Mapping QTX based on Omics Data and Their Application in Crop Breeding

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Mendelian traits

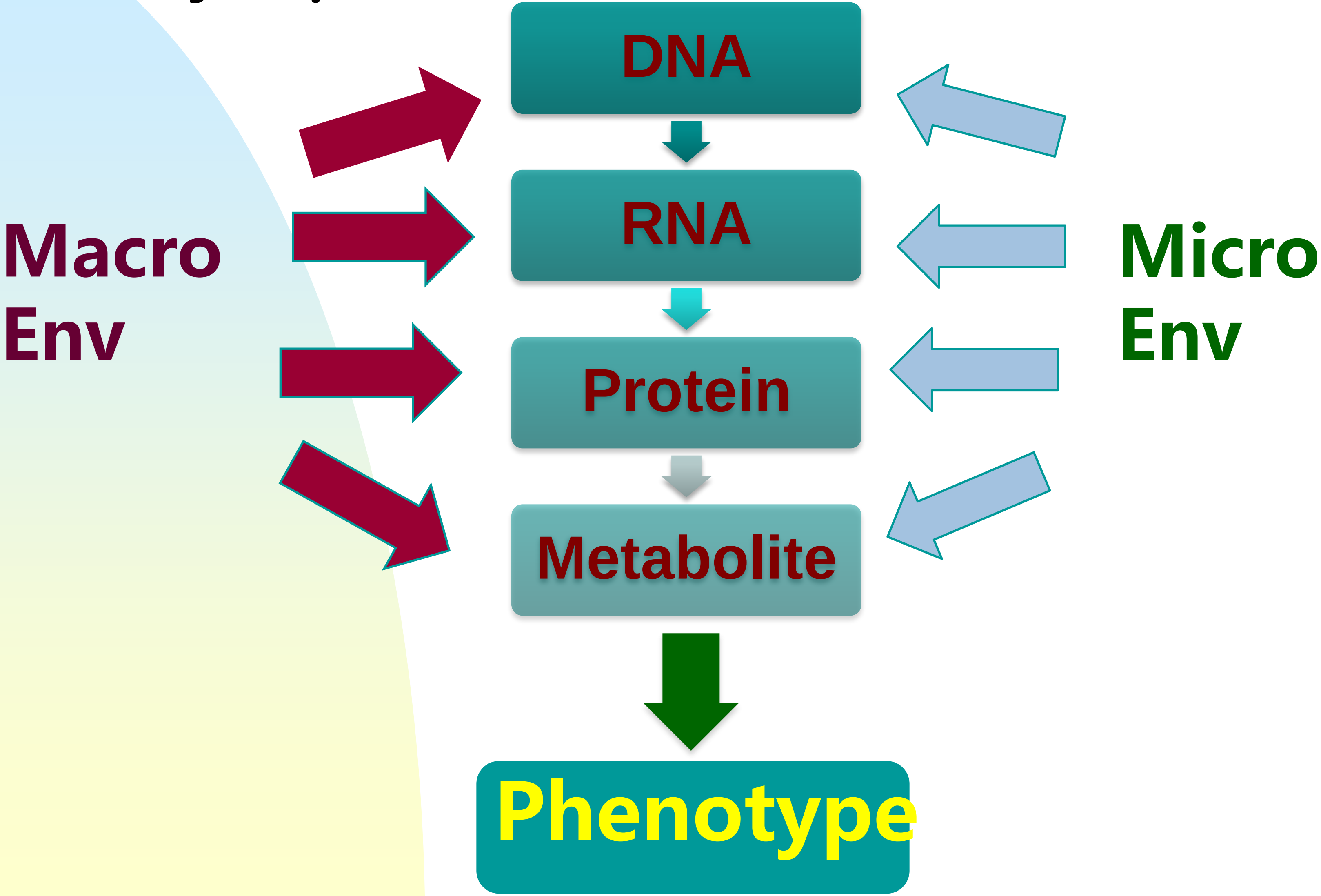
- **Phenotypes controlled by singular genes**
- **No epistasis**
- **No GE interaction**

Complex traits

- **Phenotypes controlled by multiple genes**
- **Epistasis (gene-gene interaction)**
- **Gene-environment interaction**
- **Genetic pleiotropy and heterogeneity**
- **Low heritability**
- **Limited statistical power**

Genetic Mechanism for Complex Traits

$$y = \mu + E + G + GE + e$$



Macro Env

DNA

RNA

Protein

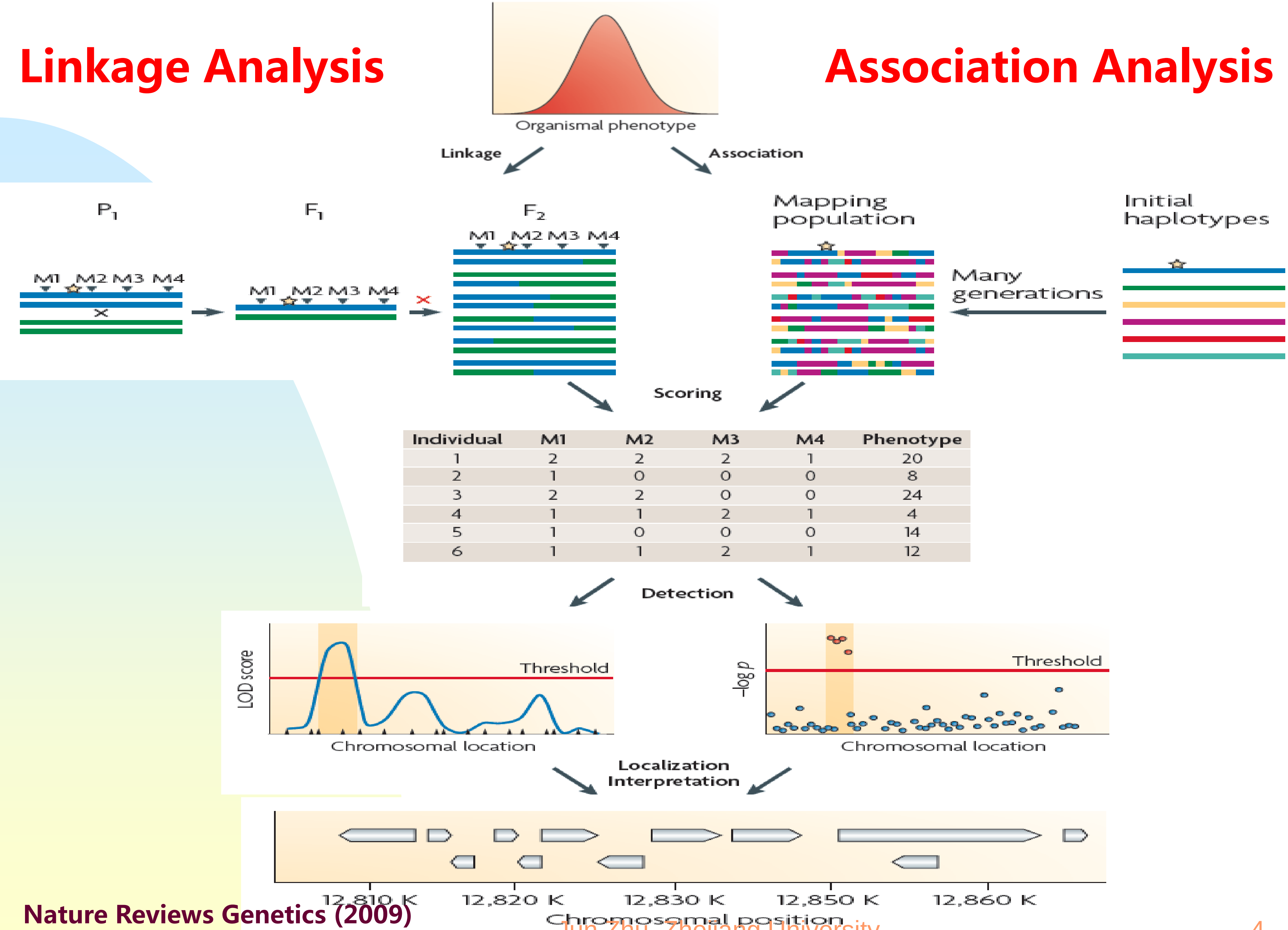
Metabolite

Micro Env

Phenotype

Linkage Analysis

Association Analysis

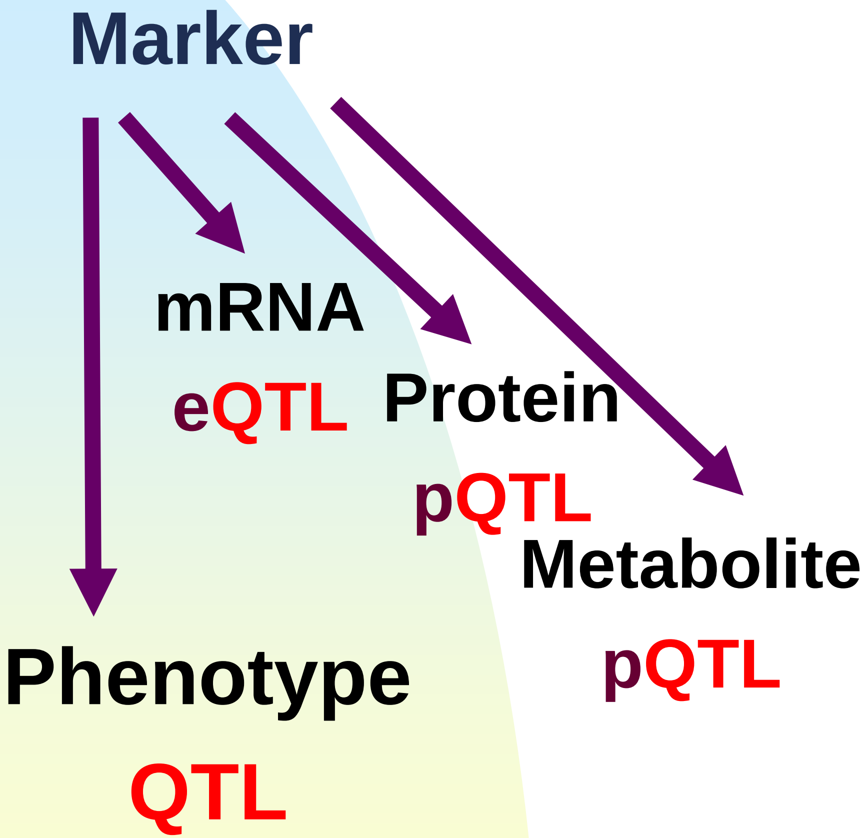


Individual	M1	M2	M3	M4	Phenotype
1	2	2	2	1	20
2	1	0	0	0	8
3	2	2	0	0	24
4	1	1	2	1	4
5	1	0	0	0	14
6	1	1	2	1	12

Nature Reviews Genetics (2009) 10:doi:10.1038/nrg2612

QTL Mapping

Linkage Analysis



Marker

mRNA

eQTL

Protein

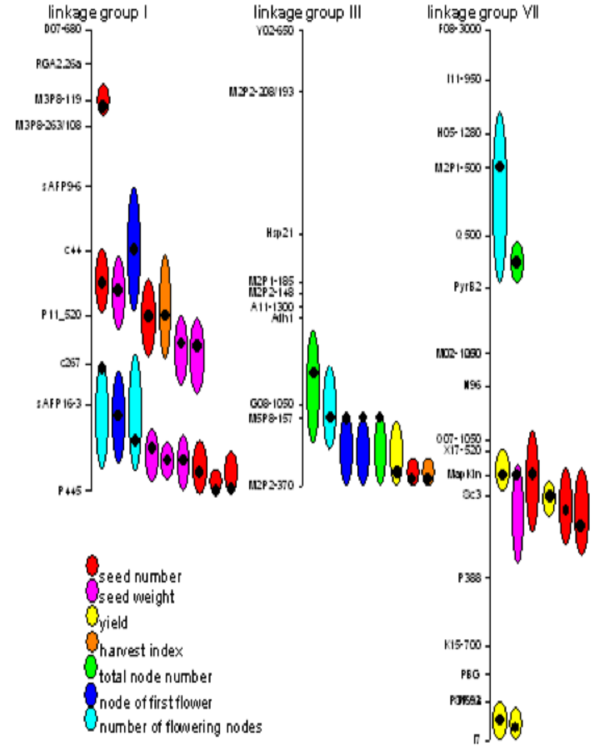
pQTL

Metabolite

pQTL

Phenotype

QTL



🟥 seed number
🟪 seed weight
🟨 yield
🟧 harvest index
🟩 total node number
🟦 node of first flower
● number of flowering nodes

Linkage mapping of QTLs for seed yield, yield components and developmental traits in pea (*Pisum sativum* L.)

Gail Timmerman-Vaughan[1], A Mills[1], TJ Frew[1], R.C. Butler[1], J.A. McCallum[1], Sarah Murray[1], C.P. Whitfield[1], A.C. Russell[2] and D.R. Wilson[1]

Google Scholar:

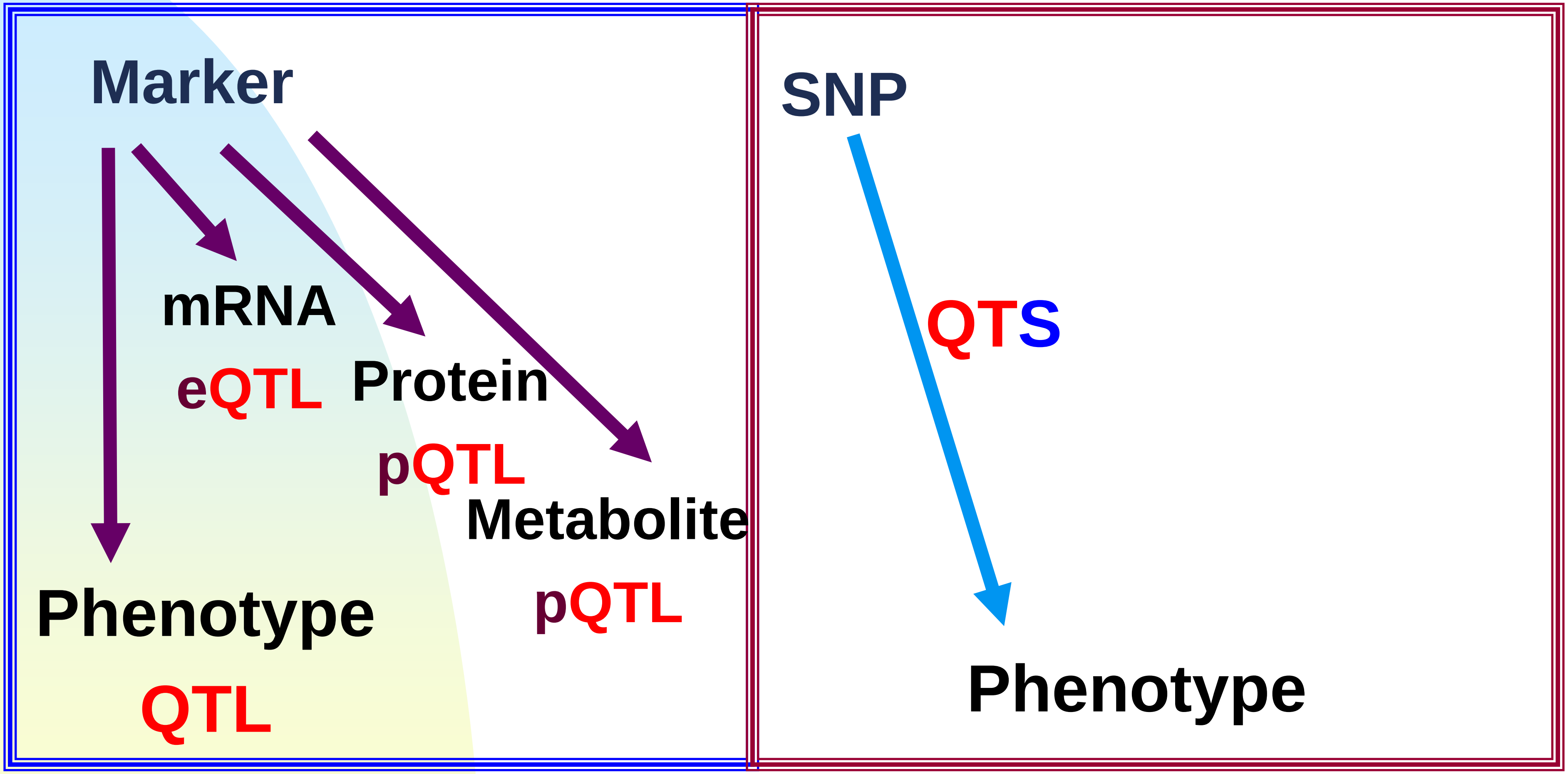
122,000 for QTL,

Limitation of QTL Mapping Based on Small Number of Markers

1. **Need linkage map of markers**
2. **QTLs detected only for mapping population derived from two parents**
3. **Mapping results cannot be applied to other parents and breeding populations**
4. **QTL mapping cannot be conducted by population involved selection/abnormal segregation**
5. **MAS may not be efficient if QTLs not closely linked to markers**
6. **QTL cannot be conducted for arbitrary breeding populations and germplasm**

