

Transcriptome-wide Association Studies

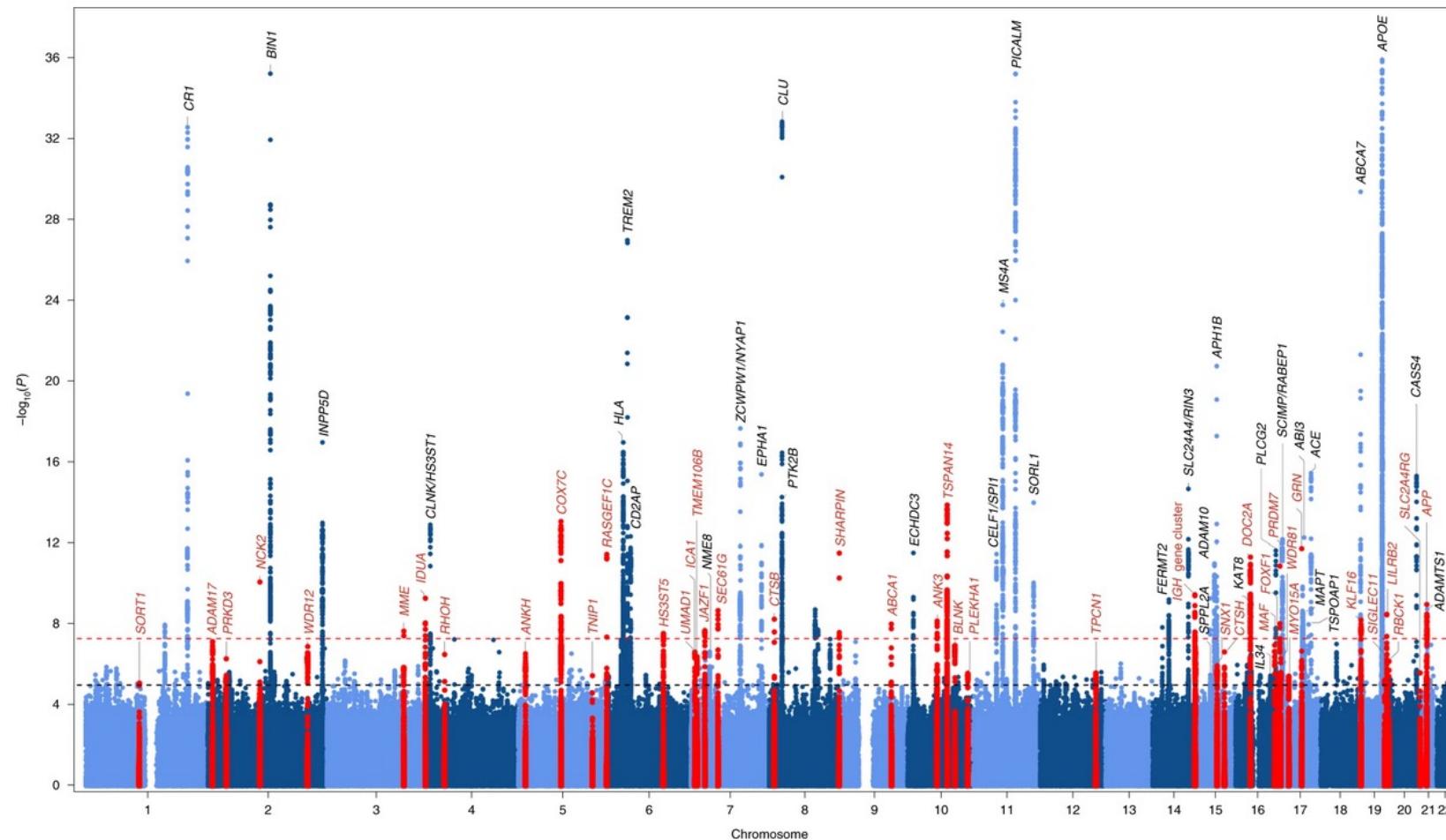
Lecture 1

Outline

- Genome-wide Association Study (GWAS)
- Transcriptome-wide Association Studies (TWAS)
 - PrediXcan
 - FUSION
 - TIGAR
 - DPR
 - VC-TWAS
 - BGW-TWAS
 - Omnibus TWAS

Genome-wide Association Study (GWAS)

- Test the association between SNPs and the phenotype of interest
 - Independent single variant test for each SNP
 - Summary data: Effect sizes, Effect size standard deviations, Z-scores, P-values



GWAS of AD dementia by Bellenguez C. et al. Nat Genetic. 2022

GWAS Catalogue Results

2019 July

>157K Associations
from 4220 Publications



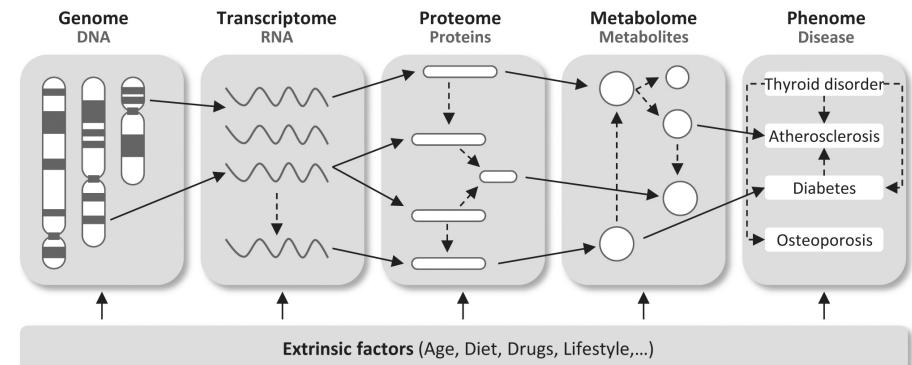
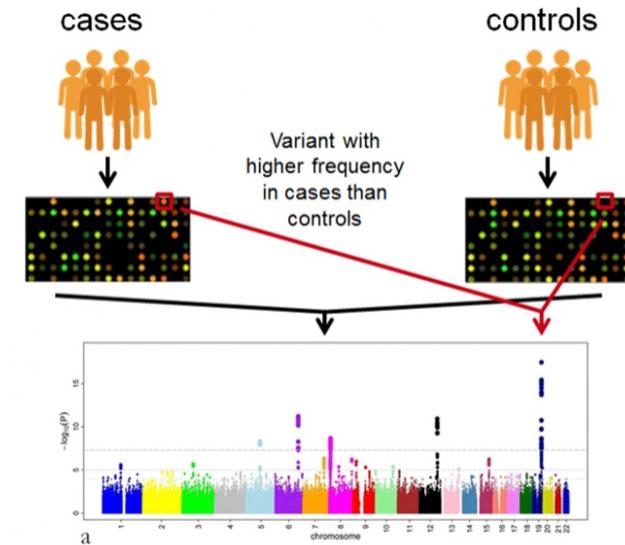
www.ebi.ac.uk/gwas

Challenge: Biological Mechanism Underlying GWAS Loci

- Mapping top significant SNP to the nearest gene?
- How to aggregate SNPs for Gene-based association tests?

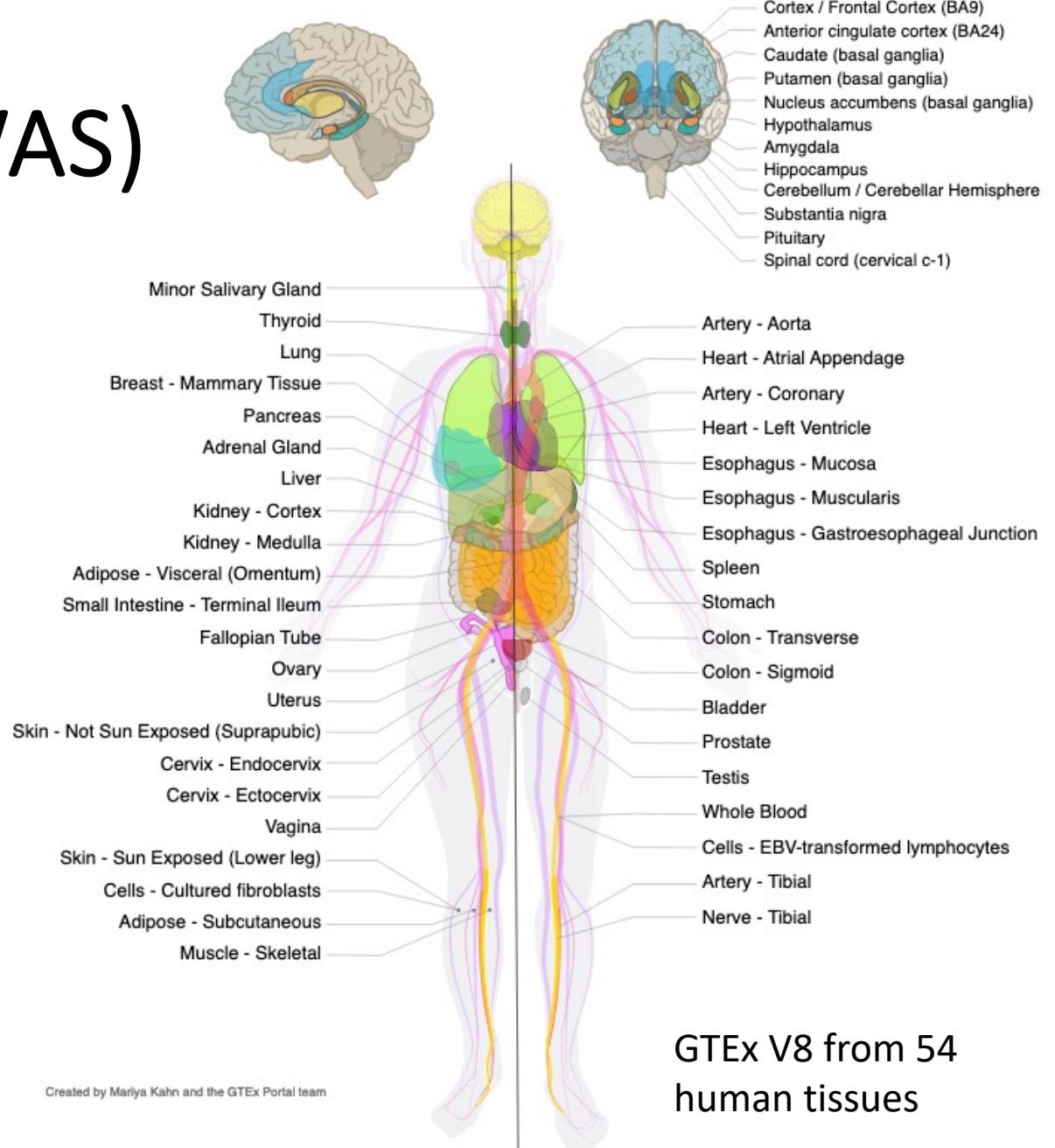
Limitations by GWAS

- Many SNP ‘hits’ are in non-coding regions with unclear molecular mechanism
- Such SNPs often enriched for expression quantitative trait loci (eQTLs)
- Suggests genetically regulated gene expression plays possible role in etiology of complex traits



Transcriptome-wide Association Study (TWAS)

- Integrate transcriptomic data with GWAS data to detect risk genes whose genetic effects are mediated through gene expressions
 - Informative of underlying biological mechanisms
- Leverage existing public transcriptomic data such as GTEx V8 from 54 human tissues

