNP2 with original Dom coding
25	RD_int_or	Interaction-only model, SNP1 with original Rec coding and SNP2 with reverse Dom coding
26	RD_int_ro	Interaction-only model, SNP1 with reverse Rec coding and SNP2 with original Dom coding
27	RD_int_rr	Interaction-only model, SNP1 with reverse Rec coding and SNP2 with reverse Dom coding
28	RR_Full	Full interaction model, SNP1 with Rec coding and SNP2 with Rec coding
29	RR_M1_int_o_1	Model with main effect of SNP1 plus an interaction, SNP1 with original Rec coding and SNP2 with Rec coding
30	RR_M1_int_r_1	Model with main effect of SNP1 plus an interaction, SNP1 with reverse Rec coding and SNP2 with Rec coding
31	RR_M2_int_o_2	Model with main effect of SNP2 plus an interaction, SNP1 with Rec coding and SNP2 with original Rec coding
32	RR_M2_int_r_2	Model with main effect of SNP2 plus an interaction, SNP1 with Rec coding and SNP2 with reverse Rec coding
33	RR_int_oo	Interaction-only model, SNP1 with original Rec coding and SNP2 with original Rec coding
34	RR_int_or	Interaction-only model, SNP1 with original Rec coding and SNP2 with reverse Rec coding
35	RR_int_ro	Interaction-only model, SNP1 with reverse Rec coding and SNP2 with original Rec coding
36	RR_int_rr	Interaction-only model, SNP1 with reverse Rec coding and SNP2 with reverse Rec coding
37	AA_Full	Full interaction model, SNP1 with Add coding and SNP2 with Add coding
38	AA_M1_int_o_1	Model with main effect of SNP1 plus an interaction, SNP1 with original Add coding and SNP2 with Add coding
39	AA_M1_int_r_1	Model with main effect of SNP1 plus an interaction, SNP1 with reverse Add coding and SNP2 with Add coding
40	AA_M2_int_o_2	Model with main effect of SNP2 plus an interaction, SNP1 with Add coding and SNP2 with original Add coding
41	AA_M2_int_r_2	Model with main effect of SNP2 plus an interaction, SNP1 with Add coding and SNP2 with reverse Add coding
42	AA_int_oo	Interaction-only model, SNP1 with original Add coding and SNP2 with original Add coding
43	AA_int_or	Interaction-only model, SNP1 with original Add coding and SNP2 with reverse Add coding
44	AA_int_ro	Interaction-only model, SNP1 with reverse Add coding and SNP2 with original Add coding
45	AA_int_rr	Interaction-only model, SNP1 with reverse Add coding and SNP2 with reverse Add coding

[1] Model label: 'D' (dominant), 'R' (recessive), 'A' (additive); 'Full' (full interaction), 'M1_int' (SNP1 main effect plus interaction); coding direction: 'o1' (original for SNP1), 'o2' (original for SNP2), r1' (reverse for SNP1), 'r2' (reverse for SNP2), 'oo' (original-original for SNP1-SNP2), 'or' (reverse-original), 'ro' (reverse-original), and 'rr' (reverse-reverse). If coding direction ('o'/'r') is not specified, the original coding is applied.

Suppl. Figure 1a. SIPI interaction models: dominant-dominant (DD) and dominant-recessive (DR) modes[1]