From QTL Mapping to QTS Mapping

Linkage Analysis **Association Analysis**



Marker

mRNA

eQTL

Protein

pQTL

Metabolite

pQTL

Phenotype

QTL

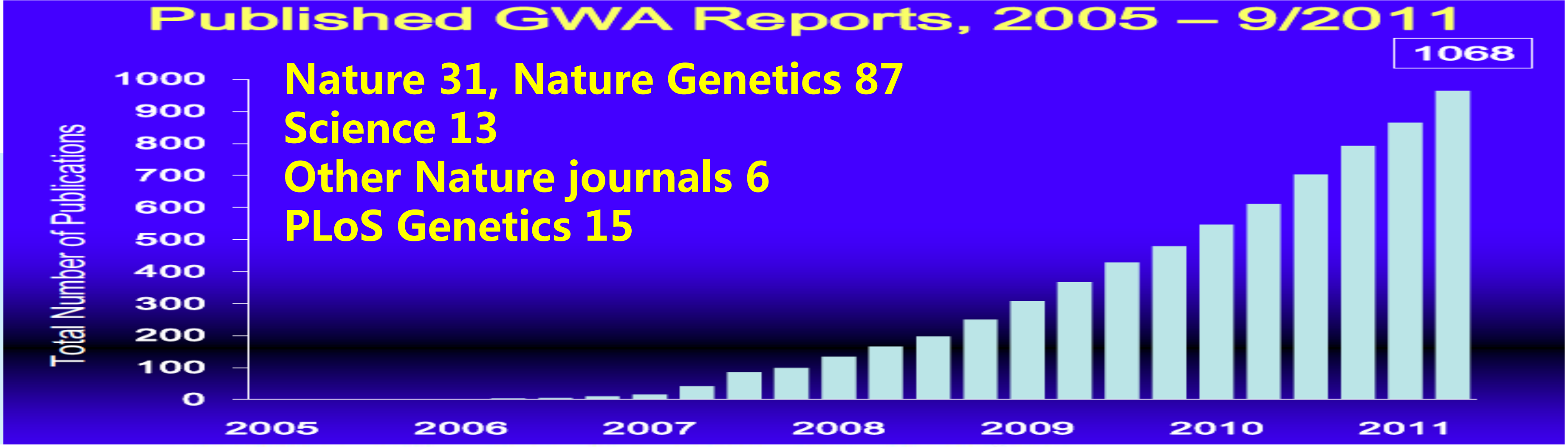
SNP

QTS

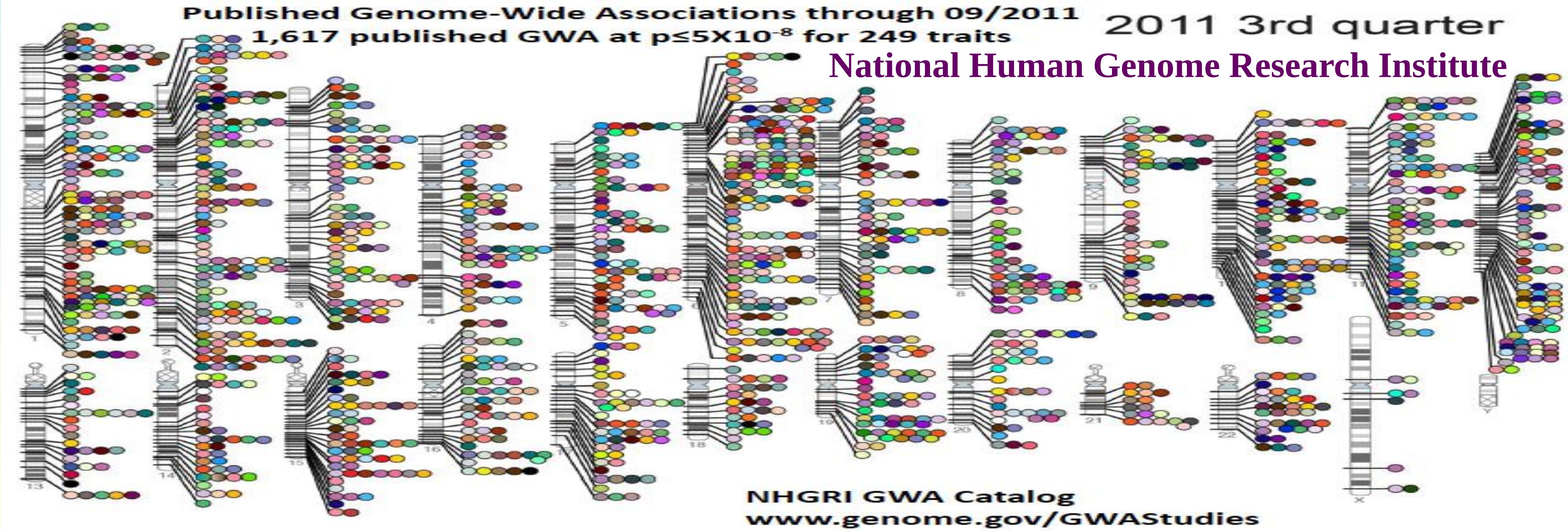
Phenotype

Google Scholar:

122,000 for QTL, 20,500 for GWAS



Nature 31, Nature Genetics 87
Science 13
Other Nature journals 6
PLoS Genetics 15



National Human Genome Research Institute

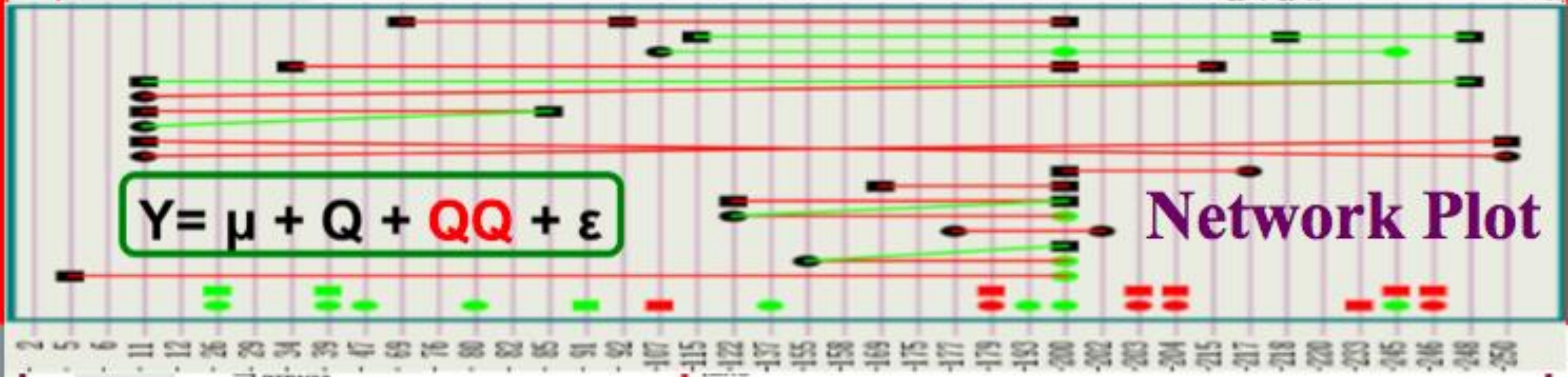
The mystery of missing heritability: Genetic interactions create phantom heritability

Or Zuk[a], Eliana Hechter[a], Shamil R. Sunyaev[a,b], and Eric S. Lander[a,1]

(2012, PNAS)

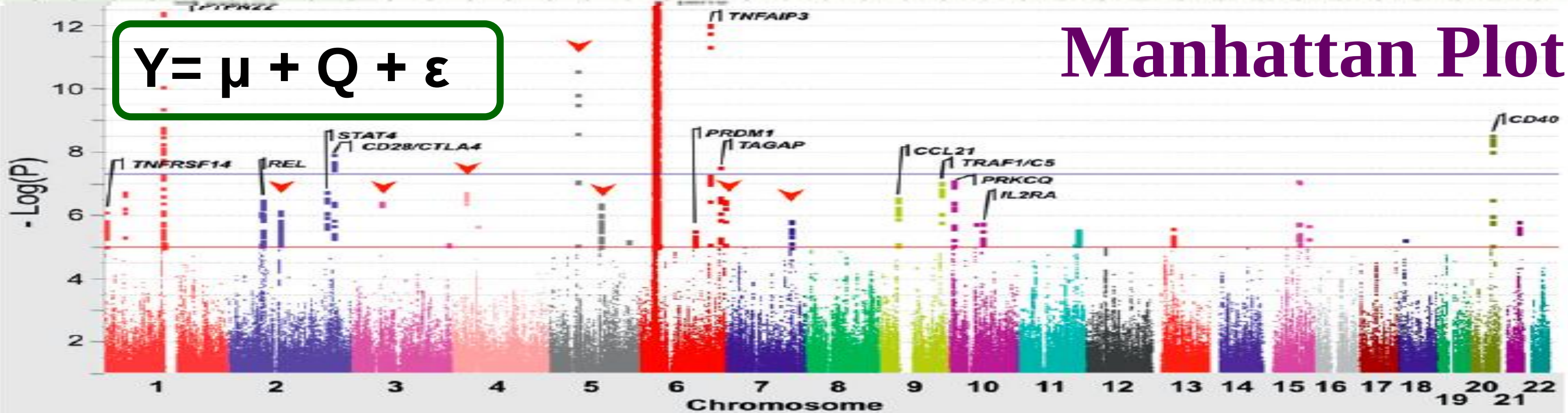
$Y = \mu + Q + QE + \varepsilon$

GxE Plot



$Y = \mu + Q + QQ + \varepsilon$

Network Plot



$Y = \mu + Q + \varepsilon$

Manhattan Plot

Stranger et al (2011, Genetics)

Partitioning of Phenotypic Variation

$$y = \mu + E + G + GE + \varepsilon$$

$$G = \text{å}\, a + \text{å}\, d + (\text{å}\,\text{å}\, aa + \text{å}\,\text{å}\, ad + + \text{å}\,\text{å}\, dd)$$

$$GE = \text{å}\, ae + \text{å}\, de + (\text{å}\,\text{å}\, aae + \text{å}\,\text{å}\, ade + + \text{å}\,\text{å}\, dde)$$

- **Environment Effects (E):**
- **QTL Effects (G):**

  Addtive (a), Dominance (d)

  QTL-QTL Interaction (aa, ad, dd)
- **QTL-Env Interaction (GE)**

  ae, de, aae, ade, dde
- **Random Error (ε)**

GMDR-GPU Parallel Computation for Genome-Wide Screening ~ 2k Candidate SNP

(n = 5,000, SNPs = 1.0×10^6)

- **GPU computation for 1D searching: 1×10^6 steps**

$$y_{ij} = \mu_j + q_k u_{ki} + qe_{kj} u_{ki} + \varepsilon_{ij}$$

- **GPU computation for 2D searching: 0.5×10^{12} steps**

$$y_{ij} = \mu_j + \sum_{k=1}^{r} (q_k u_{ki} + qe_{kj} u_{ki}) + (qq_{kh} u_{ki} u_{hi} + qqe_{khj} u_{ki} u_{hi}) + \varepsilon_{ij}$$

Computing Simulation by CPU and GPU for 10^5 SNPs and 5,000 persons

(Conducted at Microsoft Research Asia, Beijing, China)

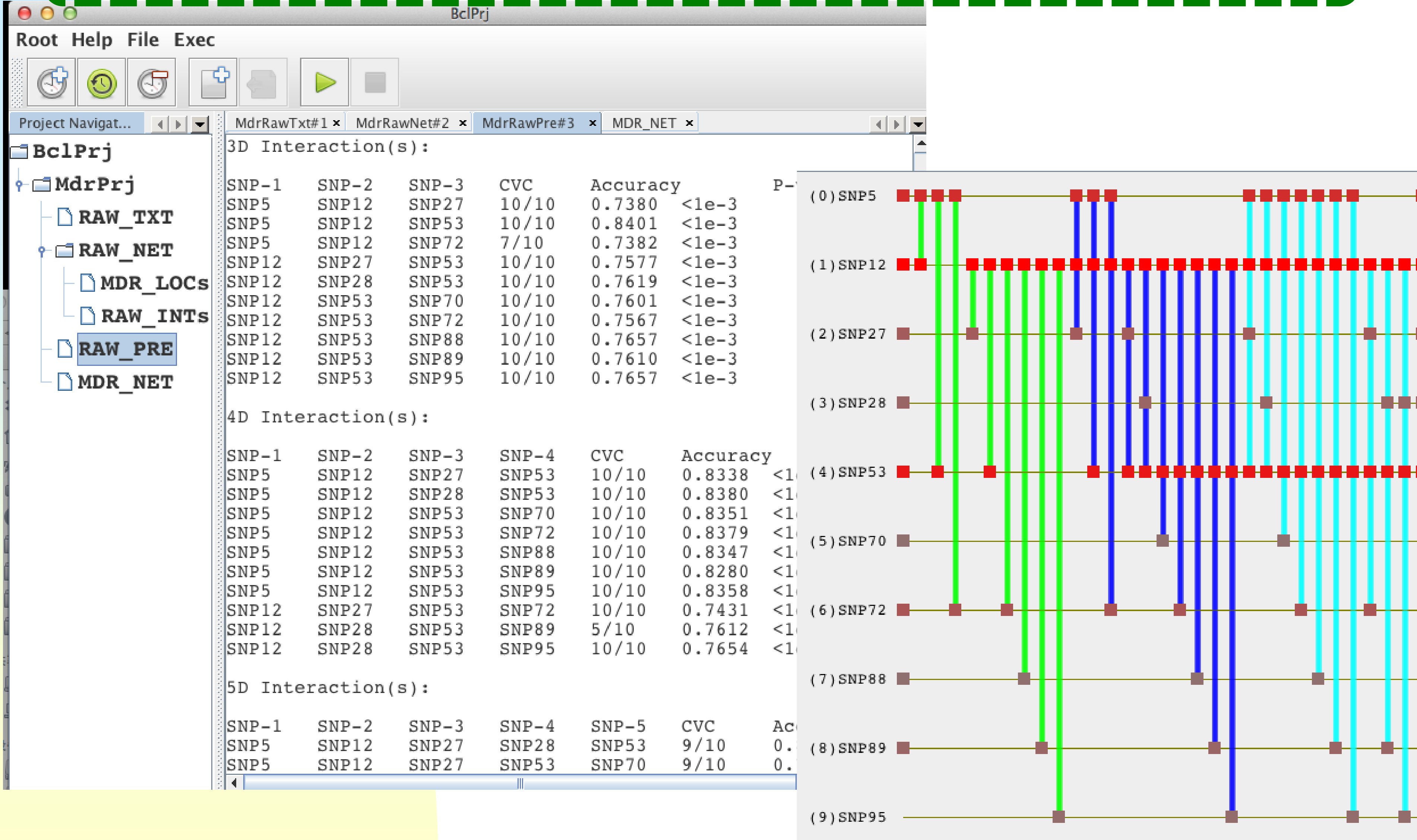
- **Four years and eight months by 24 CPU and one computer**
- **1 day by 400 CPUs and 80 computers**
- **< 1 day by 5 Tesla C2050 GPUs and one computer**

Traditional CPUs
(multi-core)

GPU
(Graphics Processing Unit)