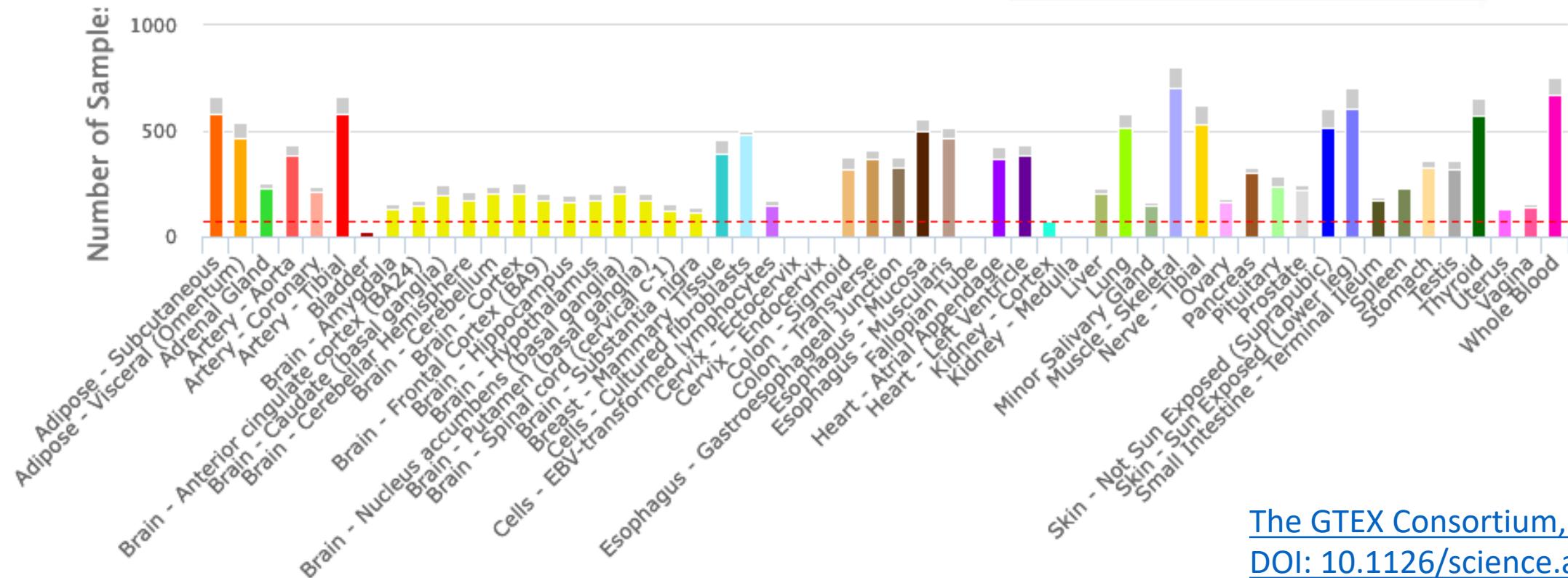


Genotype-Tissue Expression (GTEx) project

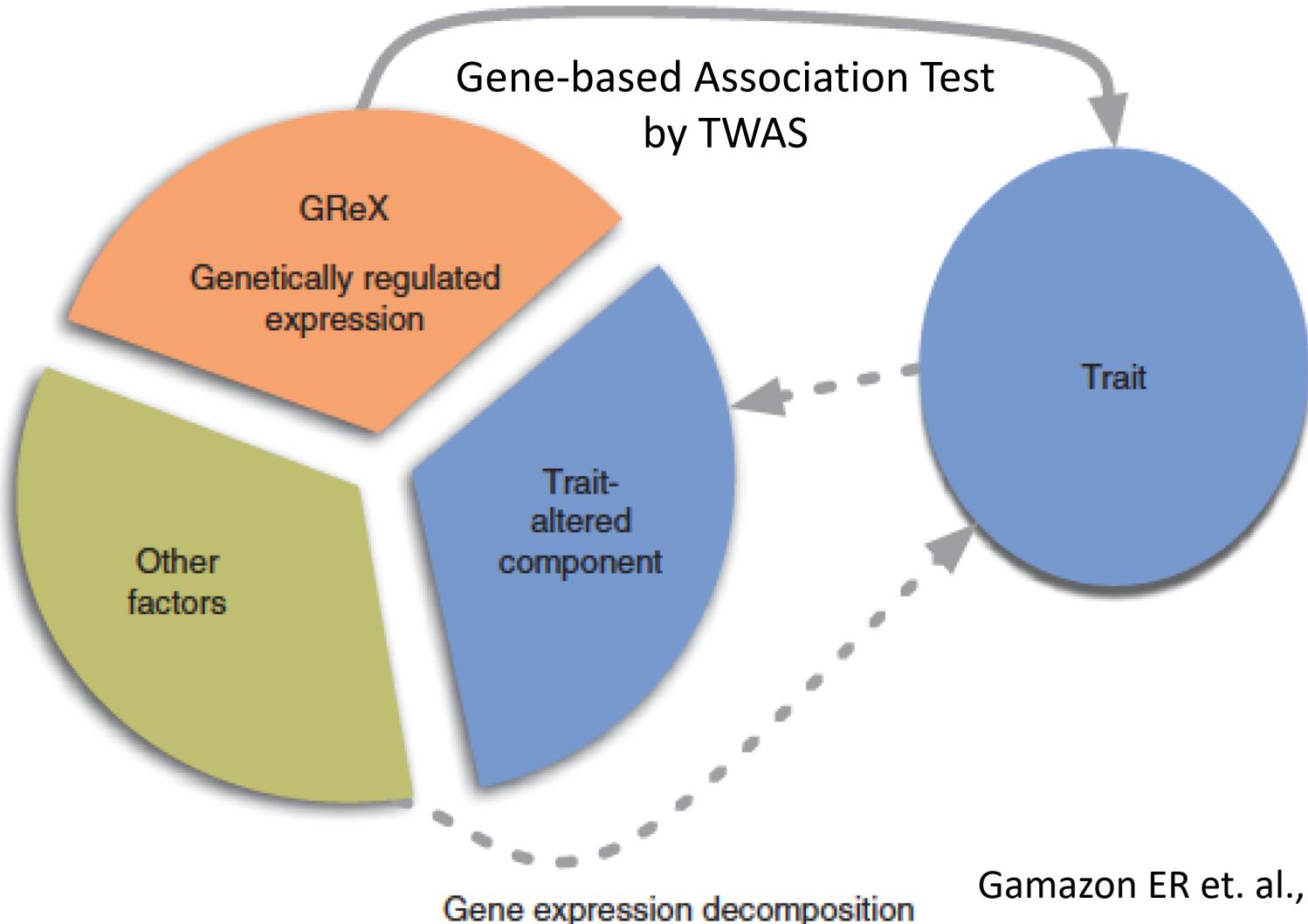
<https://www.gtexportal.org/home/>

V8 Release	# Tissues	# Donors	# Samples
Total	54	948	17382
With Genotype	54	838	15253
Has eQTL Analysis*	49	838	15201

* Number of samples with genotype ≥ 70



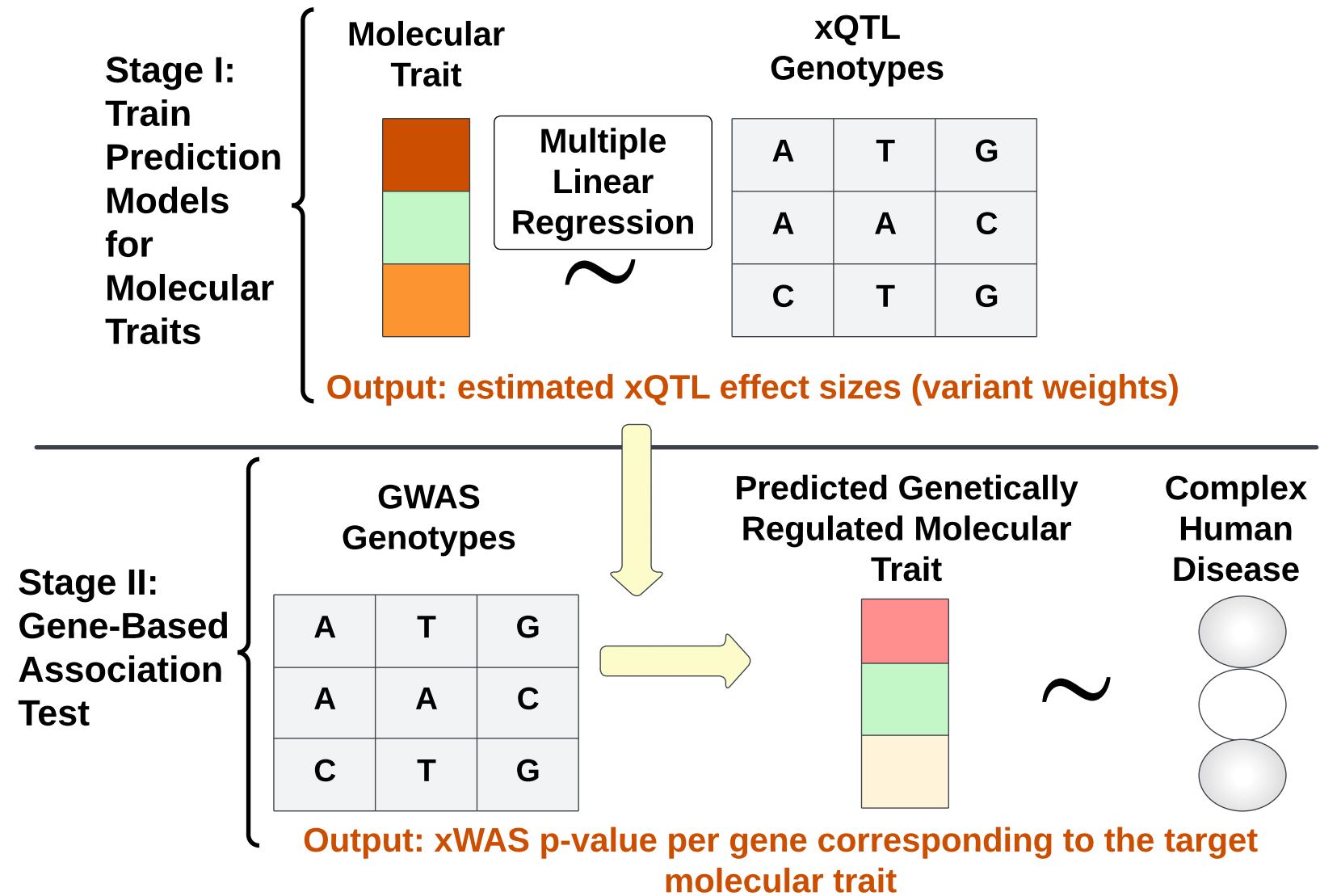
TWAS



Gamazon ER et. al., Nat Genetics, 2015.