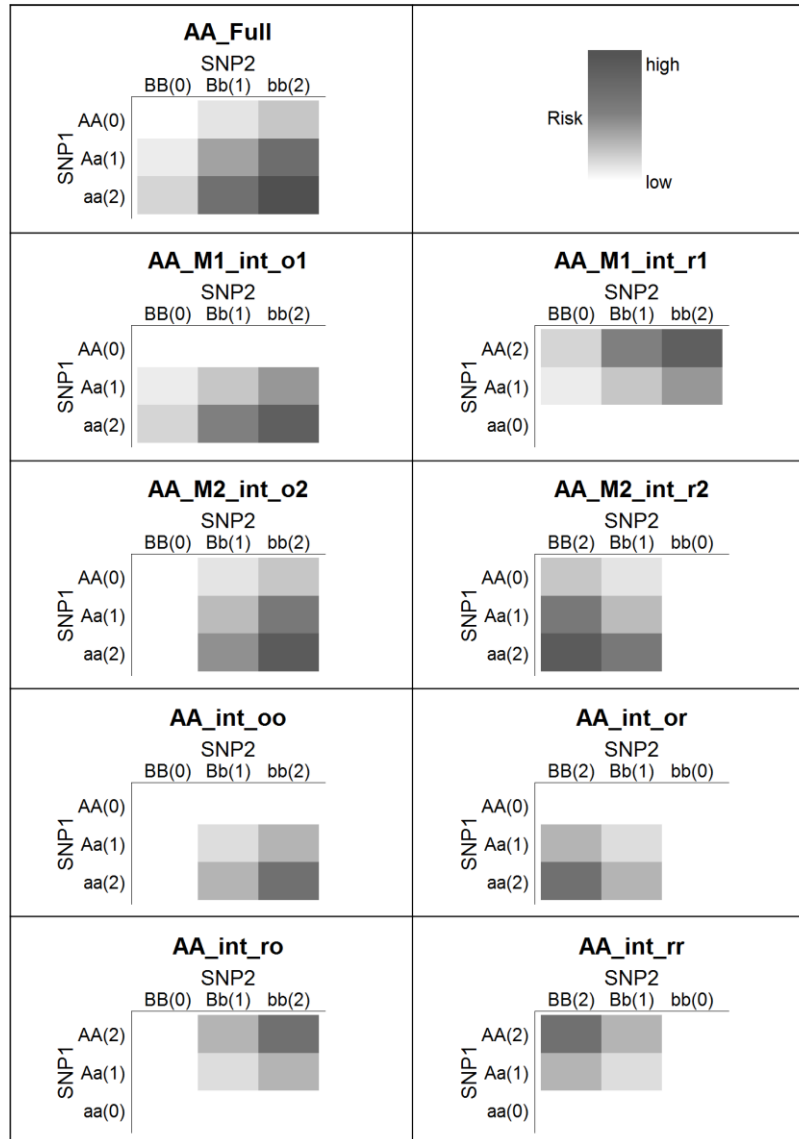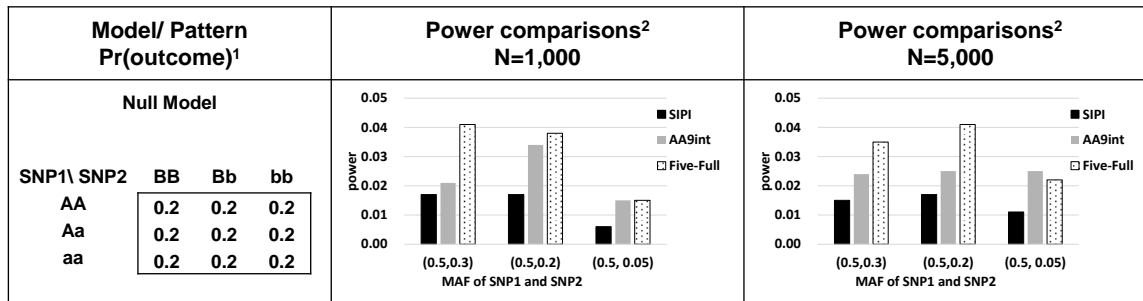Suppl. Figure 1b. SIPI interaction models: recessive-dominant (RD) and recessive-recessive (RR) modes[1]
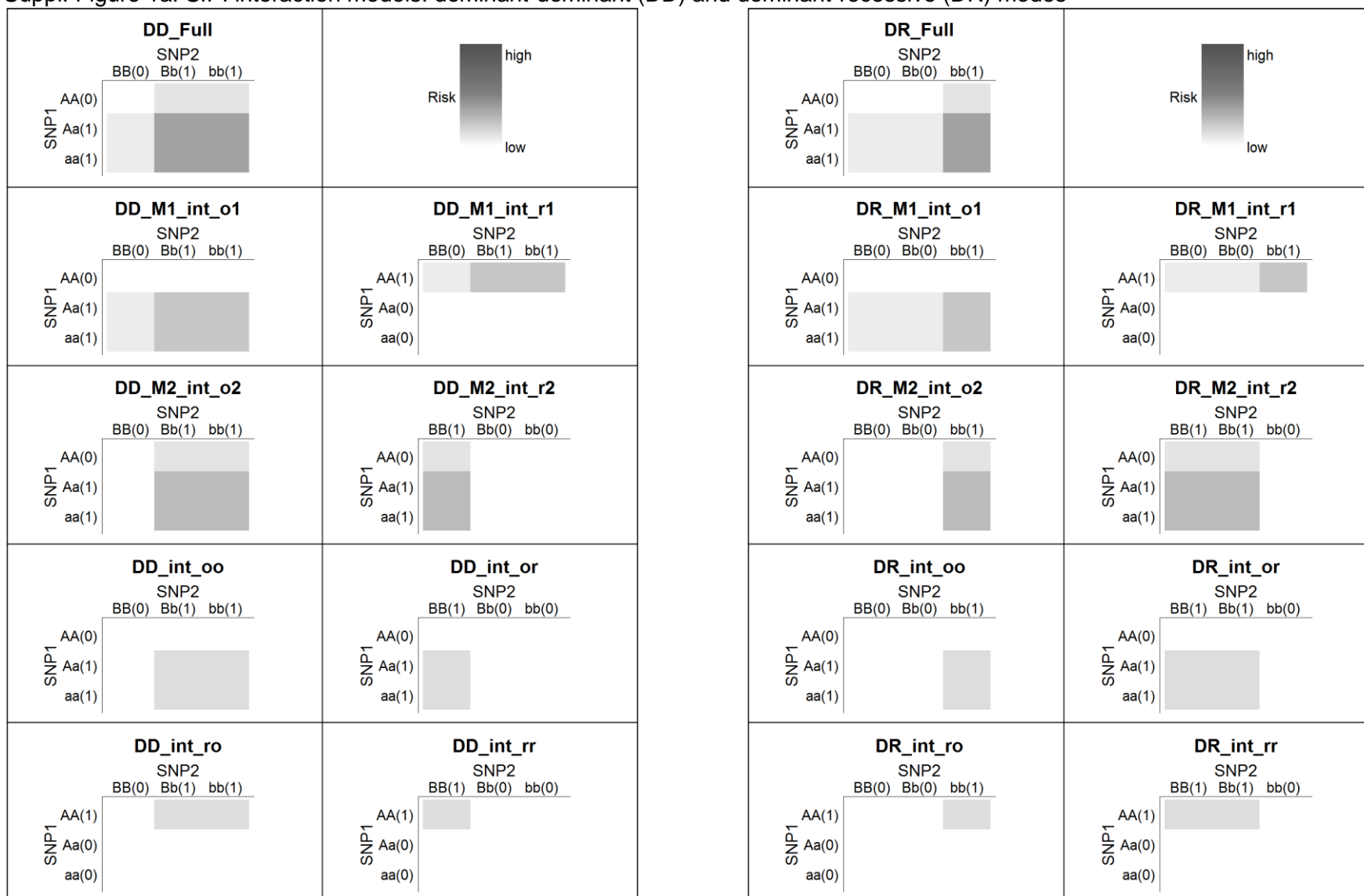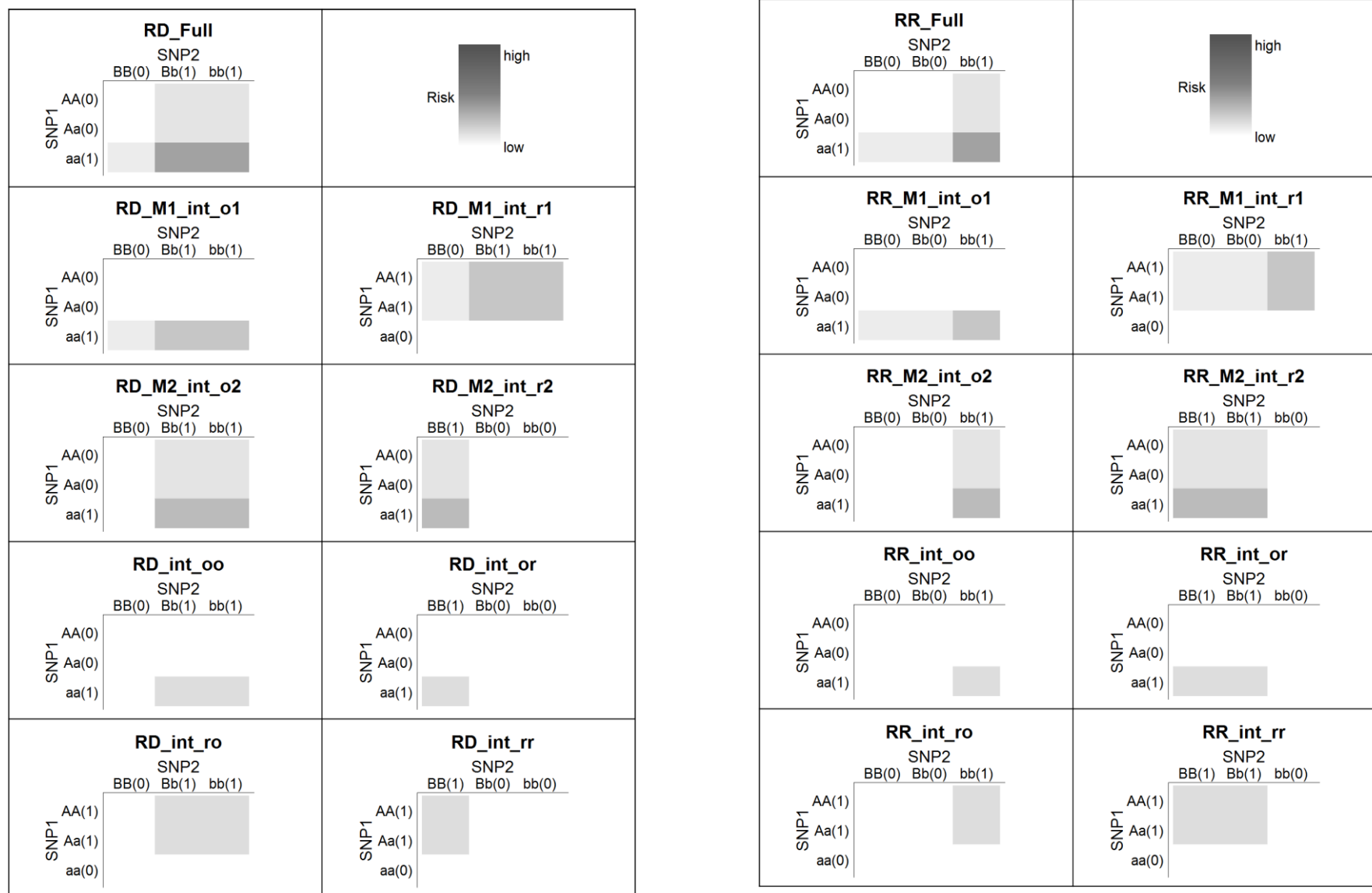
[1] **Model label**: 'D' (dominant), 'R' (recessive); 'Full' (full interaction), 'M1_int' (SNP1 main effect plus interaction); coding direction: 'o1' (original for SNP1), 'o2' (original for SNP2), r1' (reverse for SNP1), 'r2' (reverse for SNP2), 'oo' (original-original for SNP1-SNP2), 'or' (reverse-original), 'ro' (reverse-original), and 'rr' (reverse-reverse). The labels of two axes are '**genotype (coding)**'. A lowercase and capital letter denotes the minor and major allele, respectively. Color levels represent present outcome proportions. The darker the color, the higher the outcome proportion. For the 'Full' model, the figure is an example pattern based on both minor alleles as risk alleles. These plots are the SIPI pattern examples based on positive model coefficients in SIPI models. If coding direction ('o'/'r') is not specified, the original coding is applied.

Suppl. Figure 1c. SIPI interaction models: additive-additive (AA) mode[1]

Suppl. Figure 2. Comparison of Type I errors of AA9int, Five-Full and SIPI

Model/ Pattern Pr(outcome)[1]				Power comparisons[2] N=1,000	Power comparisons[2] N=5,000
Null Model					
SNP1\ SNP2	BB	Bb	bb		
AA	0.2	0.2	0.2		
Aa	0.2	0.2	0.2		
aa	0.2	0.2	0.2		

[1]Values in the 3x3 table are present outcome proportions. A lowercase and capital letter denotes the minor and major allele, respectively. [2] SIPI (SNP Interaction Pattern Identifier), AA9int (Additive-additive 9 interaction-model approach), and Five-Full (Five full interaction-model approach). MAF: minor allele frequency