GPU-Based Computation Software GMDR-GPU

3500X faster for screening one million SNPs



```
3D Interaction(s):

SNP-1    SNP-2    SNP-3    CVC      Accuracy      P-
SNP5     SNP12    SNP27    10/10    0.7380   <1e-3
SNP5     SNP12    SNP53    10/10    0.8401   <1e-3
SNP5     SNP12    SNP72    7/10     0.7382   <1e-3
SNP12    SNP27    SNP53    10/10    0.7577   <1e-3
SNP12    SNP28    SNP53    10/10    0.7619   <1e-3
SNP12    SNP53    SNP70    10/10    0.7601   <1e-3
SNP12    SNP53    SNP72    10/10    0.7567   <1e-3
SNP12    SNP53    SNP88    10/10    0.7657   <1e-3
SNP12    SNP53    SNP89    10/10    0.7610   <1e-3
SNP12    SNP53    SNP95    10/10    0.7657   <1e-3

4D Interaction(s):

SNP-1    SNP-2    SNP-3    SNP-4    CVC      Accuracy
SNP5     SNP12    SNP27    SNP53    10/10    0.8338   <1
SNP5     SNP12    SNP28    SNP53    10/10    0.8380   <1
SNP5     SNP12    SNP53    SNP70    10/10    0.8351   <1
SNP5     SNP12    SNP53    SNP72    10/10    0.8379   <1
SNP5     SNP12    SNP53    SNP88    10/10    0.8347   <1
SNP5     SNP12    SNP53    SNP89    10/10    0.8280   <1
SNP5     SNP12    SNP53    SNP95    10/10    0.8358   <1
SNP12    SNP27    SNP53    SNP72    10/10    0.7431   <1
SNP12    SNP28    SNP53    SNP89    5/10     0.7612   <1
SNP12    SNP28    SNP53    SNP95    10/10    0.7654   <1

5D Interaction(s):

SNP-1    SNP-2    SNP-3    SNP-4    SNP-5    CVC      Ac
SNP5     SNP12    SNP27    SNP28    SNP53    9/10     0.
SNP5     SNP12    SNP27    SNP53    SNP70    9/10     0.
```

QT*X*Network-GPU Parallel Computation for Genome-Wide Gene Mapping

(n = 5,000, ~2 k SNPs)

360X faster for estimating genetic effects of genes

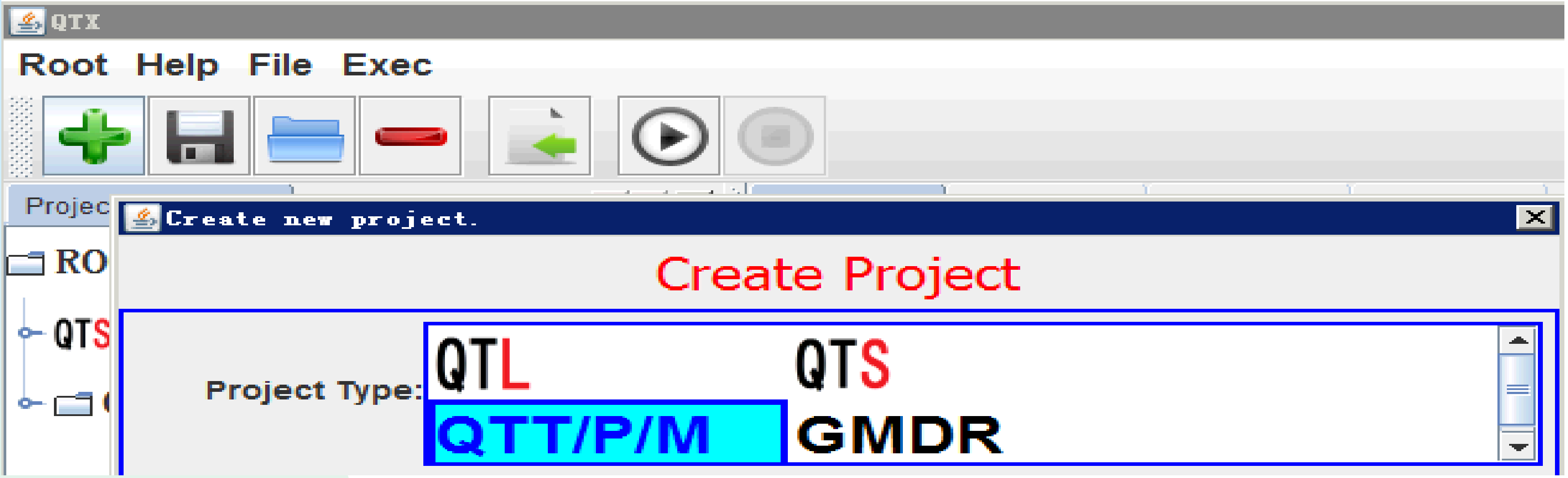
- **CPU computation for estimating gene effects in full model: 2,000 permutations, 20,000 MCMC**

$$y_{ij} = m_j + \overset{r}{\underset{k=1}{\mathring{a}}} q_k u_{ki} + \overset{s}{\underset{k,h=1,k^1 h}{\mathring{a}}} qq_{kh} u_{ki} u_{hi}$$

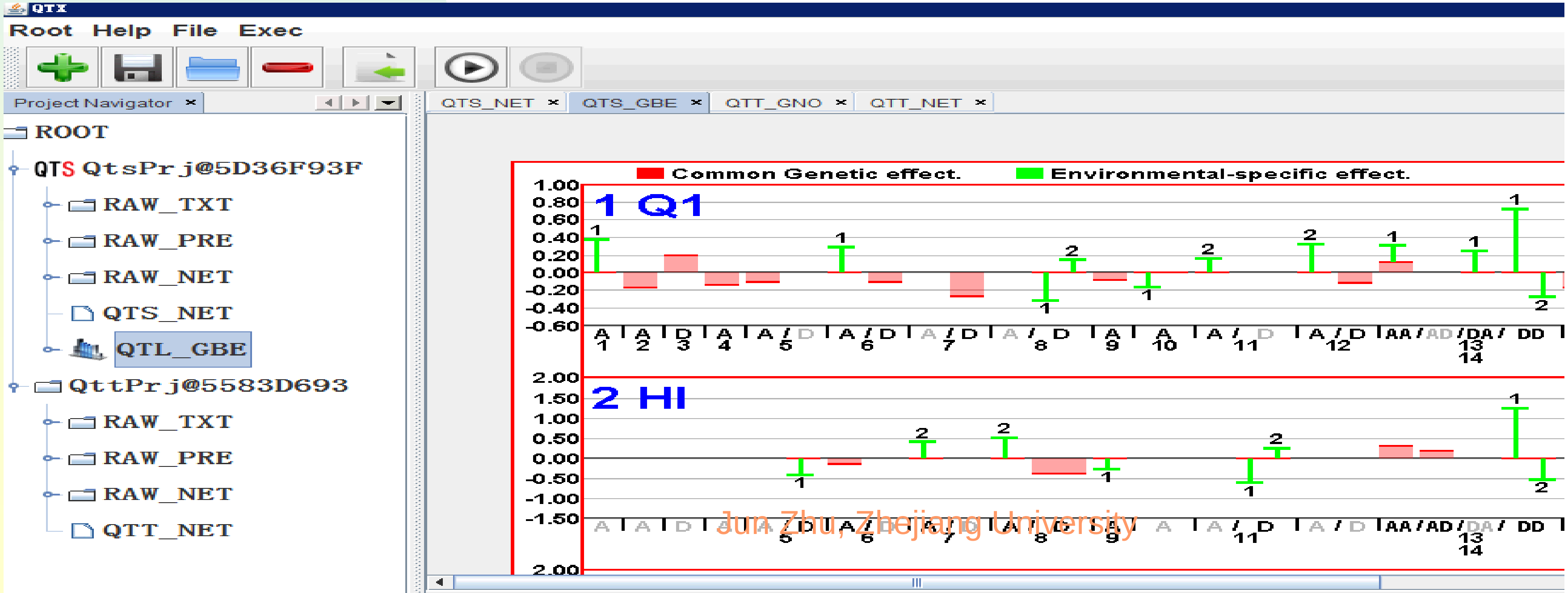
$$+ \overset{r}{\underset{k=1}{\mathring{a}}} qe_{kj} u_{ki} + \overset{s}{\underset{k,h=1,k^1 h}{\mathring{a}}} qqe_{khj} u_{ki} u_{hi} + e_{ij}$$

Mapping Software: QTXNetwork

360X faster for estimating SNP effects

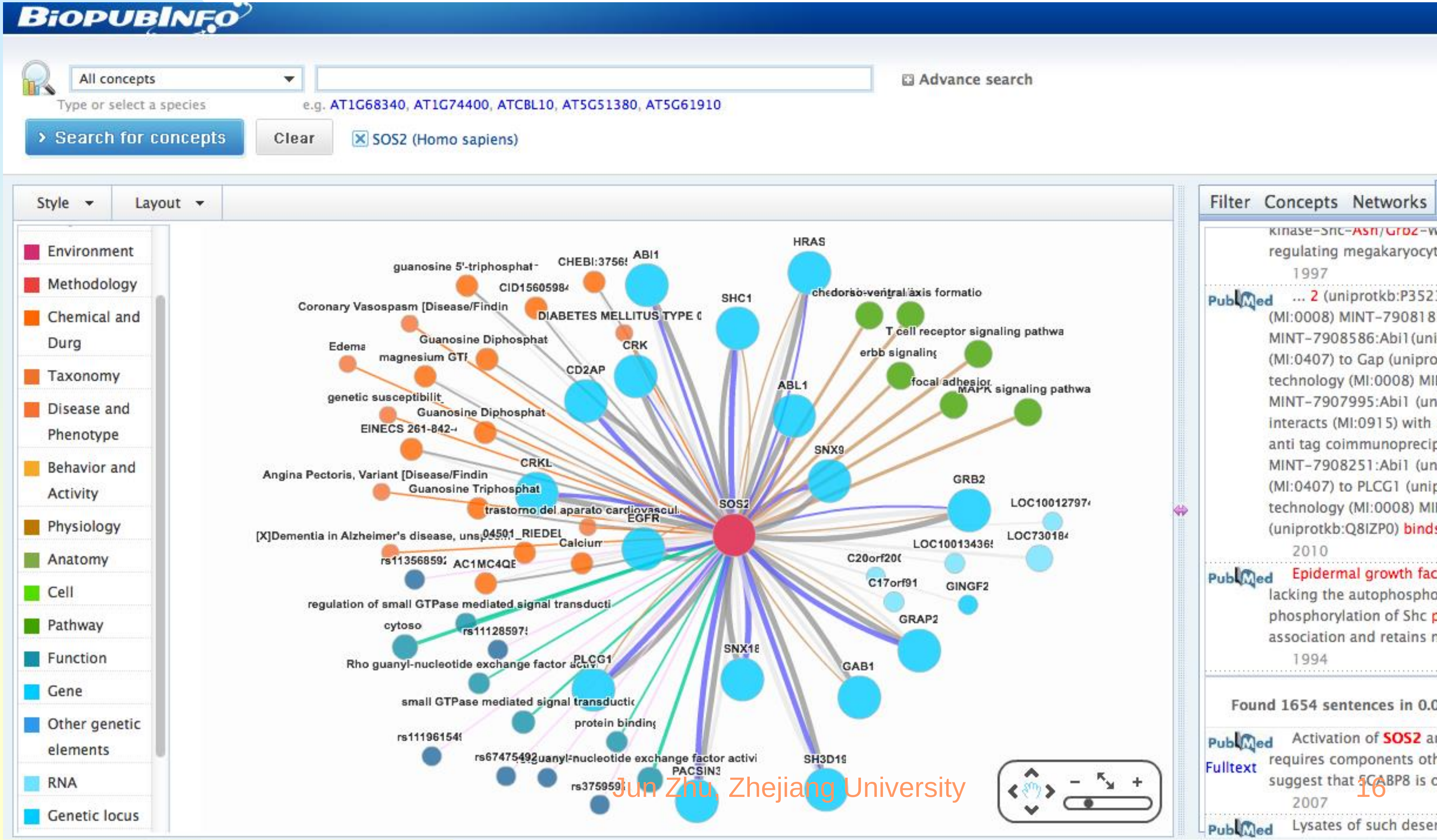


Project Type: QTT/P/M



BioPubInfo

- **Based on 1000 Databases, 6800 Species,**
- **6M Articles, 20M Abstracts, 0.3B Sentences analysis**



All concepts ▾

Type or select a species

e.g. AT1G68340, AT1G74400, ATCBL10, AT5G51380, AT5G61910

☒ SOS2 (Homo sapiens)

- 🟥 Environment
- 🟥 Methodology
- 🟧 Chemical and Durg
- 🟧 Taxonomy
- 🟧 Disease and Phenotype
- 🟨 Behavior and Activity
- 🟫 Physiology
- 🟩 Anatomy
- 🟩 Cell
- 🟩 Pathway
- 🟦 Function
- 🟦 Gene
- 🟦 Other genetic elements
- 🟦 RNA
- 🟦 Genetic locus

kinase-Shc-Ash/Grb2-W
regulating megakaryocyt
1997

PubMed ... 2 (uniprotkb:P352
(MI:0008) MINT-790818
MINT-7908586:Abi1(uni
(MI:0407) to Gap (unipro
technology (MI:0008) MI
MINT-7907995:Abi1 (un
interacts (MI:0915) with
anti tag coimmunoprecip
MINT-7908251:Abi1 (un
(MI:0407) to PLCG1 (unip
technology (MI:0008) MI
(uniprotkb:Q8IZP0) binds
2010

PubMed Epidermal growth fac
lacking the autophospho
phosphorylation of Shc p
association and retains r
1994

Found 1654 sentences in 0.0

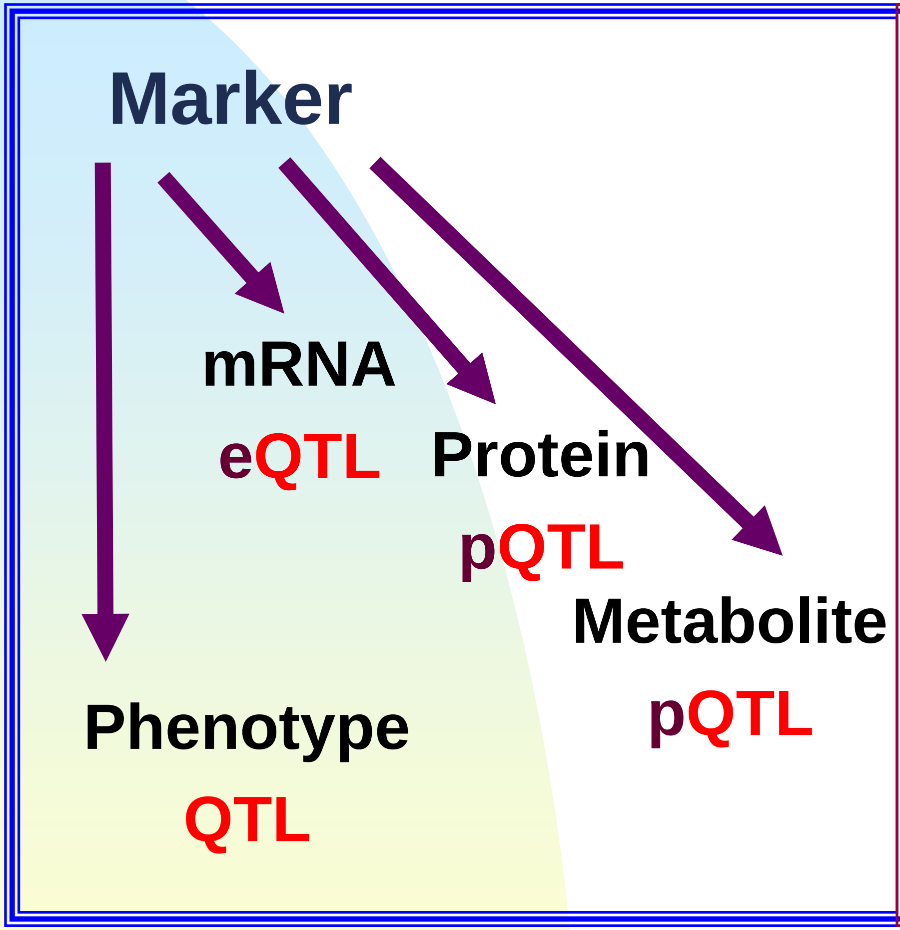
PubMed Fulltext Activation of SOS2 a
requires components oth
suggest that FCABP8 is c
2007