Standard Two-Stage TWAS Framework

- Integrates transcriptomic data (or other molecular trait) with GWAS data
- Leverage publicly available transcriptomic (or other omics) data
- Gene-based association test



Standard Two-Stage TWAS

- 1) Train GReX prediction models and estimate “eQTL” effect sizes with reference panel

$$\mathbf{E}_g = \mathbf{X}_{n \times p} \mathbf{w}_{p \times 1} + \boldsymbol{\varepsilon}, \quad \boldsymbol{\varepsilon} \sim N(0, \sigma_\varepsilon^2 \mathbf{I})$$

- \mathbf{E}_g , Gene Expression adjusted for confounding covariates, with mean 0
- $\mathbf{X}_{n \times p}$ Reference Genotypes of cis-SNPs (within +/- 1Mb around the test gene region), with column means 0
- $\mathbf{w}_{p \times 1}$: “eQTL” effect sizes, i.e., “eQTL” weights

- 2) Test gene-based association with independent GWAS test data

$$\mathbf{Y}_{\text{test}} \sim \beta * \widehat{\mathbf{GReX}}$$

- $\widehat{\mathbf{GReX}} = \mathbf{X}_{\text{test}} \widehat{\mathbf{w}}_{p \times 1}$: Predicted GReX in test cohort, with genotype data \mathbf{X}_{test}
- \mathbf{Y}_{test} : Phenotype of interest;
- Test $H_0: \beta = 0$

TWAS with GWAS Summary Data

- GWAS summary data:
 - GWAS Z-scores ($Z_l, l = 1, \dots, m$) for test SNPs with non-zero eQTL weights \hat{w} , derived from single variant tests
 - Genotype correlation and variance-covariance matrices (V) derived from reference genotype data
- TWAS Z-score statistics are given by:

$$\begin{aligned}\tilde{Z}_{g,\text{FUSION}} &= \frac{\sum_{l=1}^m (\hat{w}_l Z_l)}{\sqrt{\hat{w}' V \hat{w}}}, \quad V = \text{Corr}(G_0) \\ \tilde{Z}_{g,\text{S-PrediXcan}} &= \frac{\sum_{l=1}^m (\hat{w}_l \hat{\sigma}_l Z_l)}{\sqrt{\hat{w}' V \hat{w}}}, \quad \hat{\sigma}_l^2 = \text{Var}(G_{0,l}), \quad V = \text{Cov}(G_0).\end{aligned}$$

Both TWAS Z-score Statistics are Equivalent with Centered and Standardized Gene Expression and Genotypes in the Reference Transcriptomic Panel

TWAS

- Essentially “functional” gene-based association test
 - Aggregate associations of multiple test SNPs per target gene, with SNP weights (eQTL effect sizes) derived from reference transcriptomic data
 - Improve power than single variant tests
 - Improve power than traditional gene-based association test with equal weights for test SNPs
- Better informing the underlying biological mechanism of identified risk genes than GWAS

TWAS Tools Estimate eQTL Weights Assuming Different Statistical Model

- **PrediXcan** (Gamazon ER et al., Nat Genetics, 2015): Use penalized linear regression model with Elastic-Net penalty
- **FUSION** (Gusev et al., Nat. Genetics, 2016): Select best model out of PrediXcan/Elastic-Net, LASSO, best unbiased linear predictor (BLUP), single variant model with Top eQTL (Top1), and Bayesian sparse linear mixed model (BSLMM) with the highest cross-validation (CV) R^2
- **TIGAR** (Nagpal S. et al., AJHG, 2019): Use nonparametric Bayesian Dirichlet Process Regression (DPR) model

PrediXcan (Gamazon ER et. al., Nat Genetics, 2015)

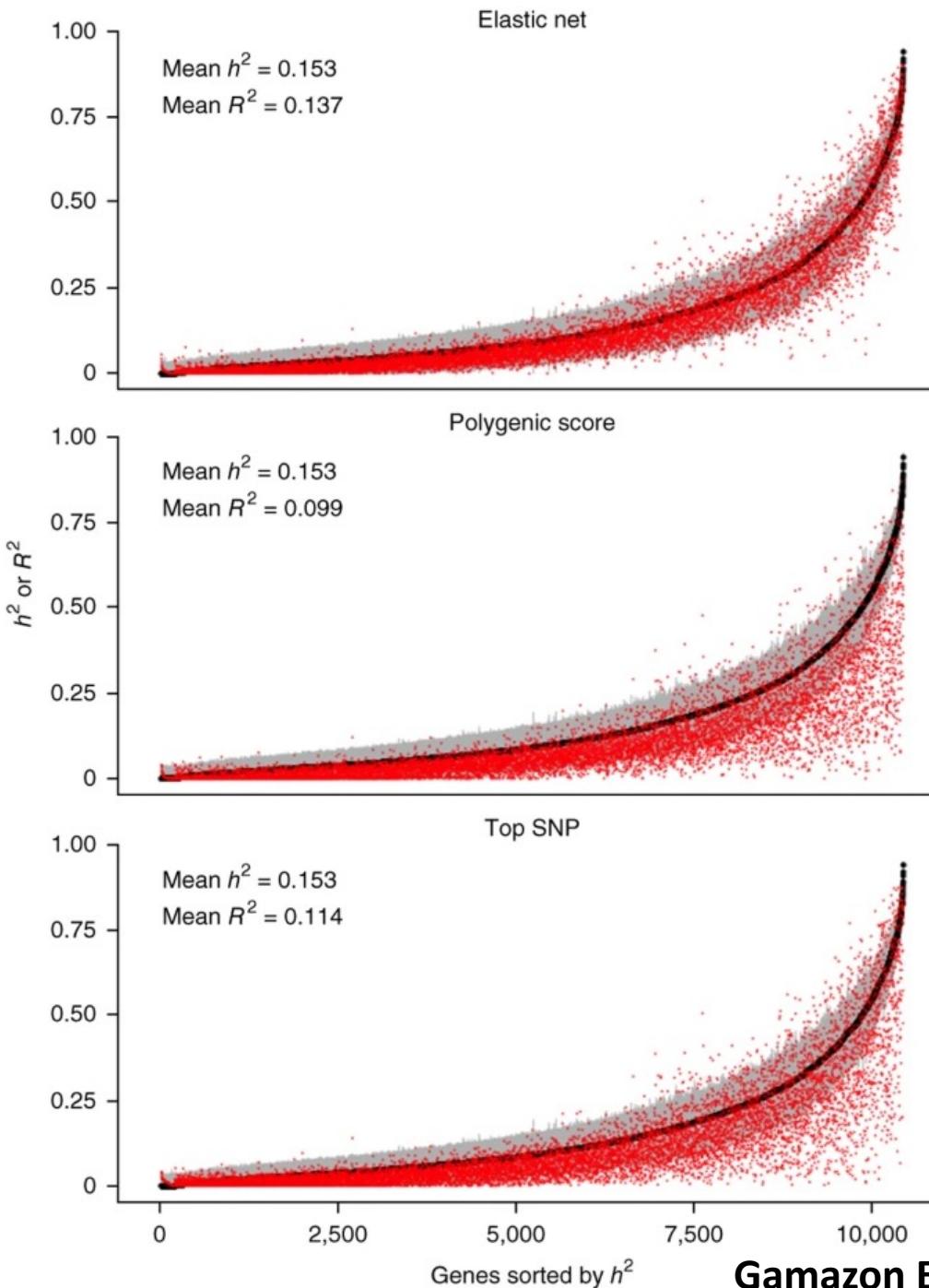
- Use Elastic-Net penalty with equal proportions of Ridge (L2) and LASSO (L1) penalties
- Minimize L2 norm of the difference between gene expression E_g and the genetically regulated component Xw

$$\hat{w} = \underset{w}{\operatorname{argmin}} \left(\|E_g - Xw\|_2^2 + \lambda \left(\alpha \|w\|_1 + \frac{1}{2} (1 - \alpha) \|w\|_2^2 \right) \right)$$

- $\|\cdot\|_2$ denotes L_2 norm, $\|\cdot\|_1$ denotes L_1 norm, $\alpha \in [0, 1]$ denotes the proportion of L_1 penalty, and λ denotes the penalty parameter
- Take $\alpha = 0.5$
- Tune the penalty parameter λ by a 5-fold cross validation
- Often estimates a sparse or null eQTL model

10-fold CV R² versus expression heritability estimates

Compare Three
Models (Elastic
net, Polygenic
score, Top eQTL)



- Red dots: Prediction R²
- Black dots: expression heritability estimates
- Gray lines: 95% confidence interval for expression heritability estimates

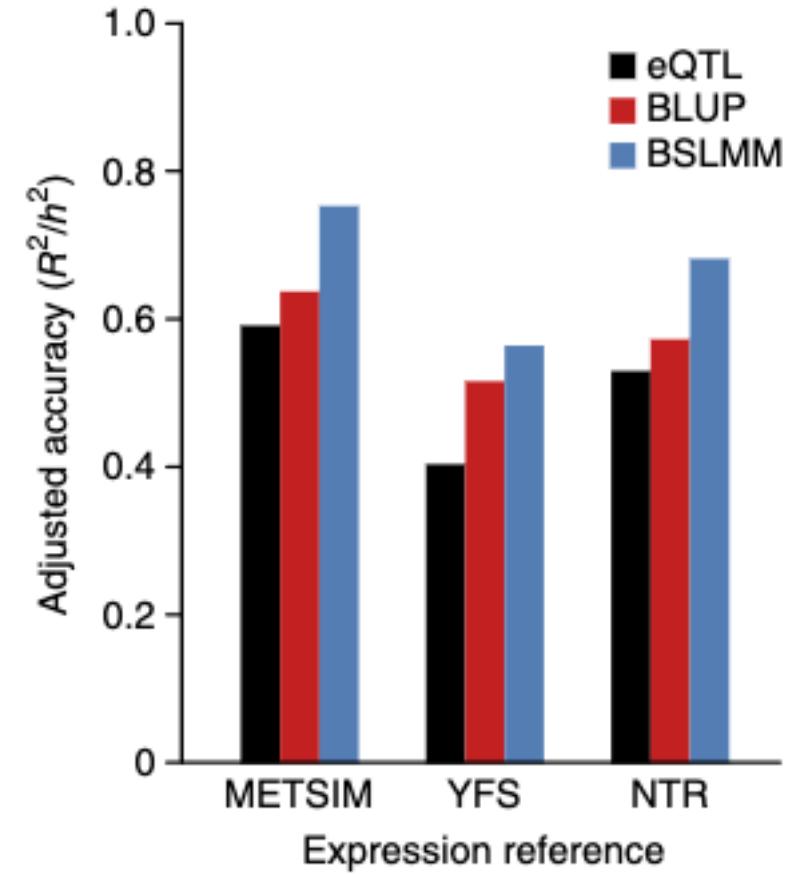
FUSION (Gusev et al., Nat. Genetics, 2016)

- Compared Top1 (most significant cis-eQTL), BLUE (standard least square estimate), and BSLMM (Zhou et al. PLOS Genetics, 2013).
- BSLMM (Zhou et al. PLOS Genetics, 2013)

$$E_g = Xw + \epsilon, \quad \epsilon \sim N(0, I\tau^{-1});$$
$$w_i \sim \pi N\left(0, \frac{\sigma_a^2 + \sigma_b^2}{\rho\tau}\right) + (1 - \pi)N\left(0, \frac{\sigma_b^2}{\rho\tau}\right)$$

$\pi=0$: Equivalent to Linear Mixed Model, BLUE

$\sigma_b^2=0$: Equivalent to Bayesian variable selection regression model (BVSR, sparse model), assuming the spike-and-slab (i.e., point-normal) prior



TIGAR: Transcriptome-Integrated Genetic Association Resource (Nagpal et. al., AJHG 2019)

- Use nonparametric Bayesian Dirichlet Process Regression (DPR) model

$$\mathbf{E}_g = \mathbf{X}_{n \times p} \mathbf{w}_{p \times 1} + \boldsymbol{\epsilon}, \quad \boldsymbol{\epsilon} \sim N(0, \sigma_\epsilon^2 \mathbf{I}), \quad \sigma_\epsilon^2 \sim IG(a_\epsilon, b_\epsilon)$$

$$w_i \sim N(0, \sigma_\epsilon^2 \sigma_w^2), \quad \sigma_w^2 \sim D, \quad D \sim DP(IG(a, b), \xi), \quad i = 1, \dots, p$$

- Estimate eQTL effect sizes $w_{p \times 1}$ by Monte Carlo Markov Chain (MCMC) algorithm or Variational Bayesian Approximation.

Nonparametric Bayesian DPR Model

Another intuitive way of viewing this nonparametric model

- σ_w^2 can be viewed as a Latent variable
- Integrating out σ_w^2 will induce a Nonparametric prior distribution on w_i
- Equivalent to a normal mixture model for w_i

Infinite Gaussian
Mixture Model

$$w_i \sim \pi_0 N(0, \sigma_\varepsilon^2 \sigma_0^2) + \sum_{k=1}^{+\infty} \pi_k N(0, \sigma_\varepsilon^2 (\sigma_k^2 + \sigma_0^2));$$

$$\pi_k = v_k \prod_{l=0}^{k-1} (1 - v_l), \quad v_k \sim Beta(1, \xi), \quad \xi \sim Gamma(a_\xi, b_\xi);$$

$$\sigma_k^2 \sim IG(a_k, b_k), \quad k = 0, 1, \dots, +\infty.$$

Advantages by using the Nonparametric Bayesian DPR model

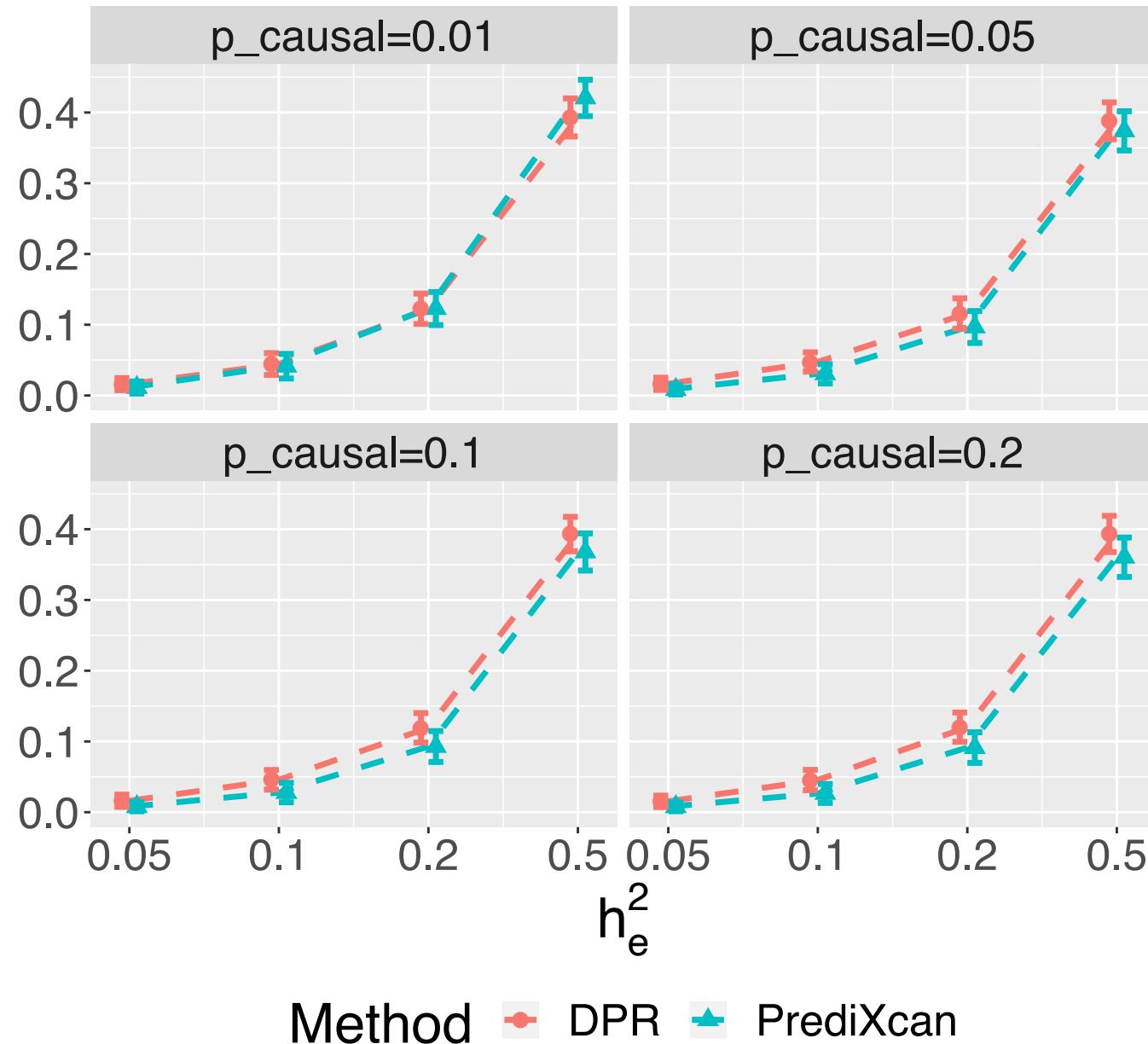
- Assume infinitesimal eQTL model: all analyzed cis-SNPs contribute to the gene expression
- Include parametric Bayesian variable selection regression model (BVR), and Bayesian sparse linear mixed model (BSLMM) as special cases
- Estimates gene expression prediction models for more genes, with higher average CV R², than PrediXcan/Elastic-Net method
- Improves TWAS power

Simulation Study Design

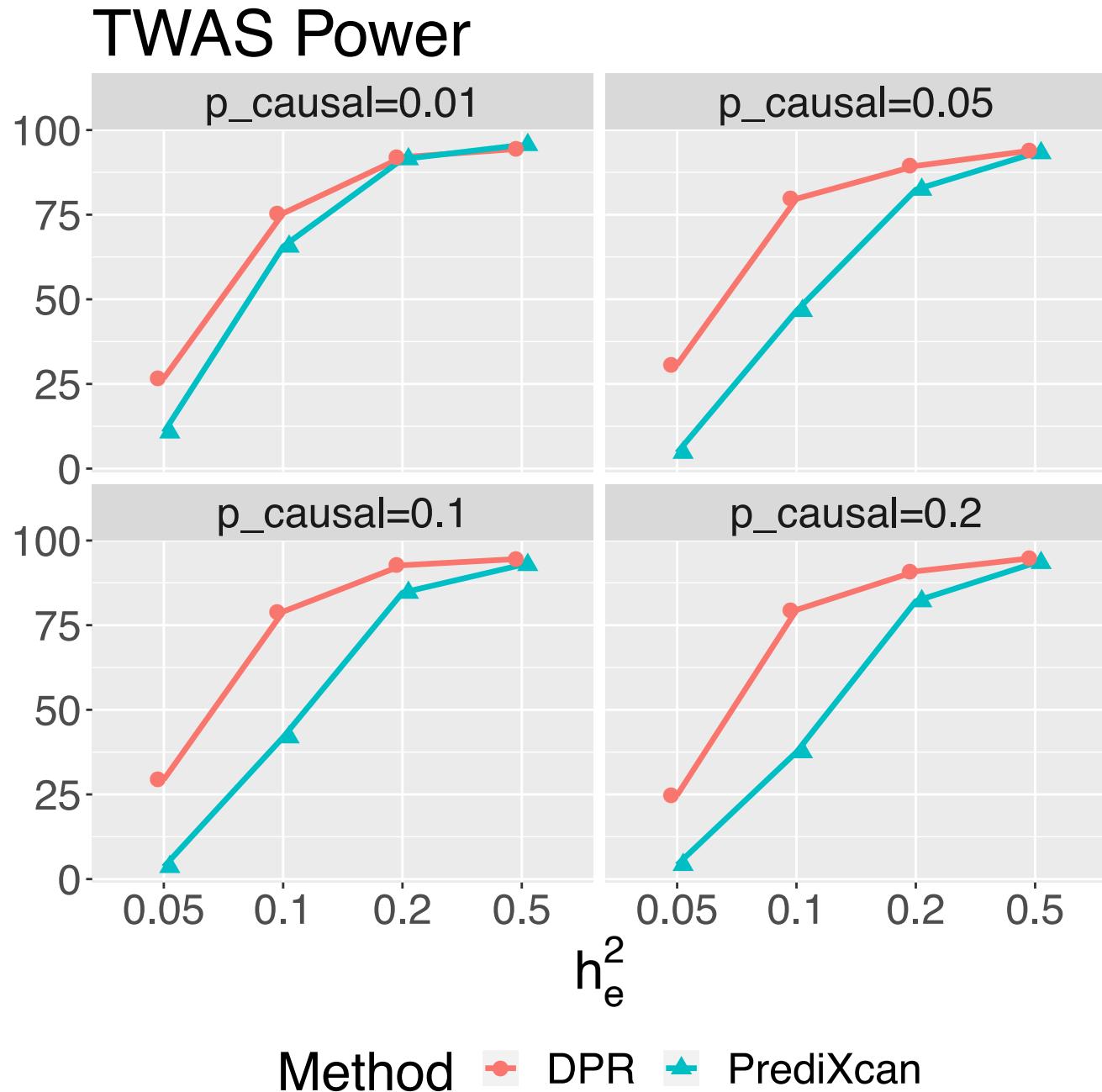
- Use the real genotype data of gene *ABCA7* with 2799 cis-SNPs with MAF > 5% and HWP > 10^{-5}
- Training sample size (100, 300, 499), test sample size 1200
- Consider scenarios with various proportion of causal SNPs for gene expression, $p_{causal} = (0.01, 0.05, 0.1, 0.2)$
- Consider scenarios with various gene expression heritability and phenotype heritability, $(p_e^2, p_h^2) = ((0.05, 0.8), (0.1, 0.5), (0.2, 0.25), (0.5, 0.1))$
- Compare PrediXcan and DPR methods with respect to gene expression prediction R^2 and TWAS power