PubMed Lysates of such deser

From QTL Mapping to QTX Mapping

Linkage Analysis

Association Analysis



Marker

mRNA

eQTL

Protein

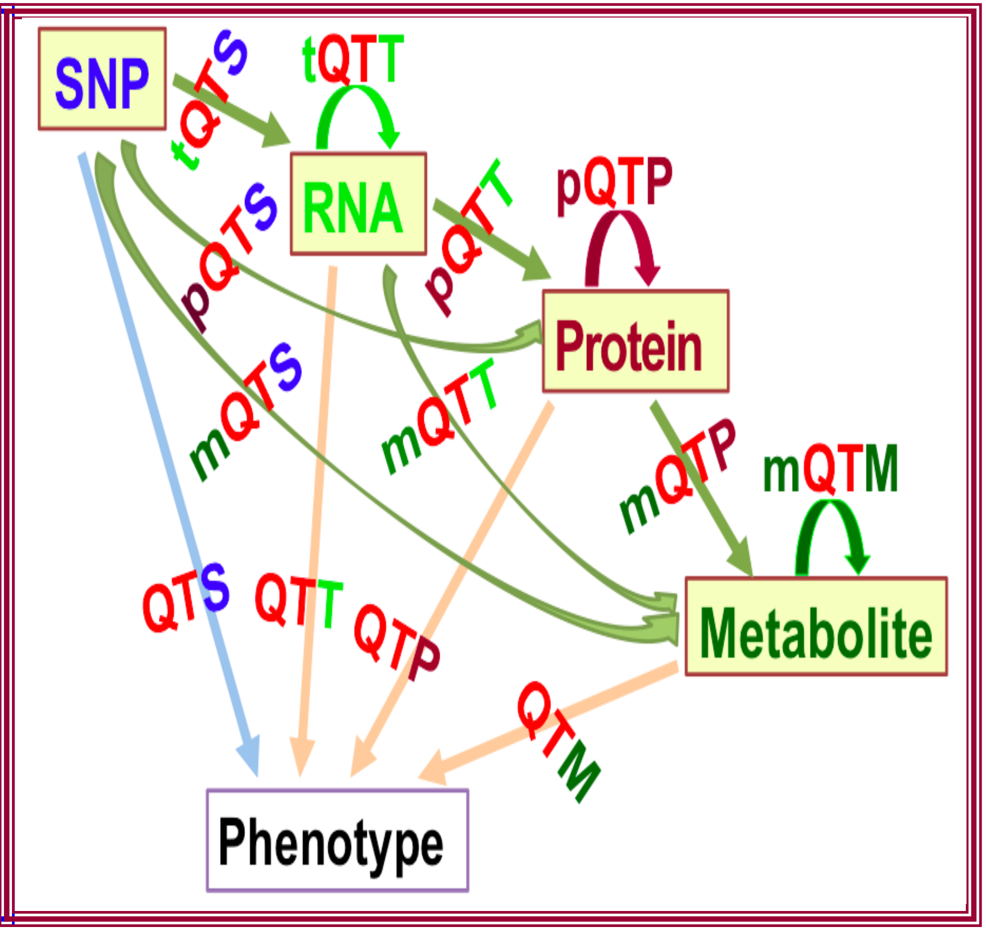
pQTL

Metabolite

pQTL

Phenotype

QTL

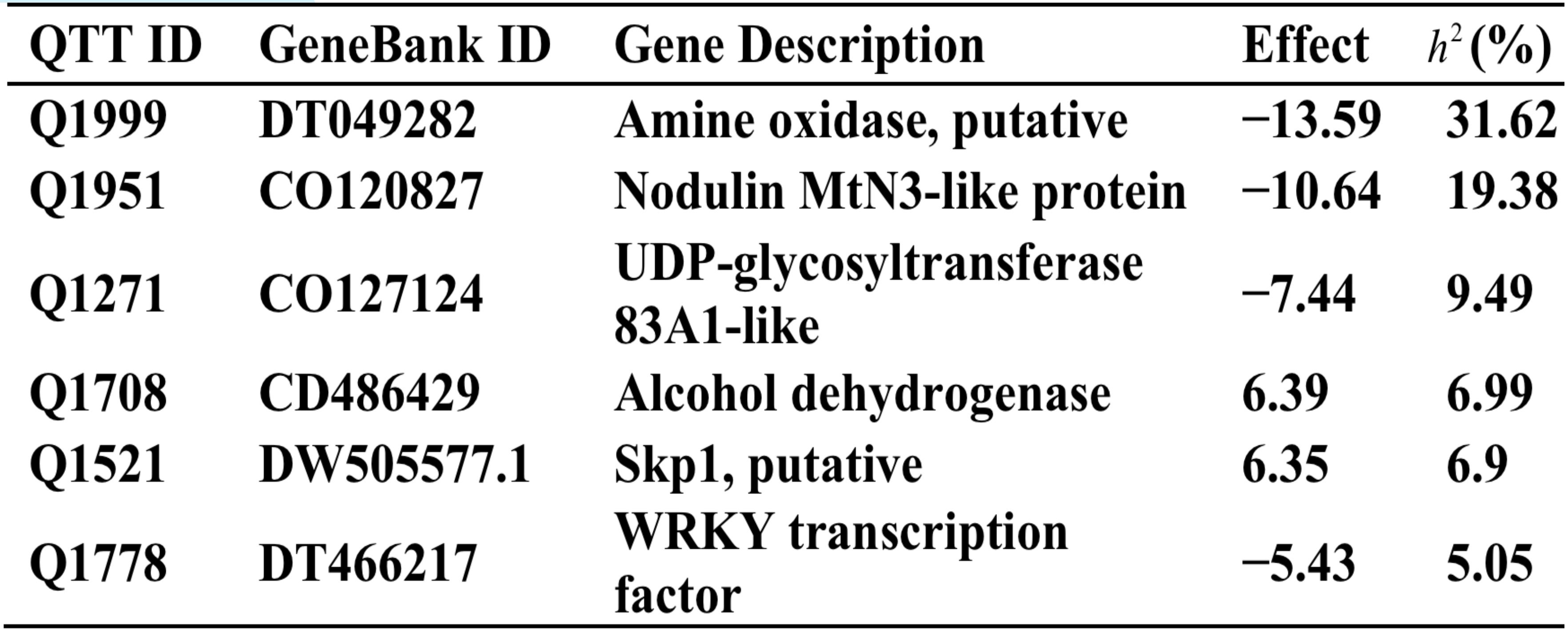


QTT Mapping for Diallel Crosses of Cotton

Chinese Sci. Bull. 2012, V57

8 Parets, 10 Crosses (1×2, 1×3, 1×5, 1×8, 2×5, 3×5, 4×5, 5×6, 5×7, 5×8)

mRNA obtained from Buds, QTT mapping for Lint yield based on 20,000 transcripts. 6 largest QTTs listed

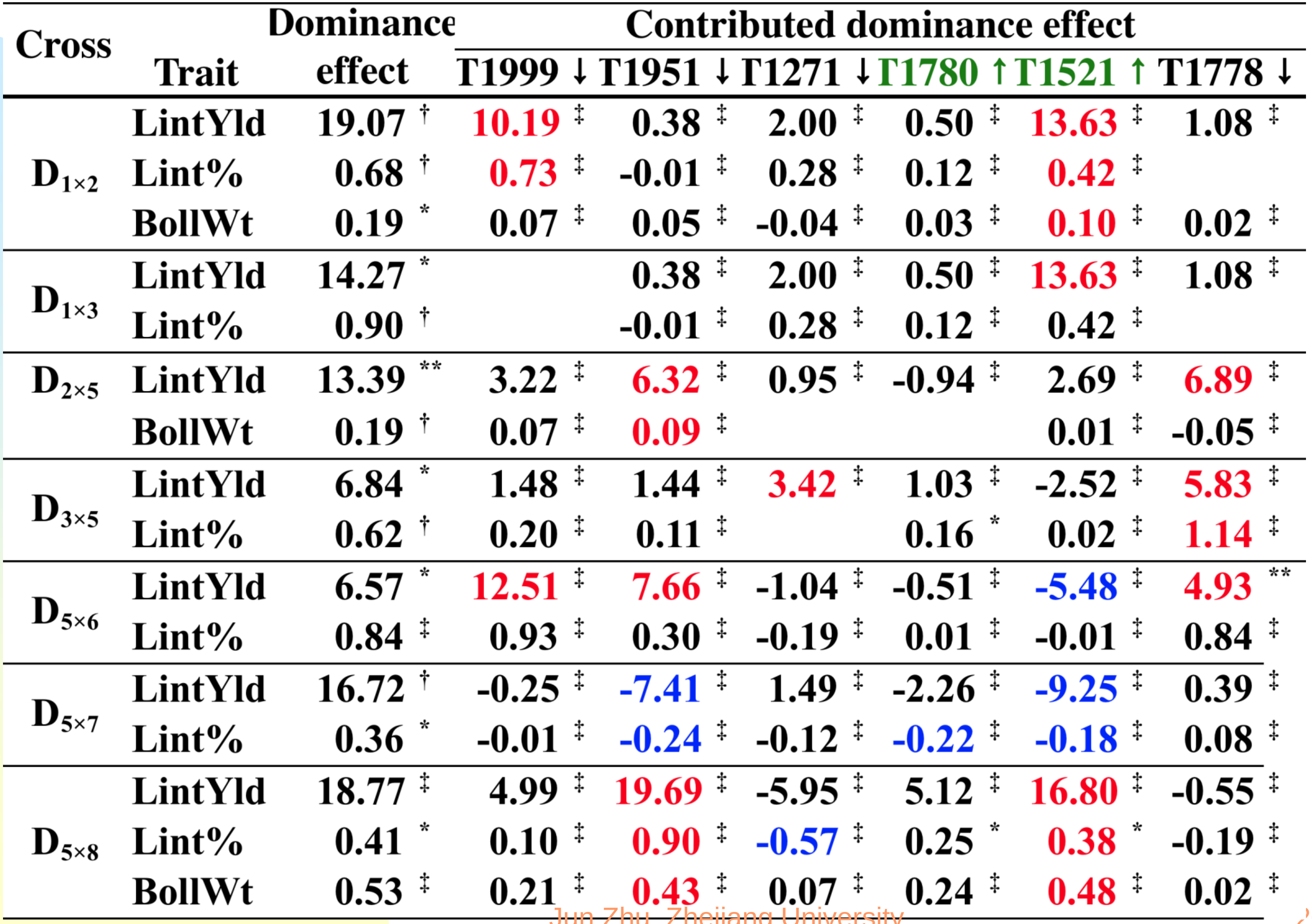


QTT ID	GeneBank ID	Gene Description	Effect	h^2 (%)
Q1999	DT049282	Amine oxidase, putative	−13.59	31.62
Q1951	CO120827	Nodulin MtN3-like protein	−10.64	19.38
Q1271	CO127124	UDP-glycosyltransferase 83A1-like	−7.44	9.49
Q1708	CD486429	Alcohol dehydrogenase	6.39	6.99
Q1521	DW505577.1	Skp1, putative	6.35	6.9
Q1778	DT466217	WRKY transcription factor	−5.43	5.05

The Contribute of QTT to Additive Effects

Parent	Trait	Additive effect	Contributed additive effect					
			T1999 ↓	T1951 ↓	T1271 ↓	T1780 ↑	T1521 ↑	T1778 ↓
A_1	LintYld	2.62^{*}	$2.12^{\ddagger}$	$1.09^{\ddagger}$	$1.01^{\ddagger}$	$0.12^{\ddagger}$	$-1.15^{\ddagger}$	$0.08^{\ddagger}$
	Lint%	$2.26^{\ddagger}$	$1.07^{\ddagger}$	$-0.25^{\ddagger}$	$1.01^{\ddagger}$	$-0.02^{\ddagger}$	$-0.78^{\ddagger}$	$-0.51^{\ddagger}$
	BollWt	$0.17^{\ddagger}$	$-0.09^{\ddagger}$	$0.05^{\ddagger}$	$-0.13^{\ddagger}$	$0.06^{\ddagger}$	$0.26^{\ddagger}$	
A_3	LintYld	-1.61^{*}	$0.22^{\ddagger}$	$0.21^{\ddagger}$	$0.07^{\ddagger}$	$-0.49^{\ddagger}$	$0.84^{\ddagger}$	$0.10^{\ddagger}$
	Lint%	$-0.35^{\ddagger}$	$-0.25^{\ddagger}$	$0.03^{\ddagger}$	$1.07^{\ddagger}$	$0.72^{\ddagger}$	$0.29^{\ddagger}$	$0.00^{\ddagger}$
	Bolls	$1.18^{\ddagger}$	$0.12^{\ddagger}$	$0.13^{\ddagger}$			$0.37^{\ddagger}$	$-0.01^{\ddagger}$
	BollWt	$-0.4^{\ddagger}$	$-0.03^{\ddagger}$	$-0.02^{\ddagger}$	$-0.03^{\ddagger}$	$0.06^{\ddagger}$	$-0.08^{\dagger}$	
A_5	LintYld	$8.52^{\dagger}$	$1.78^{\ddagger}$	$4.81^{\ddagger}$	$0.46^{\ddagger}$	$0.45^{\ddagger}$	$3.29^{\ddagger}$	
	Lint%	$-0.3^{\ddagger}$		$0.92^{\ddagger}$			$0.99^{\ddagger}$	$1.28^{\ddagger}$
	Bolls	$0.82^{\dagger}$	$0.57^{\ddagger}$	$0.51^{\ddagger}$	$0.45^{\ddagger}$		$1.12^{\ddagger}$	$-0.22^{\ddagger}$
	BollWt	0.08^{**}	$-0.06^{\ddagger}$	$-0.13^{\ddagger}$	$0.01^{\ddagger}$	$0.00^{\ddagger}$	$-0.22^{\ddagger}$	
A_8	LintYld	$-6.86^{\dagger}$	$-4.88^{\ddagger}$	$-5.04^{\ddagger}$	$-2.19^{\ddagger}$	$-1.93^{\ddagger}$	$-6.10^{\ddagger}$	$-2.92^{\ddagger}$
	Bolls	$-3.22^{\ddagger}$	$-2.21^{\ddagger}$		$-2.79^{\ddagger}$		$-3.04^{\ddagger}$	
	BollWt	$0.47^{\ddagger}$		$0.12^{\ddagger}$	$0.40^{\ddagger}$	$0.45^{\ddagger}$	$0.45^{\ddagger}$	

The Contribute of QTT to Dominance Effects



Cross	Trait	Dominance effect	Contributed dominance effect T1999 ↓	T1951 ↓	T1271 ↓	T1780 ↑	T1521 ↑	T1778 ↓
$D_{1\times2}$	LintYld	19.07†	10.19‡	0.38‡	2.00‡	0.50‡	13.63‡	1.08‡
	Lint%	0.68†	0.73‡	-0.01‡	0.28‡	0.12‡	0.42‡	
	BollWt	0.19*	0.07‡	0.05‡	-0.04‡	0.03‡	0.10‡	0.02‡
$D_{1\times3}$	LintYld	14.27*		0.38‡	2.00‡	0.50‡	13.63‡	1.08‡
	Lint%	0.90†		-0.01‡	0.28‡	0.12‡	0.42‡	
$D_{2\times5}$	LintYld	13.39**	3.22‡	6.32‡	0.95‡	-0.94‡	2.69‡	6.89‡
	BollWt	0.19†	0.07‡	0.09‡			0.01‡	-0.05‡
$D_{3\times5}$	LintYld	6.84*	1.48‡	1.44‡	3.42‡	1.03‡	-2.52‡	5.83‡
	Lint%	0.62†	0.20‡	0.11‡		0.16*	0.02‡	1.14‡
$D_{5\times6}$	LintYld	6.57*	12.51‡	7.66‡	-1.04‡	-0.51‡	-5.48‡	4.93**
	Lint%	0.84‡	0.93‡	0.30‡	-0.19‡	0.01‡	-0.01‡	0.84‡
$D_{5\times7}$	LintYld	16.72†	-0.25‡	-7.41‡	1.49‡	-2.26‡	-9.25‡	0.39‡
	Lint%	0.36*	-0.01‡	-0.24‡	-0.12‡	-0.22‡	-0.18‡	0.08‡
$D_{5\times8}$	LintYld	18.77‡	4.99‡	19.69‡	-5.95‡	5.12‡	16.80‡	-0.55‡
	Lint%	0.41*	0.10‡	0.90‡	-0.57‡	0.25*	0.38*	-0.19‡
	BollWt	0.53‡	0.21‡	0.43‡	0.07‡	0.24‡	0.48‡	0.02‡

Estimates of QTS, QTT, QTP, and QTM for Chromium in Tobacco Variety Test

Type	QTX	Effect	Predict	-lg(P)	h^2(%)
QTS	Phm1376	ae1	-0.43	2.18	30.09
		ae2	-0.37	1.72	
		ae3	-0.41	2	
		ae4	0.45	2.38	
		ae5	0.59	3.78	
		ae6	0.78	6.09	
	Phm1053/Phm1471	aae4	0.41	2.09	11.24
		aae5	0.47	2.55	
		aae6	-0.48	2.65	
QTT	mRNA2713	q	0.43	3.1	7.47
	mRNA2123	qe4	3.30	3.15	72.67
	mRNA2167	qe5	0.54	3.58	1.93
	miRNA578	qe4	-0.45	2.74	23.6
		qe5	-0.86	5.21	
QTP	Amino5	q	-0.97	1.85	32.85
	Amino5	qe6	-2.43	2.72	34.74
QTM	MetabA14	q	0.34	9.3	0.01
	MetabA21/MetabA23	qqe4	-31.53	1.76	99.96
	MetabA21/MetabA23	qqe6	105.21	6.08	

e1	L1V1
e2	L1V2
e3	L1V3
e4	L2V1
e5	L2V2
e6	L2V3

Quantitative Environment Effects of QTTs

- **One genotype with 31,100 transcripts, five treatments of drug dose (Mean = 302.4)**