Gene Expression Prediction R^2 on Test Data

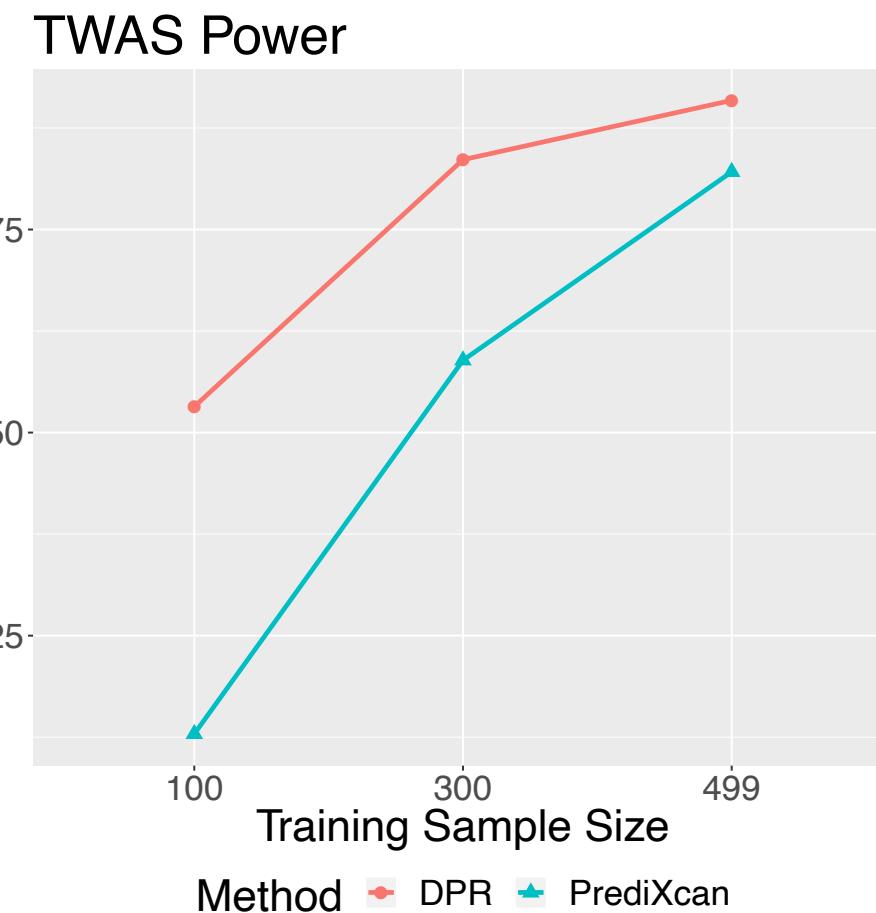
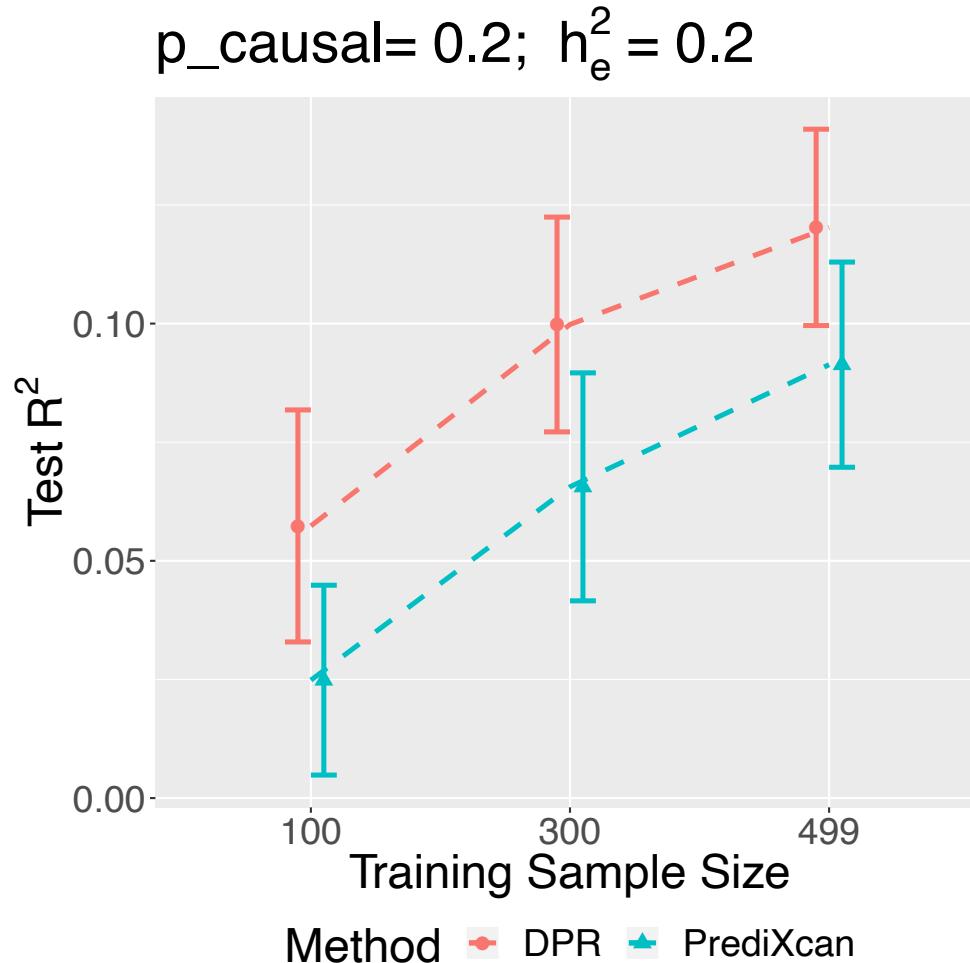
Test R^2



TWAS Power Comparison with Test Data



TWAS Power Increases as Training Sample Size Increases

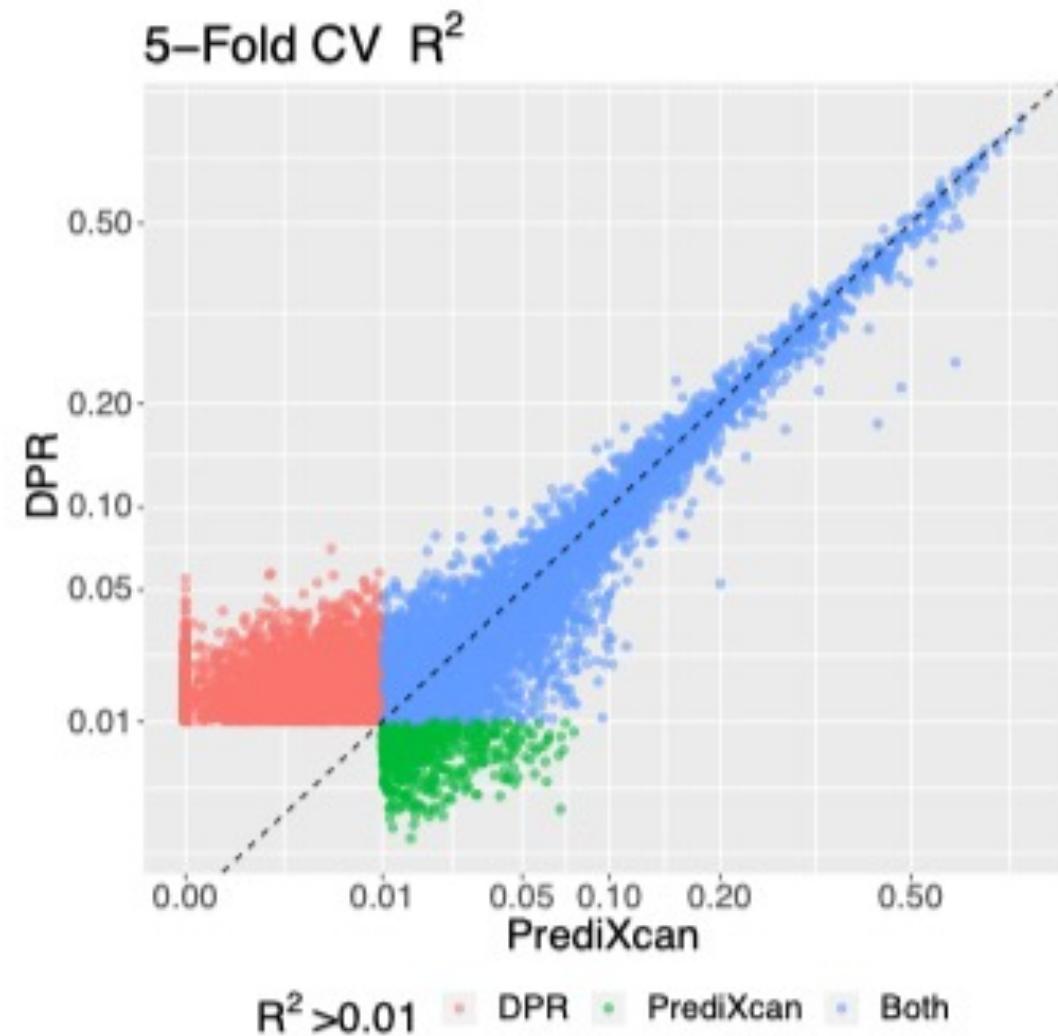


TWAS of Alzheimer's Disease Dementia

- Reference Data
 - Transcriptomic data (14K genes, RNAseq): 499 dorsolateral prefrontal cortex tissue from post-mortem brains from ROS/MAP cohorts
 - Genotype data for the same samples with profiled transcriptomic data
 - European ancestry
- GWAS summary data by International Genomics of Alzheimer's Project (IGAP)
 - ~17K cases and ~37K controls of European ancestry

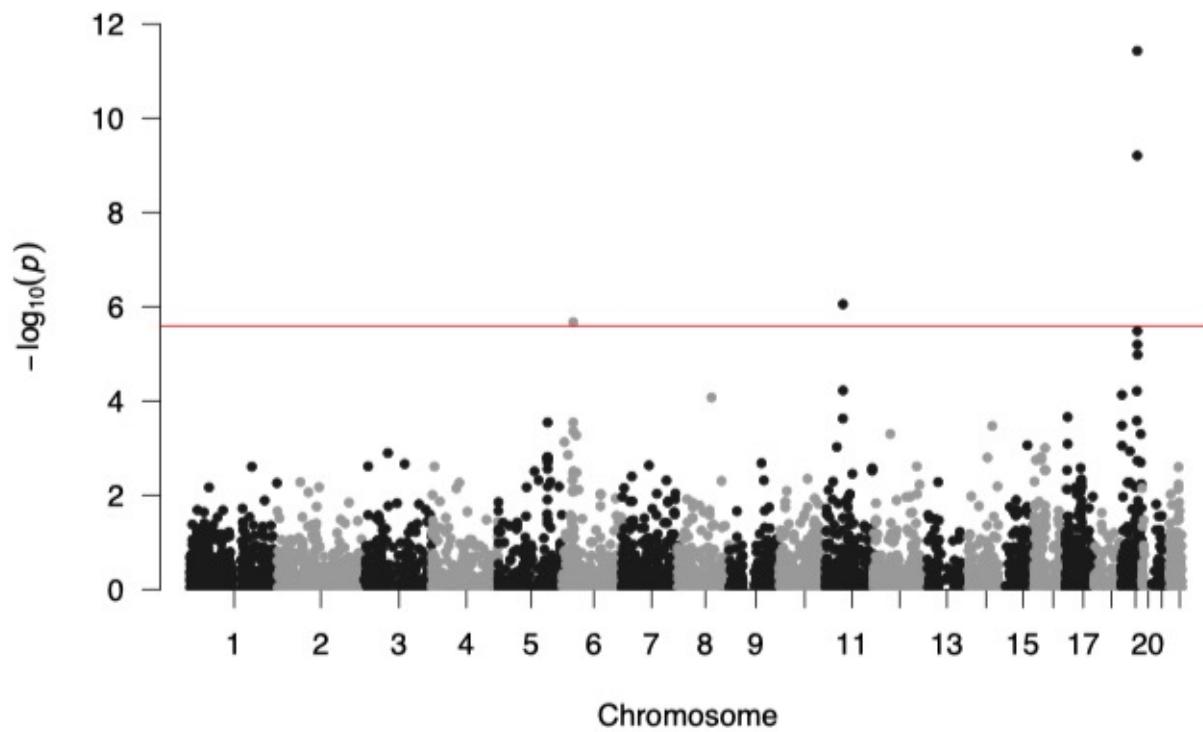
PrediXcan vs. DPR

- 5-fold cross validation
- Compare average prediction R^2
- Use threshold of prediction $R^2 > 0.01$ to identify significant gene expression prediction models