		Main Effect		Dose 5		Dose 10		Dose 20		Dose 25		
QTT	Gene ID	T	h^2(%)	TE_2	h^2(%)	TE_3	h^2(%)	TE_4	h^2(%)	TE_5	h^2(%)	h^2(%)
1-801	1398500_AT	$-61.45^{\ddagger}$	24.20	$-85.42^{\ddagger}$	14.03					-51.63^{**}	3.70	41.93
1-166	1369679_A_AT	$-46.93^{\ddagger}$	14.11									14.11
1-9	1368695_AT	-25.16^{*}	4.06			-69.75^{+}	8.83					12.89
1-531	1368829_AT	$38.82^{\ddagger}$	9.66									9.66
1-223	1387221_AT	21.86^{*}	3.06			35.91^{*}	2.34					5.40
1-1704	1388453_AT	13.92^{*}	1.24			28.38^{*}	1.46			$-41.90^{\ddagger}$	2.44	5.14
1-783	1370308_AT	-18.94^{+}	2.30							-18.04^{*}	0.45	2.75
1-988	1372306_AT	$15.81^{\ddagger}$	1.60					27.39^{*}	0.72			2.32
1-394	1367780_AT	$-9.13^{\ddagger}$	0.53							$-15.19^{\ddagger}$	0.32	0.85

SNP Mapping for Wheat F9 Population

- F$_9$ Populations, SNPs = 146, N= 499

2012 Grain Weight Mean = 78.7 Total heritability = 90.8%

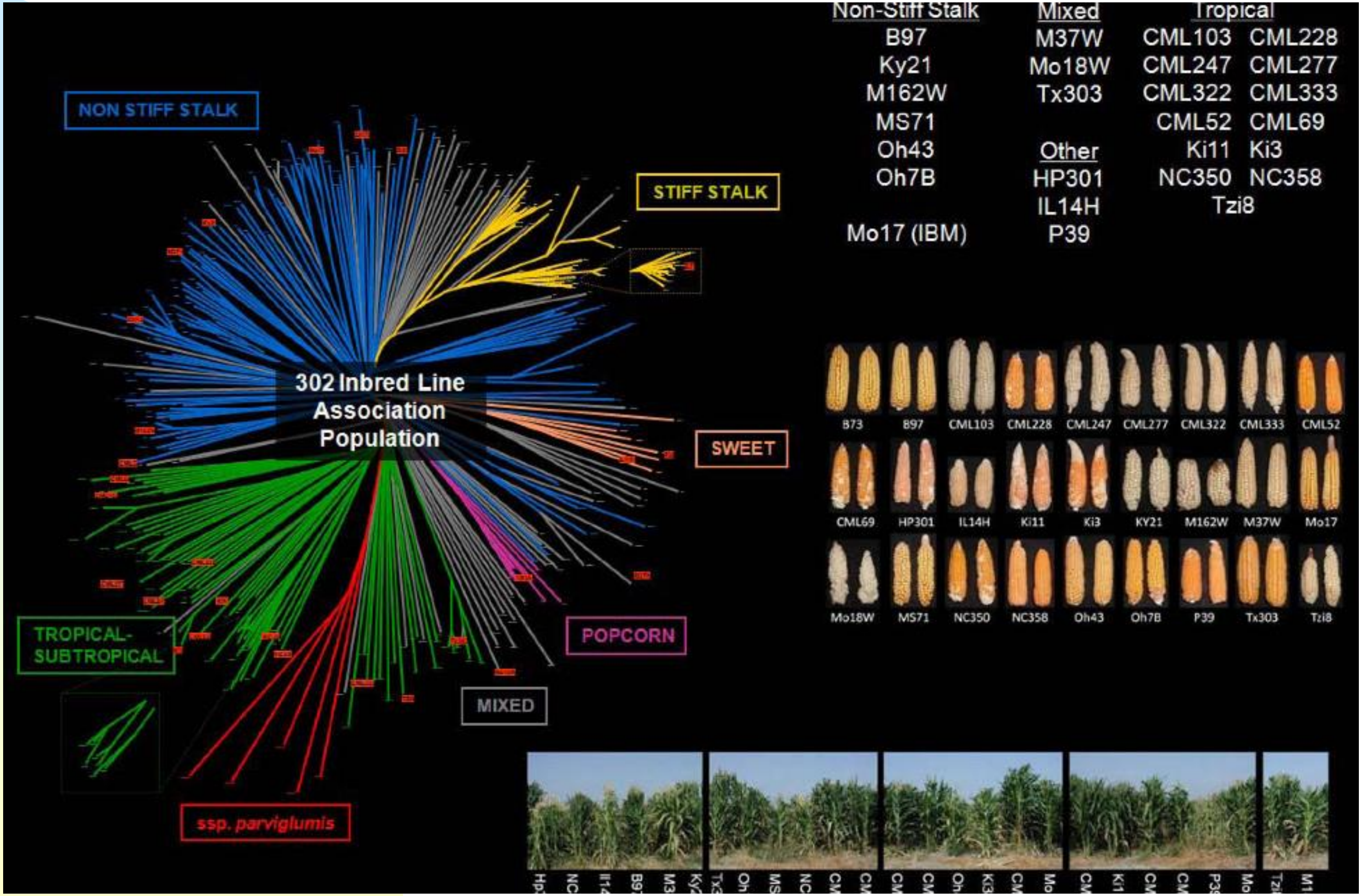
SNPID	SNPID	Type	Effect	-log(P)	h^2
BE490613_3A_1		a	3.90	36.19	8.46%
BE443010B_Ta_2_1		a	-0.80	2.01	0.35%
		d	1.33	1.55	0.98%
BE586140_1A	BG274948D_Ta_2_1	dd	-5.13	4.55	14.58%
BE586140_1A	BE445184_4B	dd	-5.57	5.27	17.23%
BE490613_3A_1	BE443010B_Ta_2_1	aa	-1.53	6.32	1.31%
		dd	-9.29	13.46	47.88%

2011Ear Humber Mean = 78.7 Total heritability = 53.5%

SNPID	SNPID	Type	Effect	-log(P)	h^2
BE444579_3B_1		a	5.68	2.89	2.39%
BE443010B_Ta_2_1		a	8.22	5.48	5.02%
		d	-14.18	4.25	14.90%
BE442700_7B	BE498985A_Ta_2_1	ad	-13.24	3.83	13.01%
		dd	-0.84	6.92	18.20%

GWAS for Maize NAM Populations

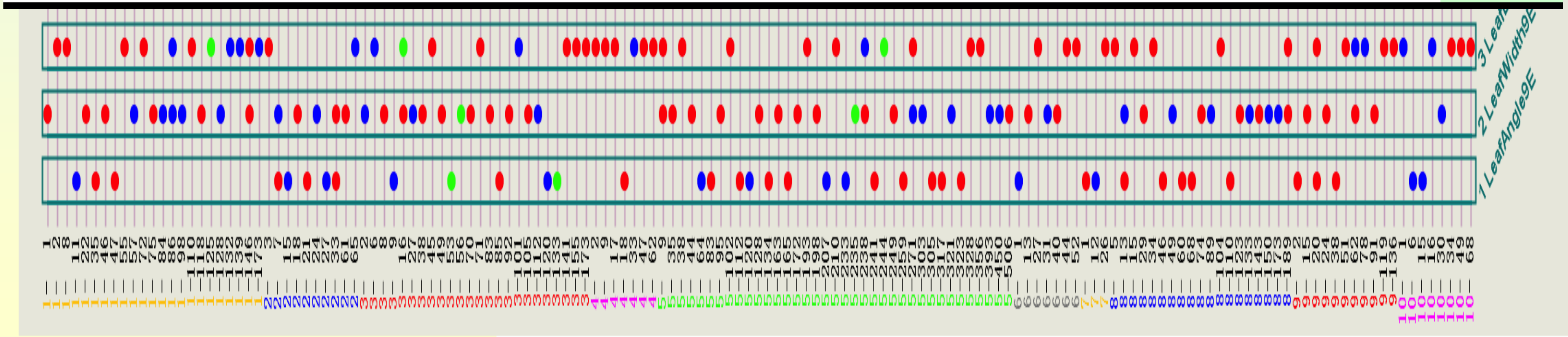
McMullen, et al. 2009. Science, 325(7): 737-740



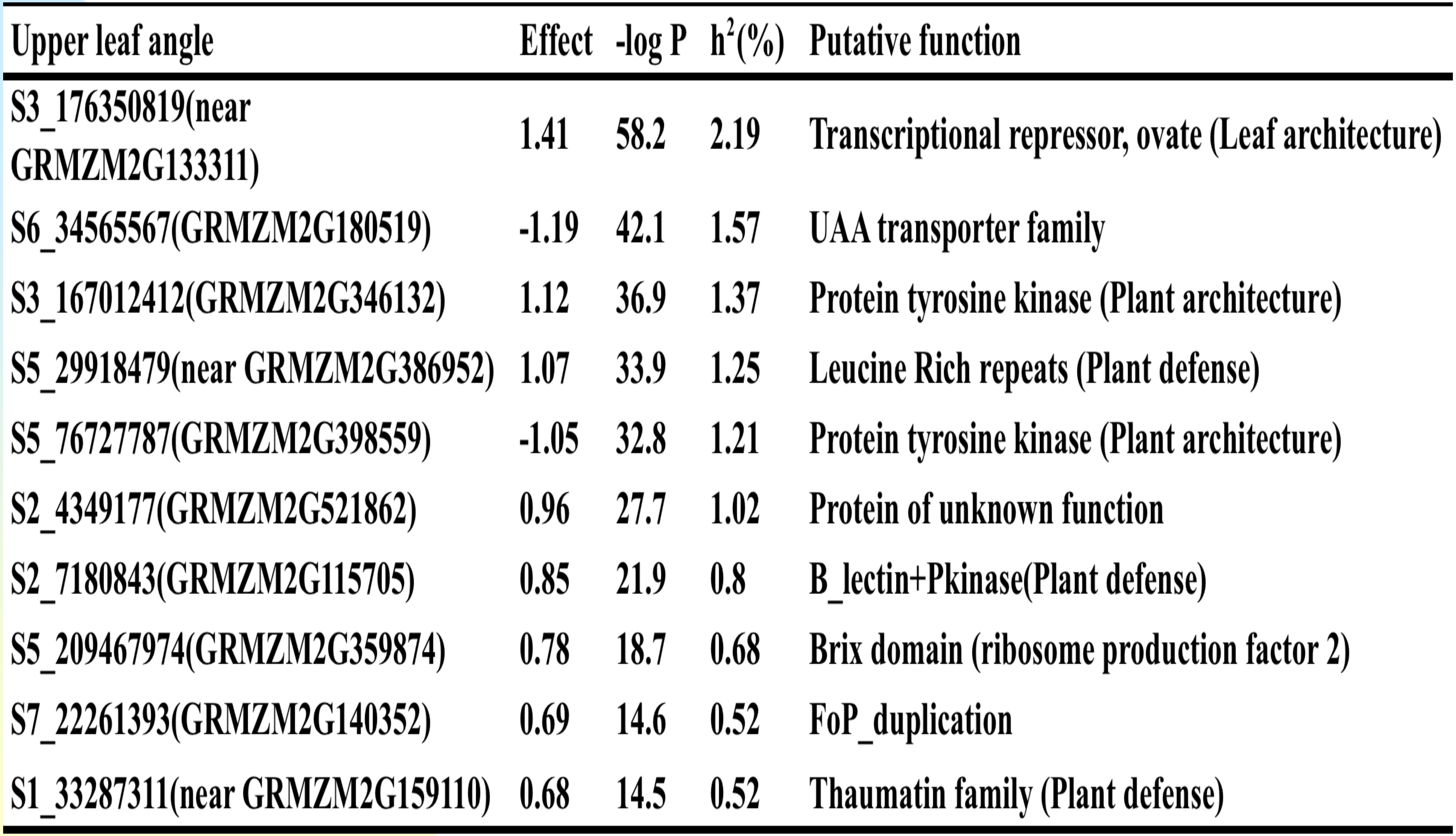
Detected Significant SNPs of Leaf Traits for Maize NAM Population in 9 Environments (N=44,055, SNPs=0.47M)

124 SNPs located within genes and 44 SNPs close to genes

Trait		Chr1	Chr2	Chr3	Chr4	Chr5	Chr6	Chr7	Chr8	Chr9	Chr10	Total
Leaf Angle	SNPs	3	5	5	1	13	1	2	5	3	2	40
	h^2(%)	0.77	2.2	3.56	0.13	4.56	1.57	0.89	1.21	0.89	0.68	16.46
	h^2(%)	0.03	0.18	1.29	0	0.17	0.02	0.25	0	0	0.52	2.46
Leaf Length	SNPs	11	2	8	6	10	3	1	5	6	5	57
	h^2(%)	4.4	0.28	3.69	1.64	4.84	0.89	0.18	2.73	3.6	3.61	25.86
	h^2(%)	0.77	0.02	0.55	0.02	0.13	0	0	0	0.61	0.66	2.76
Leaf Width	SNPs	11	5	12	0	17	3	0	11	4	1	64
	h^2(%)	6.47	3.08	3.61	0	8	1.77	0	7.44	1.61	0.22	32.2
	h^2(%)	0.55	0.06	0.04	0	0.23	0.03	0	0.8	0	0	1.71

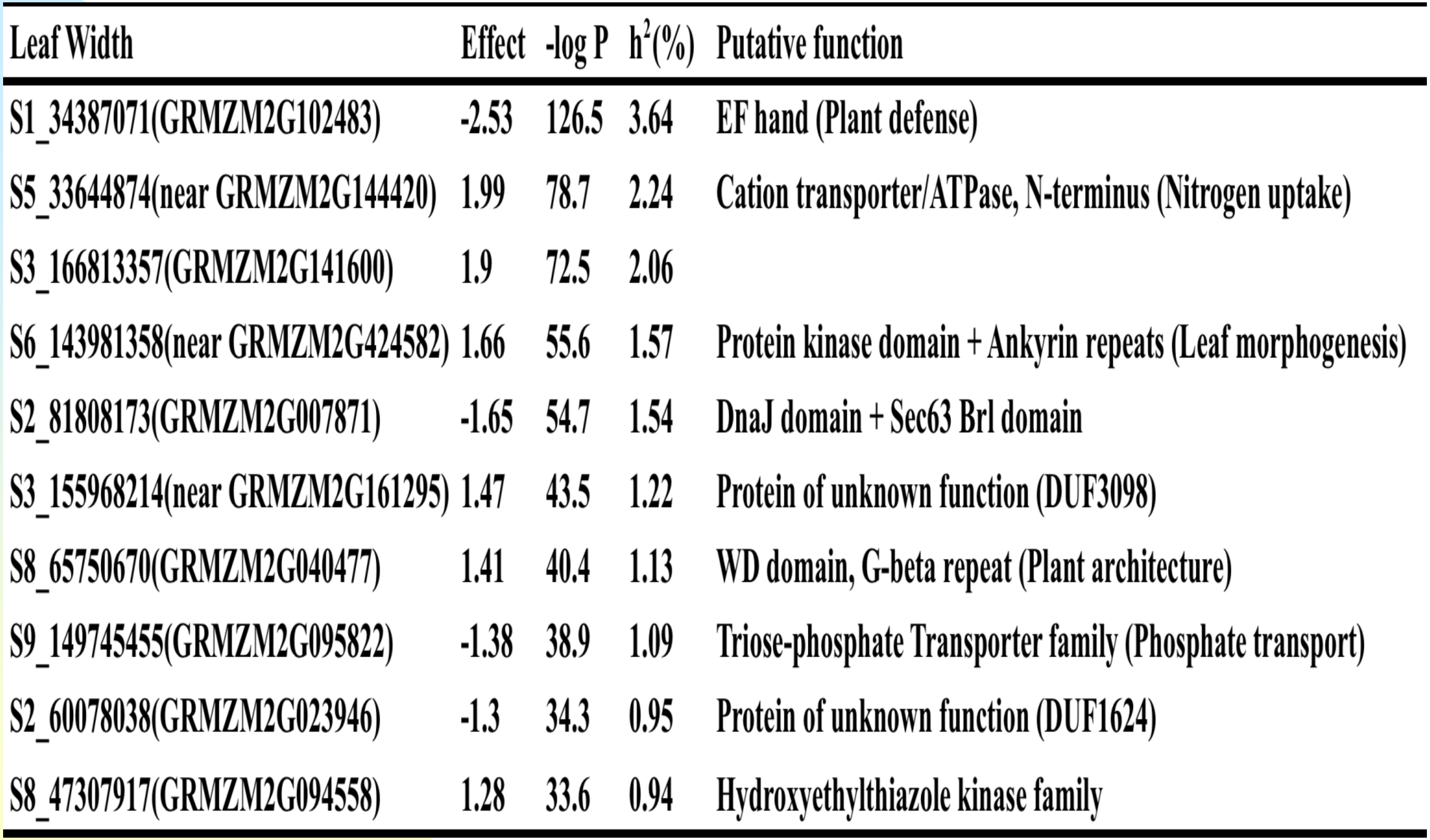


Top 10 Major SNPs with Large Additive Effect for LUA in NAM Population



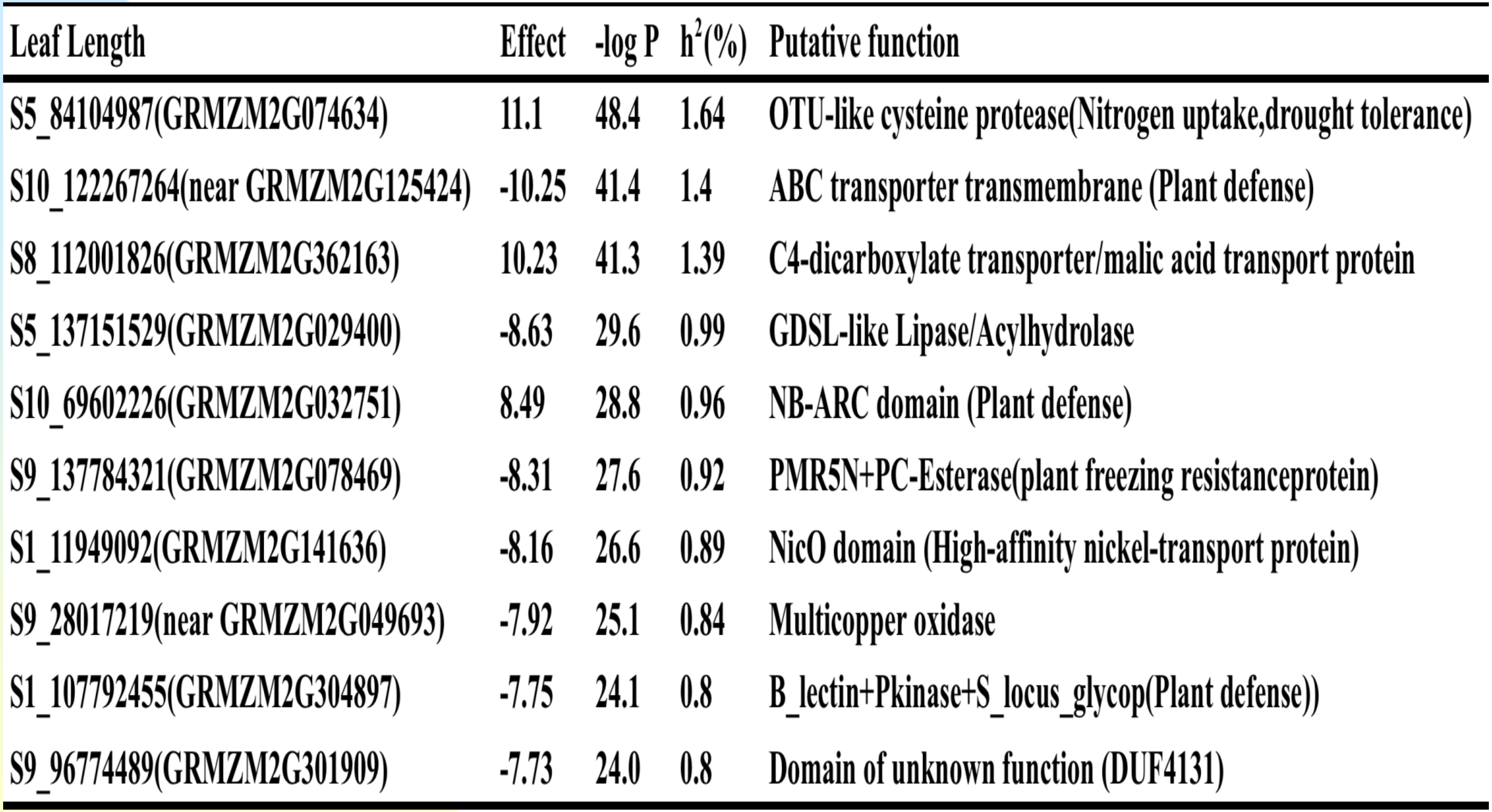
Upper leaf angle	Effect	-log P	h^2(%)	Putative function
S3_176350819(near GRMZM2G133311)	1.41	58.2	2.19	Transcriptional repressor, ovate (Leaf architecture)
S6_34565567(GRMZM2G180519)	-1.19	42.1	1.57	UAA transporter family
S3_167012412(GRMZM2G346132)	1.12	36.9	1.37	Protein tyrosine kinase (Plant architecture)
S5_29918479(near GRMZM2G386952)	1.07	33.9	1.25	Leucine Rich repeats (Plant defense)
S5_76727787(GRMZM2G398559)	-1.05	32.8	1.21	Protein tyrosine kinase (Plant architecture)
S2_4349177(GRMZM2G521862)	0.96	27.7	1.02	Protein of unknown function
S2_7180843(GRMZM2G115705)	0.85	21.9	0.8	B_lectin+Pkinase(Plant defense)
S5_209467974(GRMZM2G359874)	0.78	18.7	0.68	Brix domain (ribosome production factor 2)
S7_22261393(GRMZM2G140352)	0.69	14.6	0.52	FoP_duplication
S1_33287311(near GRMZM2G159110)	0.68	14.5	0.52	Thaumatin family (Plant defense)

Top 10 Major SNPs with Large Additive Effect for LW in NAM Population



Leaf Width	Effect	-log P	h^2(%)	Putative function
S1_34387071(GRMZM2G102483)	-2.53	126.5	3.64	EF hand (Plant defense)
S5_33644874(near GRMZM2G144420)	1.99	78.7	2.24	Cation transporter/ATPase, N-terminus (Nitrogen uptake)
S3_166813357(GRMZM2G141600)	1.9	72.5	2.06	
S6_143981358(near GRMZM2G424582)	1.66	55.6	1.57	Protein kinase domain + Ankyrin repeats (Leaf morphogenesis)
S2_81808173(GRMZM2G007871)	-1.65	54.7	1.54	DnaJ domain + Sec63 Brl domain
S3_155968214(near GRMZM2G161295)	1.47	43.5	1.22	Protein of unknown function (DUF3098)
S8_65750670(GRMZM2G040477)	1.41	40.4	1.13	WD domain, G-beta repeat (Plant architecture)
S9_149745455(GRMZM2G095822)	-1.38	38.9	1.09	Triose-phosphate Transporter family (Phosphate transport)
S2_60078038(GRMZM2G023946)	-1.3	34.3	0.95	Protein of unknown function (DUF1624)
S8_47307917(GRMZM2G094558)	1.28	33.6	0.94	Hydroxyethylthiazole kinase family

Top 10 Major SNPs with Large Additive Effect for LL in NAM Population



Leaf Length	Effect	-log P	h^2(%)	Putative function
S5_84104987(GRMZM2G074634)	11.1	48.4	1.64	OTU-like cysteine protease(Nitrogen uptake,drought tolerance)
S10_122267264(near GRMZM2G125424)	-10.25	41.4	1.4	ABC transporter transmembrane (Plant defense)
S8_112001826(GRMZM2G362163)	10.23	41.3	1.39	C4-dicarboxylate transporter/malic acid transport protein
S5_137151529(GRMZM2G029400)	-8.63	29.6	0.99	GDSL-like Lipase/Acylhydrolase
S10_69602226(GRMZM2G032751)	8.49	28.8	0.96	NB-ARC domain (Plant defense)
S9_137784321(GRMZM2G078469)	-8.31	27.6	0.92	PMR5N+PC-Esterase(plant freezing resistanceprotein)
S1_11949092(GRMZM2G141636)	-8.16	26.6	0.89	NicO domain (High-affinity nickel-transport protein)
S9_28017219(near GRMZM2G049693)	-7.92	25.1	0.84	Multicopper oxidase
S1_107792455(GRMZM2G304897)	-7.75	24.1	0.8	B_lectin+Pkinase+S_locus_glycop(Plant defense))
S9_96774489(GRMZM2G301909)	-7.73	24.0	0.8	Domain of unknown function (DUF4131)

Additive × Evironment Effects of SNPs in 9 Environments

Upper leaf angle	ae (-log P, h^2 %)
S3_176350819	ae1: 0.71 (2.3, 0.56)
	ae2: 1.29 (6.6, 1.82)
	ae3: 0.56 (1.6, 0.35)
	ae5: 0.59 (1.5, 0.38)
	ae6: 1.80 (12.4, 3.55)
	ae7: 1.18 (5.5, 1.53)
	ae9: -1.38 (7.3, 2.08)
S6_34565567	ae3: -0.40 (1.4, 0.18)
S5_29918479	ae9: 0.46 (1.4, 0.23)
S5_76727787	ae1: -0.50 (1.9, 0.27)
S2_7180843	ae6: 0.59 (2.3, 0.39)
S1_33287311	ae6: 0.50 (1.8, 0.28)

Leaf Width	ae (-log P, h^2 %)
S6_143981358	ae3: -0.66 (1.7, 0.25)
S8_65750670	ae8: 0.59 (1.6, 0.20)
S2_60078038	ae5: 0.66 (1.9, 0.25)
S8_47307917	ae1: 1.75 (8.1, 1.74)
	ae3: -1.37 (5.1, 1.07)
	ae7: 1.09 (3.6, 0.68)
	ae9: 0.71 (1.8, 0.29)

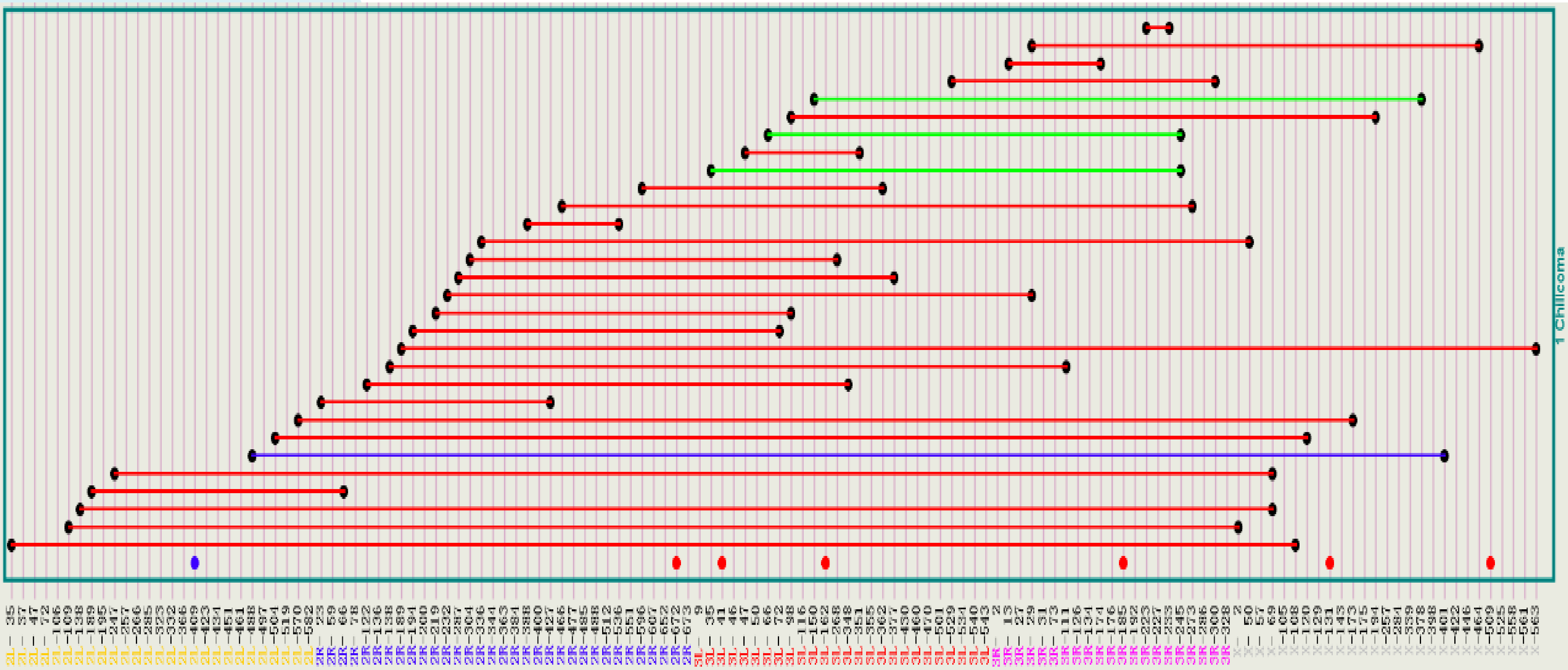
Leaf Length	ae (-log P, h^2 %)
S5_84104987	ae9: 5.44 (2.4, 0.40)
S10_69602226	ae1: 8.29 (3.9, 0.92)
	ae5: -8.99 (4.4, 1.08)
	ae6: 5.72 (2.2, 0.44)
	ae8: 11.57 (6.4, 1.78)
S1_107792455	ae1: -4.78 (1.7, 0.30)
	ae3: 4.79 (1.6, 0.31)
	ae8: -5.15 (1.8, 0.35)
	ae9: -6.39 (2.8, 0.54)
S9_96774489	ae3: 5.68 (2.2, 0.43)
	ae9: -4.01 (1.4, 0.21)

Predicted P1, Best Lines & Superior Lines

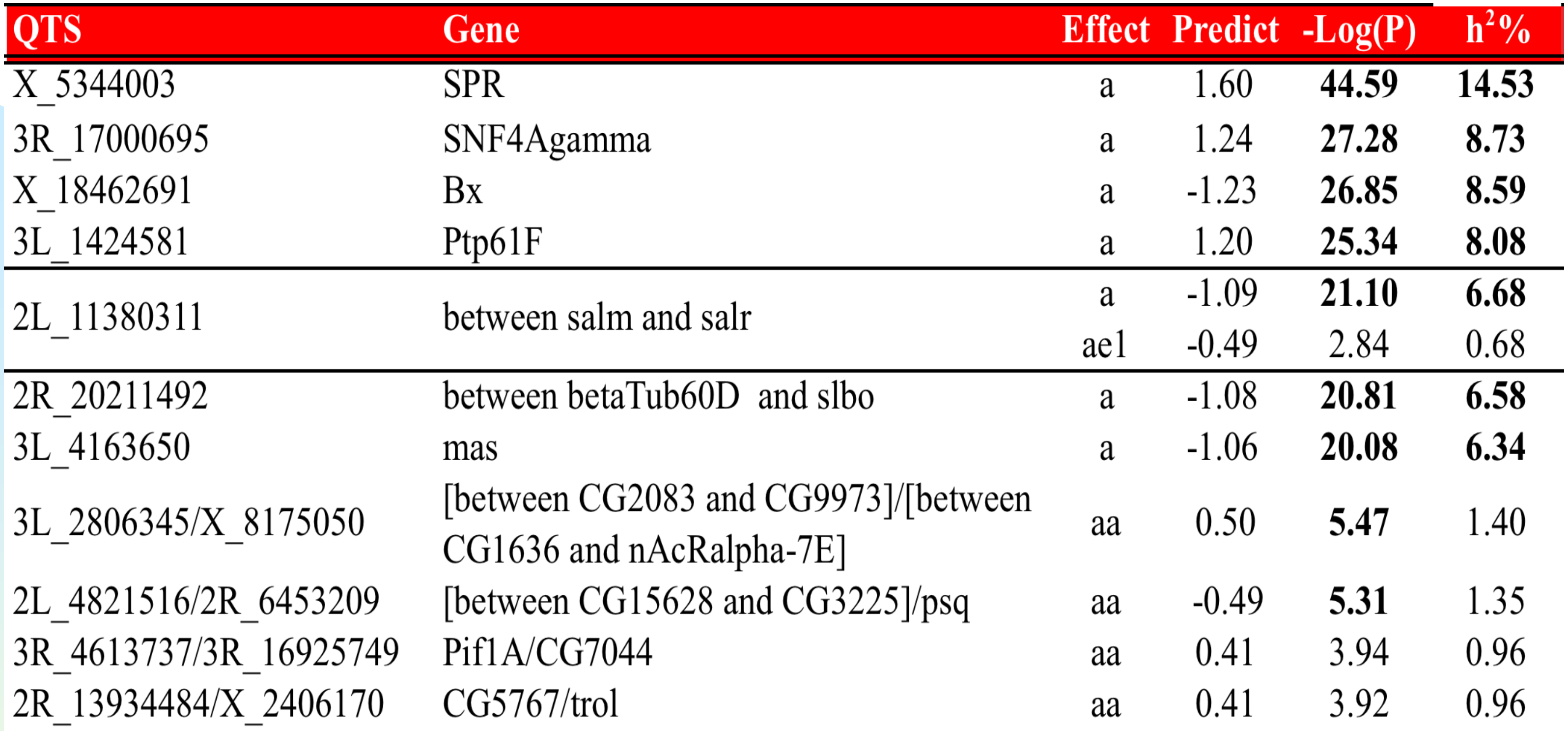
Entry	G	G+GE1	G+GE2	G+GE3	G+GE4	G+GE5	G+GE6	G+GE7	G+GE8	G+GE9
Leaf Angle	Mean = 61.0									
P1	11.2	12.5	12.5	11.1	10.1	11.8	16.0	13.6	10.7	10.3
Best Line	17.7	19.0	19.0	18.4	16.6	18.3	22.5	20.1	18.3	16.8
Superior Line	21.2	23.5	22.5	23.6	21.4	21.8	26.4	23.6	21.7	21.5
Select SNP	3	7	3	3	5	3	4	3	3	3
Leaf Width	Mean = 87.4									
P2	-6.8	-6.8	-6.1	-5.5	-8.4	-7.7	-6.1	-9.6	-8.0	-7.5
Best Line	-28.8	-30.9	-26.6	-26.1	-30.3	-26.9	-29.5	-33.6	-30.3	-30.2
Superior Line	-51.2	-56.2	-50.6	-49.1	-50.6	-49.5	-51.9	-57.9	-54.3	-55.6
Select SNP	18	19	18	19	16	20	19	18	21	14
Leaf Length	Mean = 752.7									
P1	-15.8	1.0	-22.8	-18.7	-18.4	-22.1	3.9	-5.5	7.9	-29.6
Best Line	-144.2	-146.4	-144.6	-134.2	-137.7	-134.9	-153.6	-145.2	-148.8	-197.8
Superior Line	-294.9	-321.2	-301.9	-290.6	-294.8	-301.7	-321.3	-305.1	-328.9	-344.1
Select SNP	13	13	12	11	13	15	15	17	14	13