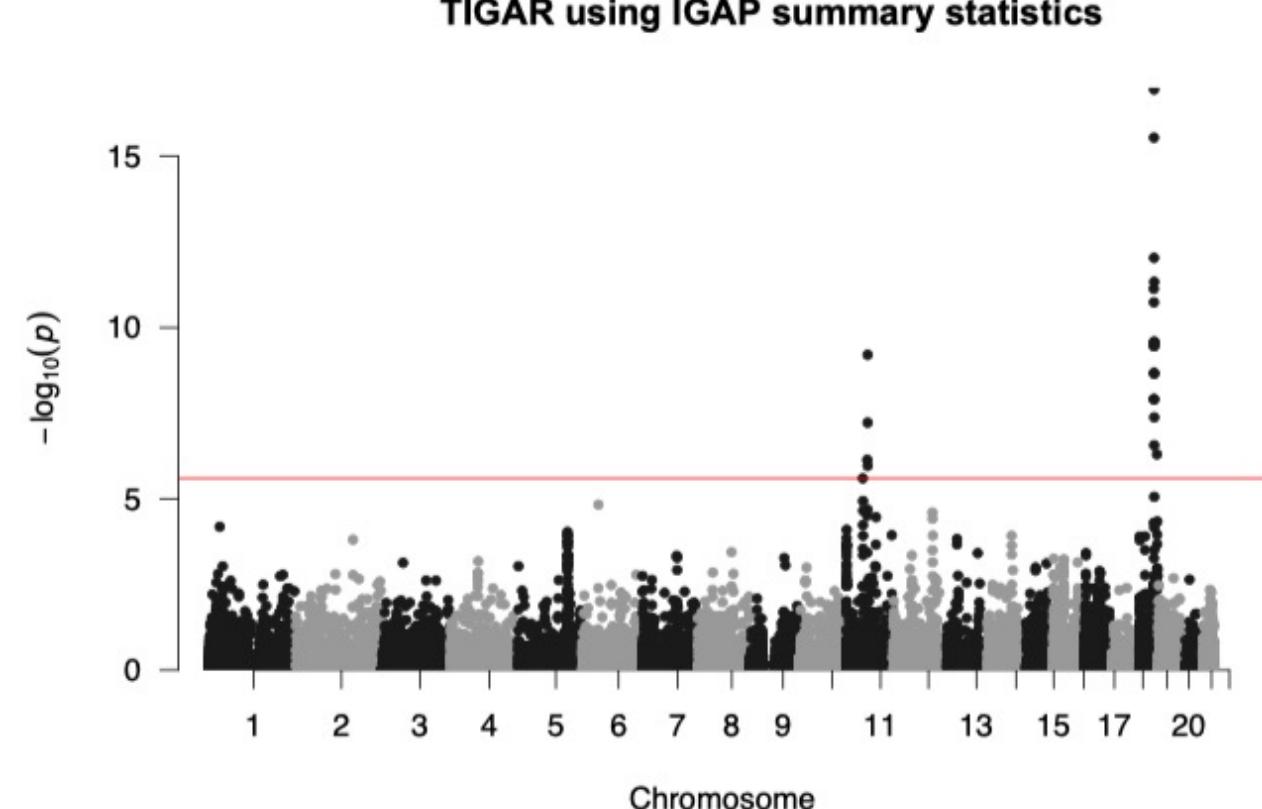


Manhattan Plots of TWAS results by S-PrediXcan Z-score Test Statistic

PrediXcan using IGAP summary statistics



TIGAR using IGAP summary statistics



Increased Sample Sizes for Both Training and Test Cohorts

- Training transcriptomic reference data profiled by RNAseq:
 - ~1K samples of dorsolateral prefrontal cortex from ROS/MAP cohorts
 - European ancestry
- Training genotype data profiled by Whole Genome Sequencing
- Test GWAS summary data by Bellenguez C. et al,
Nat. Genetics, 2022
 - 39,106 European ancestry clinically diagnosed cases
 - 46,828 European ancestry proxy cases
 - 401,577 European ancestry controls
 - 75 GWAS Loci were identified

Article | [Open access](#) | Published: 04 April 2022

New insights into the genetic etiology of Alzheimer's disease and related dementias

[Céline Bellenguez](#) , [Fahri Küçükali](#), [Iris E. Jansen](#), [Luca Kleineidam](#), [Sonia Moreno-Grau](#), [Najaf Amin](#), [Adam C. Naj](#), [Rafael Campos-Martin](#), [Benjamin Grenier-Boley](#), [Victor Andrade](#), [Peter A. Holmans](#), [Anne Boland](#), [Vincent Damotte](#), [Sven J. van der Lee](#), [Marcos R. Costa](#), [Teemu Kuulasmaa](#), [Qiong Yang](#), [Itziar de Rojas](#), [Joshua C. Bis](#), [Amber Yaqub](#), [Ivana Prokic](#), [Julien Chapuis](#), [Shahzad Ahmad](#), [Vilmantas Giedraitis](#), [EADB](#), [GR@ACE](#), [DEGESCO](#), [EADI](#), [GERAD](#), [Demgene](#), [FinnGen](#), [ADGC](#), [CHARGE](#), ... [Jean-Charles Lambert](#)  + Show authors

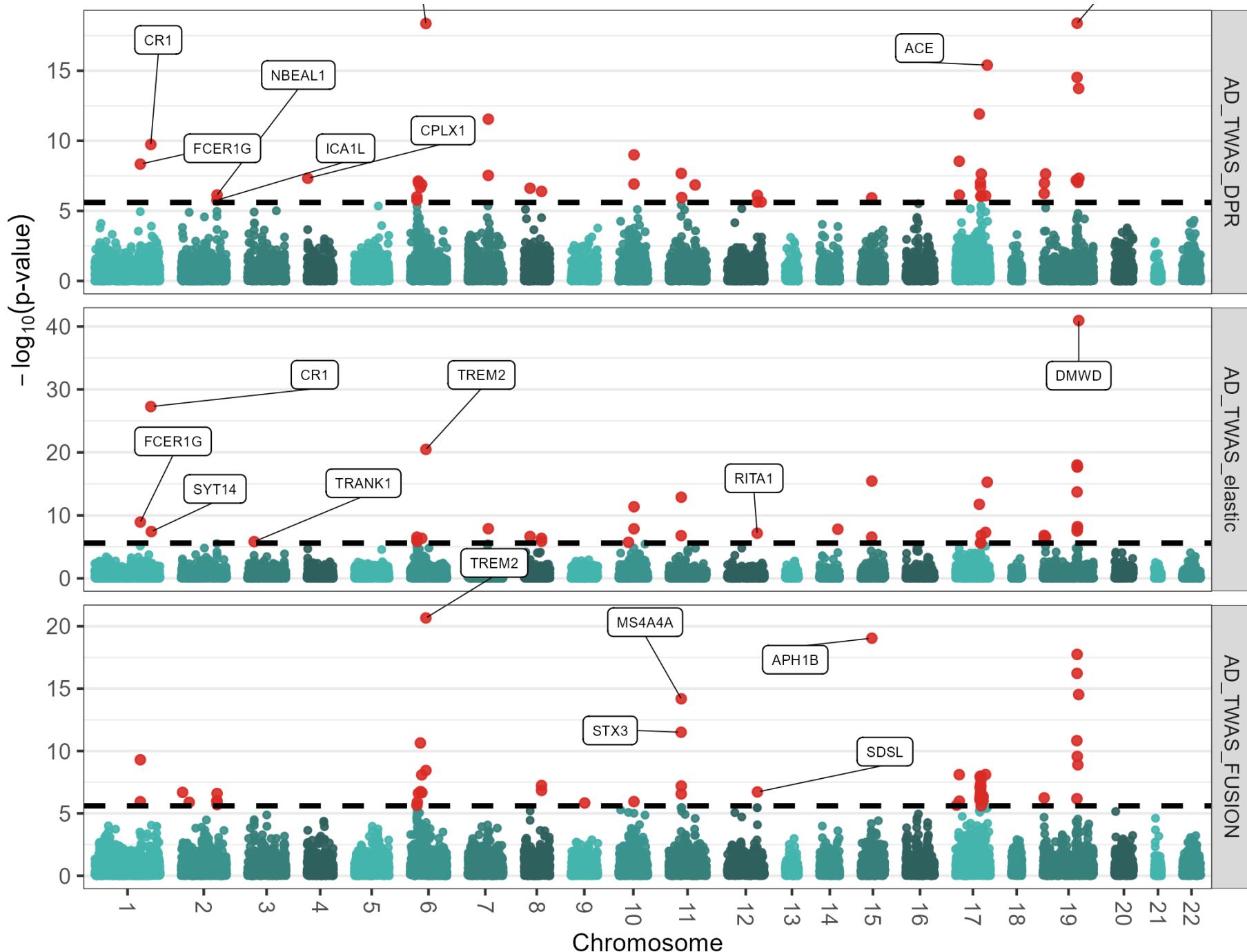
Nature Genetics 54, 412–436 (2022) | [Cite this article](#)

TWAS of AD Dementia by

-TIGAR/DPR

-PrediXcan

-FUSION



Limitations of the Two-Stage Framework

- Not accounting for the uncertainty of estimating eQTL weights from reference transcriptomic data
 - Account for the estimation uncertainty of eQTL weights
 - Variance component TWAS by Tang S. et al. PLOS Genetics 2021.
- Only accounting for cis-eQTL
 - Account for both cis- and trans-eQTL?
 - Bayesian Genome-wide TWAS by Luningham J.M. et al. AJHG 2020.
- Only use one statistical model for estimating eQTL weights
 - Aggregating TWAS results by multiple statistical models?
 - By Aggregated Cauchy Association Test (ACAT)

Variance Component TWAS

- Tests if the phenotype variance component due to $GReX_g$ is non-zero:
- $\widehat{\mu}$ denotes the phenotype mean under the null model

$$E[g(\mathbf{Y}_{pheno} | \mathbf{X}^*, \widehat{\mathbf{w}})] = \sum_{i=1}^m (\gamma \widehat{w}_i) x_i^* = \mathbf{X}^* \boldsymbol{\beta},$$

$$\beta_i \sim N(0, \widehat{w}_i^2 \tau)$$

- Estimated eQTL effect sizes \widehat{w}_i from the reference panel will be taken as SNP weights
- Variance Component test: $H_0 : \tau = 0$

$$Q = (\mathbf{Y} - \widehat{\mu}) \mathbf{K} (\mathbf{Y} - \widehat{\mu})'$$

$$\mathbf{W} = \text{diag}(\widehat{w}_1^2, \dots, \widehat{w}_m^2)$$

- Test statistic Q follows a mixture of chi-square distributions under the null hypothesis
- P-value can be easily calculated by Davies exact method as used by SKAT
- P-value calculation is also derived for using GWAS summary statistics

Tang S. et. al. PLOS Genetics, 2021.

<https://doi.org/10.1371/journal.pgen.1009482>

Variance Component TWAS with GWAS Summary Data

Assume the phenotype mean $\hat{\mu}$ under H_0 is 0, the test statistic is given by

$$Q = \sum_{j=1}^m w_j^2 s_j^2$$

- $s_j = \mathbf{X}'_{\cdot j} \mathbf{Y} / \widehat{\sigma_Y}^2$ is the single variant score statistic of the j^{th} variant
- Numerator of s_j which can be estimated by

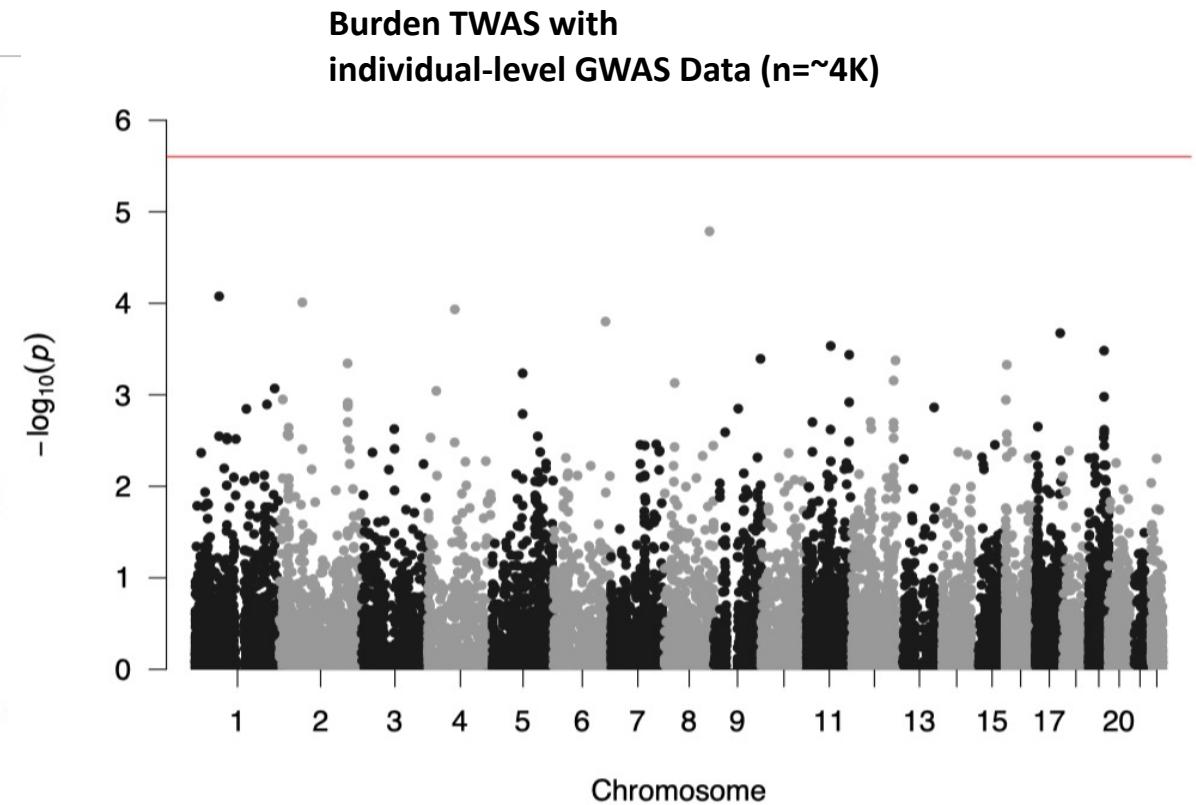
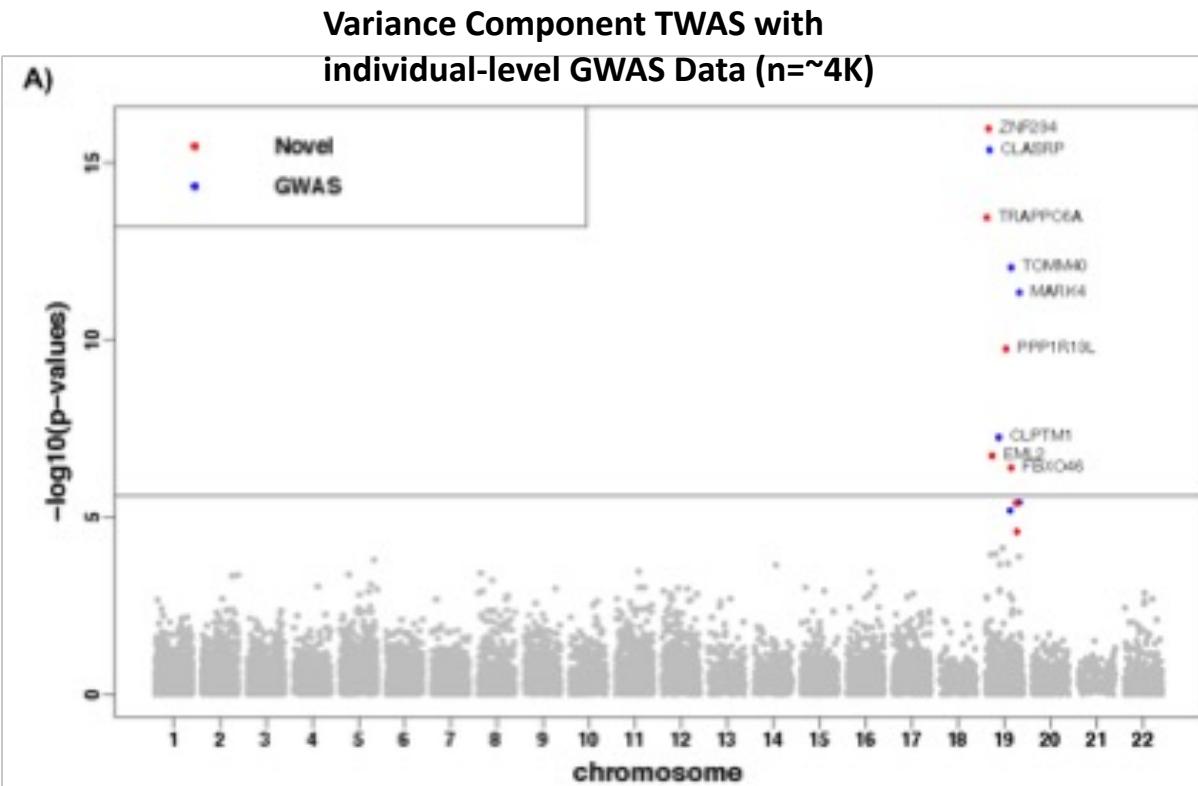
$$\mathbf{X}'_{\cdot j} \mathbf{Y} = (n - 1) \widehat{\beta}_j \Sigma_{j,j}$$

- Denominator of s_j is the estimated phenotype variance $\widehat{\sigma_Y}^2$, which can be estimated by,

$$\widehat{\sigma_Y}^2 = \text{median} \left(\Sigma_{j,j} \widehat{\sigma_j}^2 (n - 1) + \Sigma_{j,j} \widehat{\beta}_j^2; j = 1, \dots, m \right)$$

TWAS of Alzheimer's Disease by TIGAR

- eQTL weights trained by Bayesian DPR model with reference transcriptomic data of brain tissue were used
- Using ~4K individual-level GWAS data

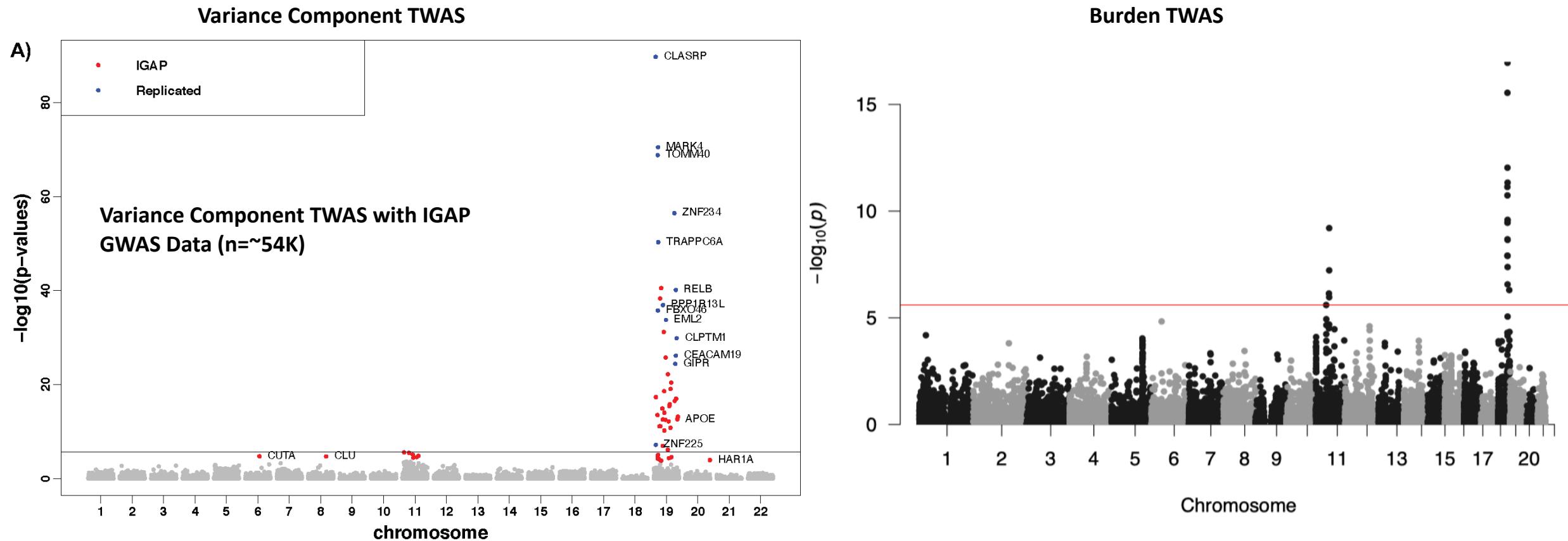


Tang S. et. al. PLOS Genetics, 2021.
<https://doi.org/10.1371/journal.pgen.1009482>