Importance of Epistasis on Chill Coma Recovery in Drosophila

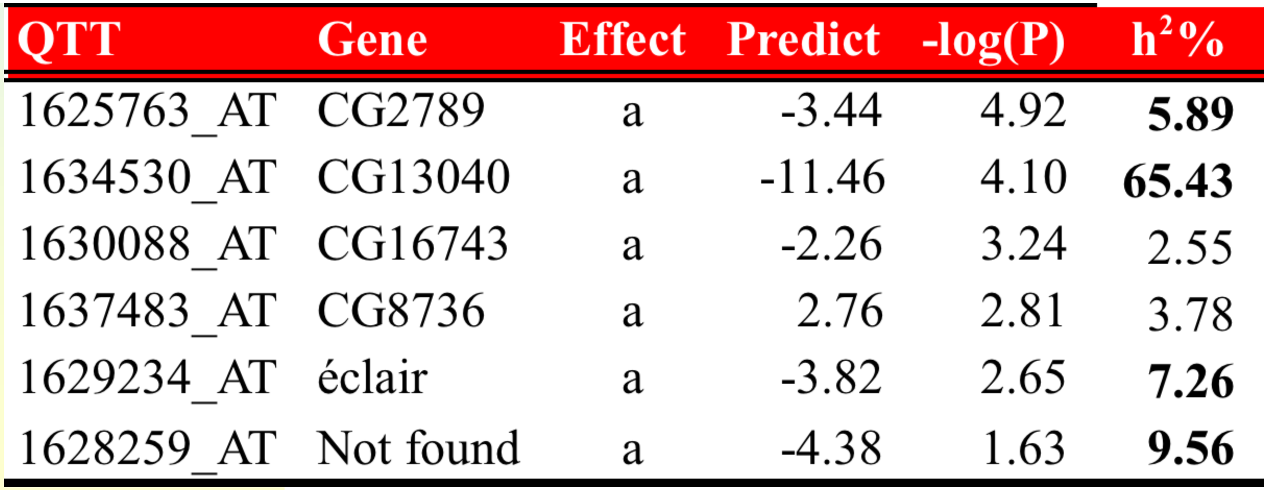
- SNPs=5.2M, Transcripts=10.1K, N=322
- 7 QTSs, 30 Epistasis QTSs, 5 GxE QTSs
- Total h^2(G+GE)=78.3%, h^2(A)=59.5%, h^2(AA)=16.9%, R_G^2
- R_G^2=0.862, R_{G+GE1}^2=0.892 for female, R_{G+GE2}^2=0.872 for male



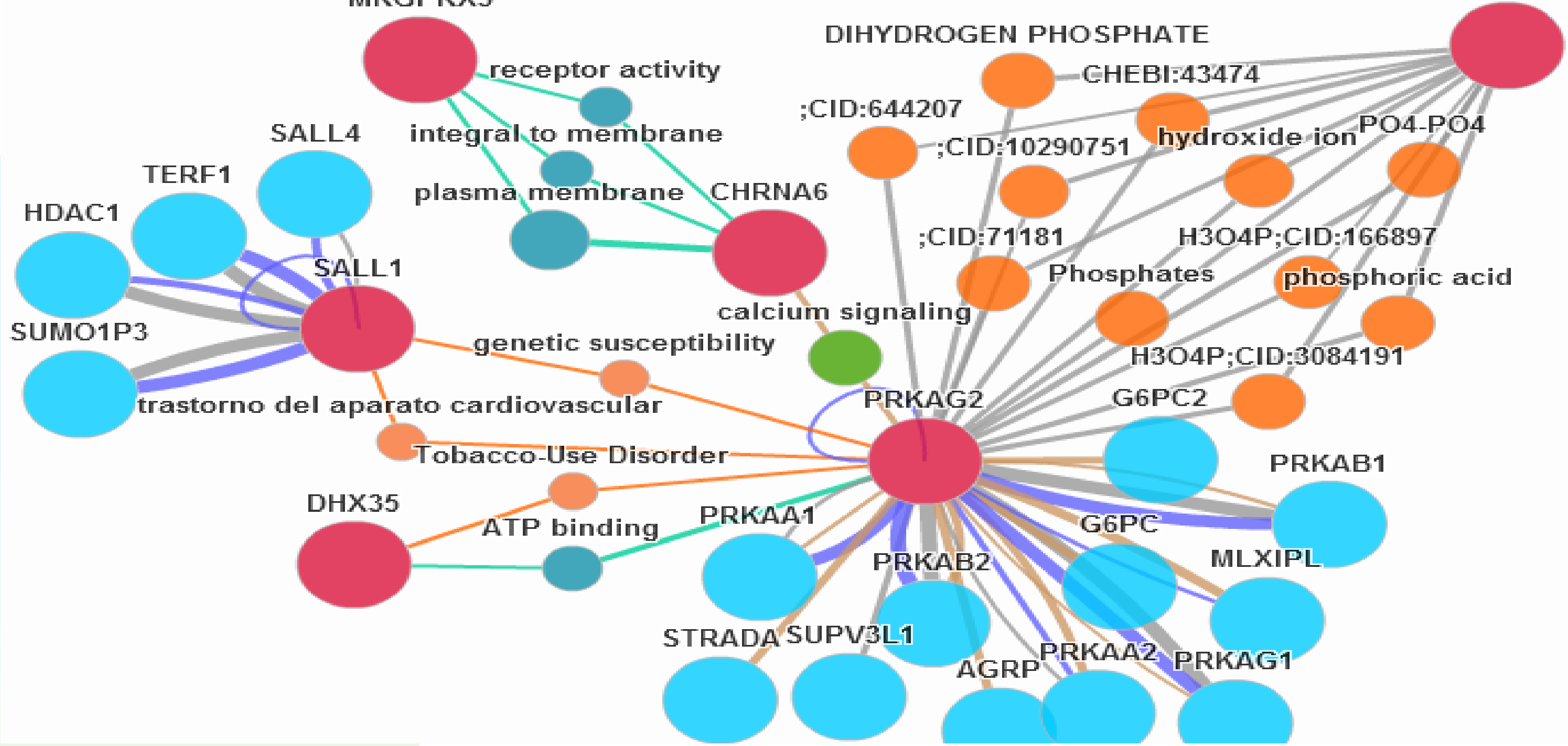
Estimates of QTS & QTT for Chill Coma Recovery



QTS	Gene	Effect	Predict	-Log(P)	h^2%
X_5344003	SPR	a	1.60	**44.59**	**14.53**
3R_17000695	SNF4Agamma	a	1.24	**27.28**	**8.73**
X_18462691	Bx	a	-1.23	**26.85**	**8.59**
3L_1424581	Ptp61F	a	1.20	**25.34**	**8.08**
2L_11380311	between salm and salr	a	-1.09	**21.10**	**6.68**
		ae1	-0.49	2.84	0.68
2R_20211492	between betaTub60D and slbo	a	-1.08	**20.81**	**6.58**
3L_4163650	mas	a	-1.06	**20.08**	**6.34**
3L_2806345/X_8175050	[between CG2083 and CG9973]/[between CG1636 and nAcRalpha-7E]	aa	0.50	**5.47**	1.40
2L_4821516/2R_6453209	[between CG15628 and CG3225]/psq	aa	-0.49	**5.31**	1.35
3R_4613737/3R_16925749	Pif1A/CG7044	aa	0.41	3.94	0.96
2R_13934484/X_2406170	CG5767/trol	aa	0.41	3.92	0.96



QTT	Gene	Effect	Predict	-log(P)	h^2%
1625763_AT	CG2789	a	-3.44	4.92	**5.89**
1634530_AT	CG13040	a	-11.46	4.10	**65.43**
1630088_AT	CG16743	a	-2.26	3.24	2.55
1637483_AT	CG8736	a	2.76	2.81	3.78
1629234_AT	éclair	a	-3.82	2.65	**7.26**
1628259_AT	Not found	a	-4.38	1.63	**9.56**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;CID:644207
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SALL4
;CID:10290751
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PO4-PO4
TERF1
HDAC1
plasma membrane
CHRNA6
SALL1
;CID:71181
H3O4P;CID:166897
Phosphates
phosphoric acid
calcium signaling
SUMO1P3
genetic susceptibility
H3O4P;CID:3084191
PRKAG2
G6PC2
trastorno del aparato cardiovascular
Tobacco-Use Disorder
PRKAB1
DHX35
ATP binding
PRKAA1
G6PC
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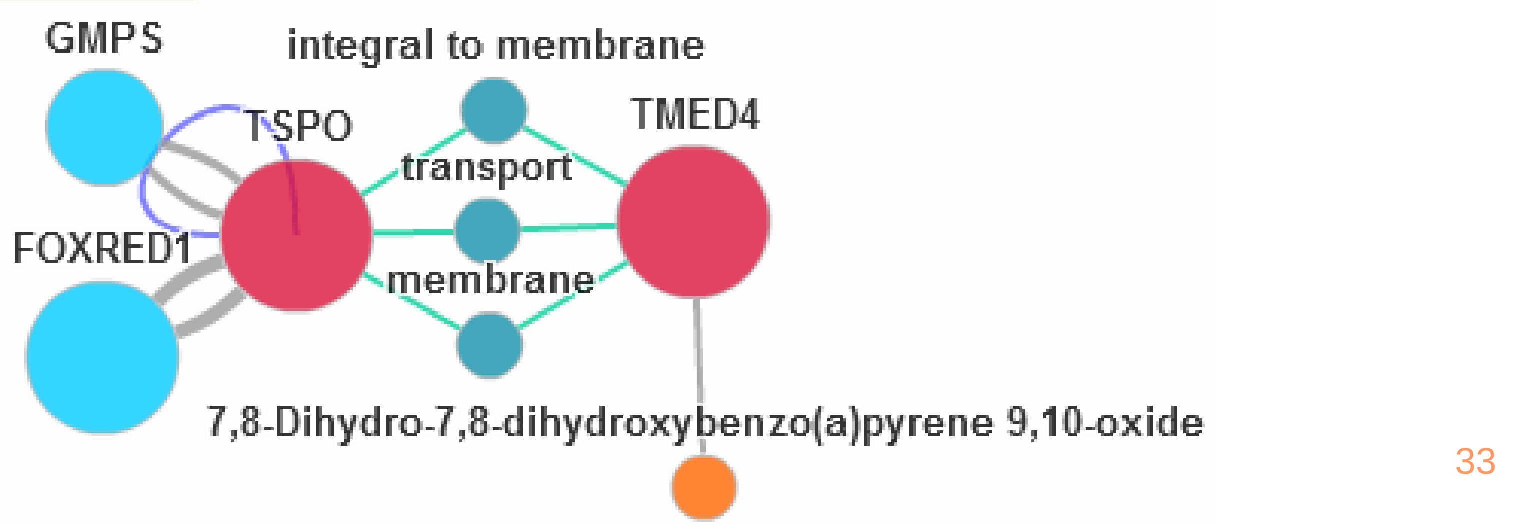
MLXIPL
STRADA
SUPV3L1
AGRP
PRKAA2
PRKAG1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TSPO
TMED4
transport
FOXRED1
membrane
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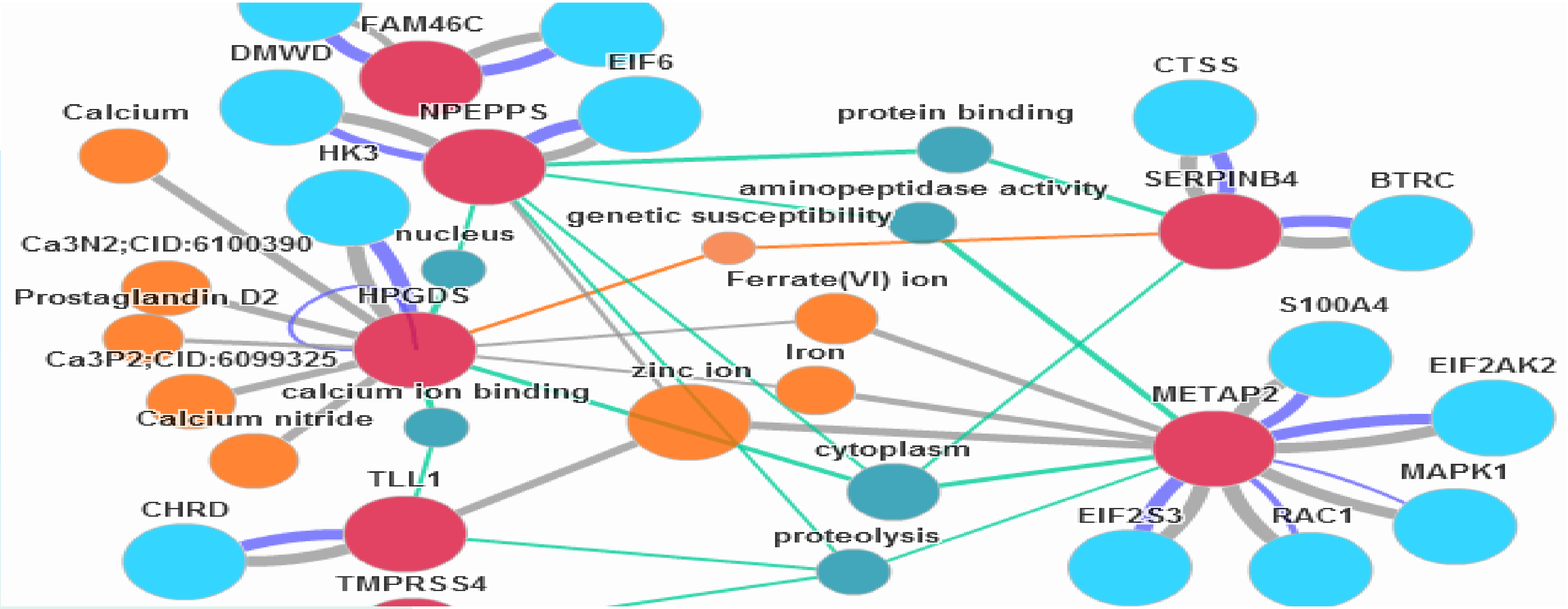
Estimates of tQTSs for Chill Coma Recovery

SNP	Gene	Effect	Predict	-log(P)	h^2%	mRNA	Gene
chillcoma							
2L_11380311	between salm and salr	a	-0.10	**32.92**	**31.38**	1625975_at	CG31052
2R_20211492	between betaTub60D and slbo	a	0.29	**13.73**	**41.63**	1638991_at	CG5506
2R_3662220	CG30497	ae1	-0.26	**6.18**	**57.90**	1635129_at	CG6332
		a	0.09	**5.41**	**26.38**	1626253_at	Glutathione S transferase D4
		ae1	-0.23	**8.36**	**72.93**	1640649_at	CG15878
		a	-0.17	**12.26**	**36.86**	1634444_at	CG12736
		ae1	-0.15	**8.47**	**72.87**	1639860_at	Unknown
		a	-0.13	**5.10**	**24.73**	1627059_at	uninitiated
		a	-0.08	**8.22**	**22.82**	1639748_at	CG15922
2R_12981799	GstS1	a	0.09	**6.62**	**14.22**	1632245_a_at	Serine protease inhibitor 4
		a	-0.06	**14.58**	**44.70**	1636814_at	Unknown
		a	-0.07	**7.12**	**13.79**	1640463_at	Unknown
		a	0.16	**6.42**	**30.03**	1641465_at	CG6153
2R_16439355	CG13430	ae1	-0.22	**9.85**	**80.89**	1640044_at	CG7329
3L_1519297	Psa	a	-0.20	**6.89**	**18.33**	1623398_at	CG4830
3L_8283282	between CG7201 and cert	a	0.10	**5.94**	**22.11**	1631633_a_at	Gram-negative bacteria binding protein 2
3R_4613737	Pif1A or Pif1B	a	-0.19	**14.79**	**32.81**	1637366_at	CG16876
3R_10857239	between CG14861 and RpL10Aa	a	-0.06	**6.02**	**28.49**	1636121_at	CG12924
3R_20569151	tok	a	-0.16	**6.92**	**17.33**	1634158_at	CG6164
		a	-0.24	**28.16**	**38.06**	1629199_at	Antigen 5-related 2
2R_18181213	CG5819	a	0.26	**24.70**	**35.85**	1630088_AT	CG16743
3L_612891	between CG42719 and Reg-2	a	-0.22	**19.05**	**27.32**		
2L_1763460	between CG17650 and Gr22e	a	-0.21	**94.39**	**50.94**	1637483_AT	CG8736
2L_3854056	between CG3964 and slp2	a	0.14	**42.67**	**22.43**		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SERPINB4
BTRC
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genetic susceptibility
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nucleus
Ferrate(VI) ion
Prostaglandin D2
HPGDS
S100A4
Ca3P2;CID:6099325
Iron
EIF2AK2
zinc ion
METAP2
calcium ion binding
Calcium nitride
cytoplasm
TLL1
MAPK1
CHRD
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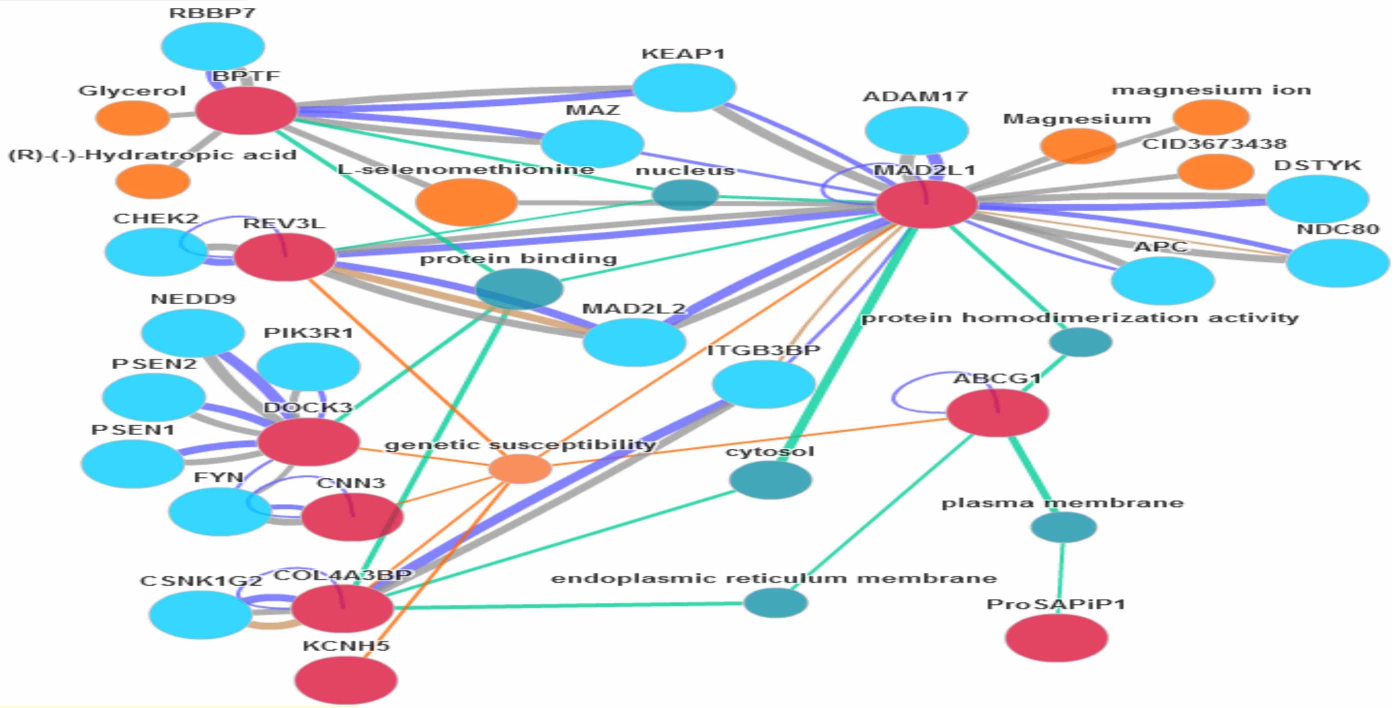
RAC1
proteolysis
TMPRSS4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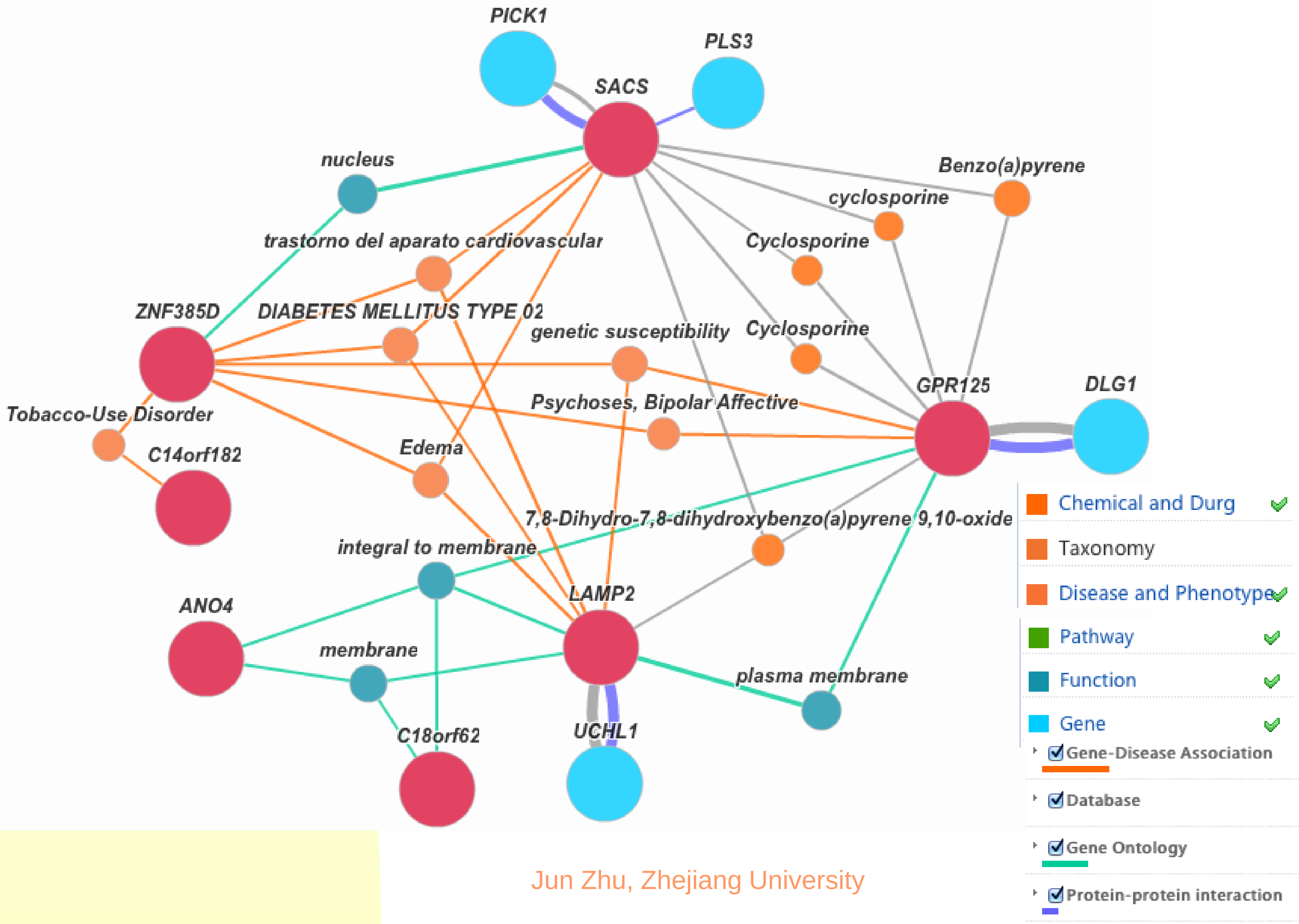
nucleus
MAD2L1
DSTYK
CHEK2
REV3L
NDC80
APC
protein binding
NEDD9
MAD2L2
protein homodimerization activity
PIK3R1
ITGB3BP
PSEN2
ABCG1
DOCK3
PSEN1
genetic susceptibility
cytosol
FYN
CNN3
plasma membrane
CSNK1G2
COL4A3BP
endoplasmic reticulum membrane
ProSAPiP1
KCNH5

Impact of Smoking on Genetic Architecture of BMI Behavior (1)

Table 1. Detected SNPs for no cofactor and smoking cigarettes per day as cofactor

			No cofactor			CigPD cofactor		
SNPID	Gene Name	Effect	Predict	-L(P)	h^2%	Predict	-L(P)	h^2%
3_rs2620535	ZNF385D	d	-1.11	3.20	2.09	-1.13	3.56	1.80
7_rs2178628	SDK1	d	-1.31	4.24	2.90	-0.82	2.06	0.94
9_rs10514834	GAS1	d	-0.92	2.34	1.44	-0.71	1.65	0.71
		de1	-0.99	1.71	1.65	-1.22	2.39	2.10
12_rs1902753	CDK17	d	-1.77	7.27	5.30	-1.39	5.12	2.73
13_rs7983587	GPR12	d	1.97	8.85	6.57	1.57	6.34	3.47
14_rs10873029	C14orf182	de2	1.14	2.00	2.19	1.22	2.34	2.09
14_rs4905888	CYP46A1	a	0.39	1.31	0.26	0.60	2.50	0.51
		d	-1.01	2.74	1.74	-0.81	2.02	0.91
19_rs3848535	SLC8A2	d	1.02	2.78	1.77	0.96	2.67	1.29
X_rs5957379	LAMP2	d	-1.68	6.61	4.77	-1.21	3.97	2.04

Gene Network for BMI Not Affected by Smoking

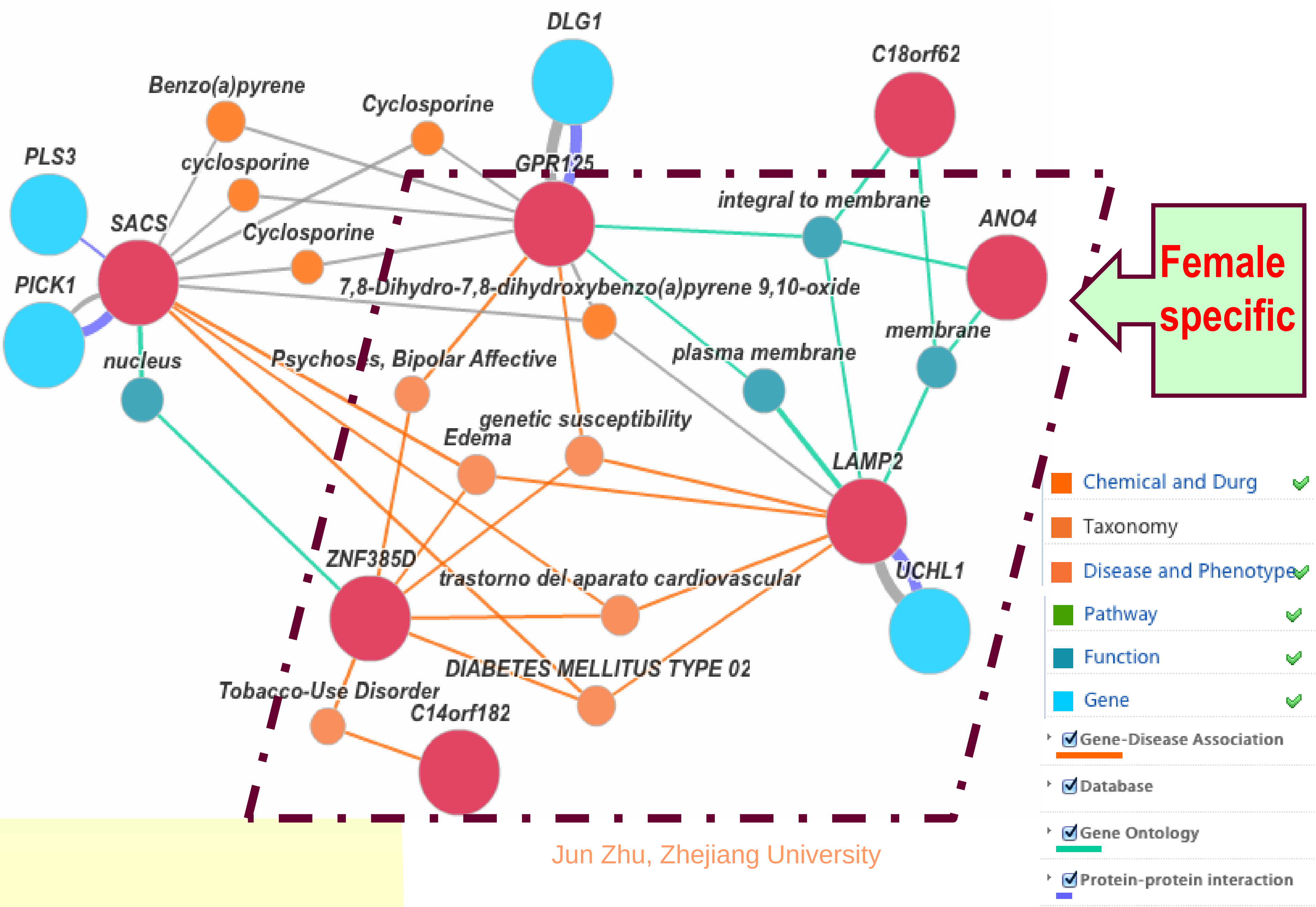


Impact of Smoking on Genetic Architecture of BMI Behavior (2)

Table 2. Detected SNPs for only setting no cofactor

SNPID	Gene Name	Effect	Predict	-L(P)	h^2%
3_rs2620535	ZNF385D	a	0.44	1.71	0.33
4_rs7674804	GPR125	d	1.02	2.77	1.76
		de1	1.13	1.97	2.16
12_rs10778062	ANO4	d	1.02	2.75	1.75
		de1	1.08	1.88	1.96
13_rs7983587	GPR12	ae1	0.80	2.27	1.09
13_rs9580631	SACS	d	1.25	3.92	2.65
14_rs10873029	C14orf182	aae1	1.60	4.16	4.34
18_rs1982114	C18orf62	d	-1.36	4.52	3.12
X_rs5957379	LAMP2	ae1	-0.68	1.63	0.79
3_rs2620535/14_rs10873029	ZNF385D/C14orf182	dd	2.33	3.53	9.22
		aae1	1.60	4.16	4.34

Gene Network for BMI Caused by Smoking



Female specific

Advantage of Mapping QTX Based on Genome-Wide OMICS Data

1. **No need for linkage map**
2. **QTX mapping can be conducted for arbitrary breeding populations and germplasm**
3. **Mapping results can be applied to parents and breeding populations**
4. **QTX mapping can be conducted by population involved selection/abnormal segregation**
5. **Not MAS but SNP/Gene/Protein/Metabolite selection can be applied**

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