Luningham J.M. et. al. AJHG, 2020.
<https://doi.org/10.1016/j.ajhg.2020.08.022>

TWAS of Alzheimer's Disease by TIGAR

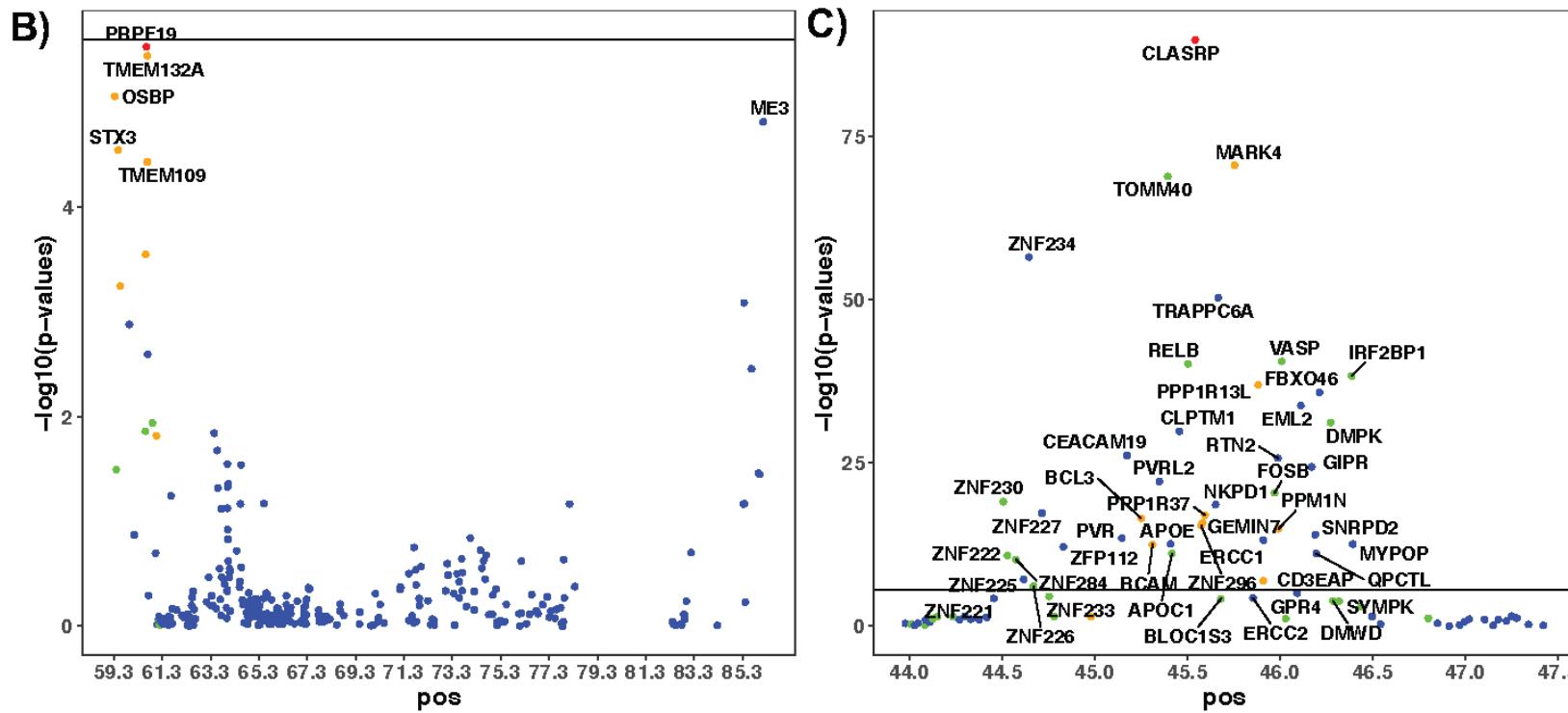
- eQTL weights trained by Bayesian DPR model with reference transcriptomic data of brain tissue were used
- Using IGAP summary-level GWAS data ($n \approx 54K$)



Tang S. et. al. PLOS Genetics, 2021.
<https://doi.org/10.1371/journal.pgen.1009482>

Lunningham J.M. et. al. AJHG, 2020.
<https://doi.org/10.1016/j.ajhg.2020.08.022>

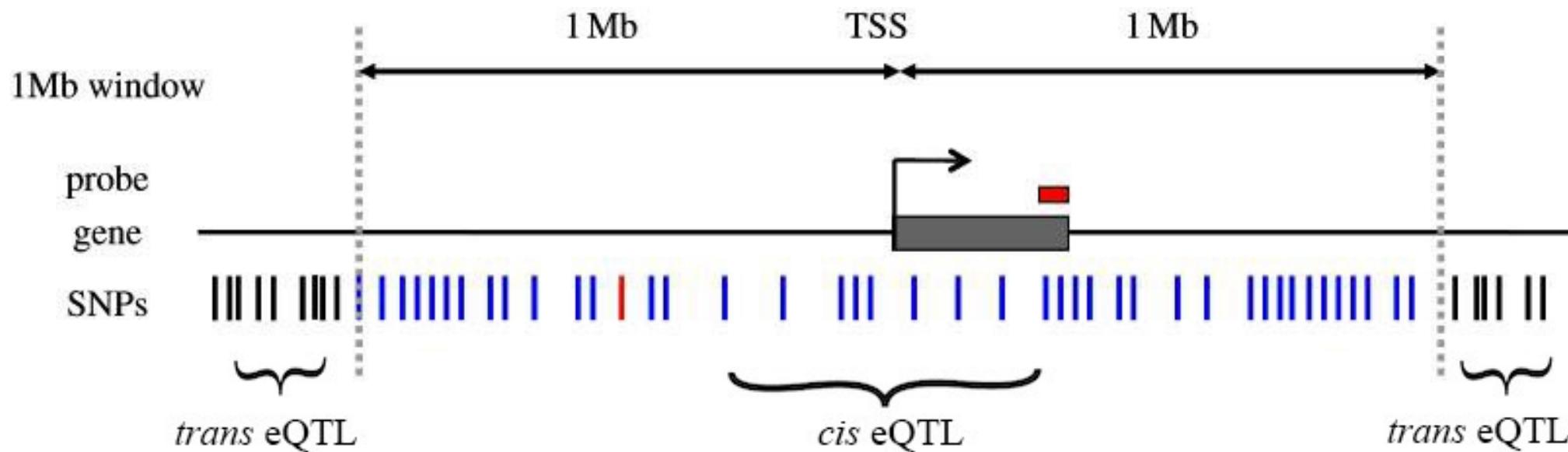
Locus Zoom Plot of TWAS Loci of Alzheimer's Disease by TIGAR (each dot represents a gene)



Tang S. et. al. PLOS
Genetics, 2021.
<https://doi.org/10.1371/journal.pgen.1009482>

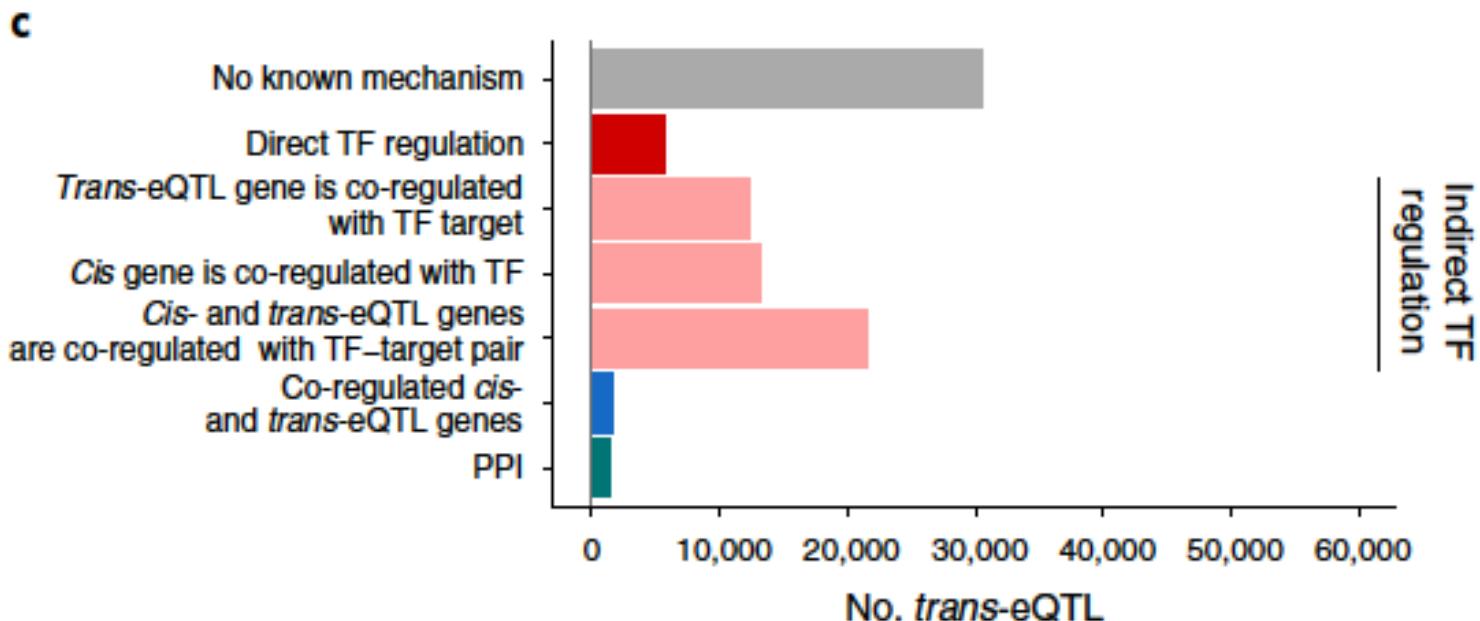
Bayesian Genome-wide TWAS

- Using both cis- and trans- SNPs as predictors for training the gene expression prediction models



Importance of *trans*-eQTL

- Gene expression levels are affected by both *cis* and *trans*-eQTL.
[Gusev et al., *Nat. Genetics*. 2016]
- In whole blood tissue, > 30% genes have significant *trans*-eQTL.
[Lloyd-Jones et al., *AJHG*, 2017]
- In eQTLGen Consortium studies of 31,684 blood samples, *trans*-eQTL were detected for 37% of 10,317 trait-associated GWAS signals, which primarily working through **regulations by transcription factors**. [Vosa U. et al., *Nat. Genetics*. 2021]



Bayesian Genome-wide TWAS

Bayesian Variable Selection Regression (BVSR) Model

1. Consider quantitative gene expression trait \mathbf{T}_g and "spike-and-slab" priors for "eQTL" effect size w_i

$$\mathbf{T}_g = \mathbf{X}\mathbf{w} + \boldsymbol{\epsilon}$$

$$w_i \sim \pi_q N(0, \sigma_\varepsilon^2 \sigma_q^2) + (1 - \pi_q) \delta_0(w_i)$$

$$\varepsilon_i \sim N(0, \sigma_\varepsilon^2)$$

2. Consider an indicator variable γ_i per SNP i , *cis* or *trans* as denoted by q

$$\gamma_i \sim \text{Bernoulli}(\pi_q) \text{ such that } w_i \sim \begin{cases} N(0, \sigma_\varepsilon^2 \sigma_q^2) & \text{if } \gamma_i = 1 \\ 0 & \text{if } \gamma_i = 0 \end{cases}$$

Allow respective "spike-and-slab" prior for effect sizes of *cis* and *trans* "eQTL".

Bayesian Genome-wide TWAS

3. Estimate “eQTL” effect size \hat{w}_i and *Posterior Causal Probability* (PP), $\hat{\gamma}_i = E[\gamma_i] = \text{Prob}(\gamma_i = 1)$, by MCMC.
4. With GWAS data of additional test samples, predict Genetically Regulated gene eXpression (*GReX*) by

$$\widehat{GReX}_g = \sum_{i=1}^m \hat{\gamma}_i \hat{w}_i x_i^*$$

$$E[g(\mathbf{Y}_{pheno} | \mathbf{X}, \hat{\mathbf{w}}, \hat{\boldsymbol{\gamma}})] = \beta \widehat{GReX}_g = \beta \left(\sum_{i=1}^m \hat{\gamma}_i \hat{w}_i x_i^* \right)$$

5. TWAS is to test $H_0 : \beta = 0$

Bayesian Genome-wide TWAS

Segment and Prune Genome Blocks

- Genome-wide SNPs segmented into blocks with $\sim 3,000$ - $10,000$ variants based on block-wise LD structure
- Prune to genome blocks that:
 - have variants in *cis*
 - have potential marginally significant (p -value $< 10^{-5}$) variant by single variant tests
 - up to 50 blocks, ranked by top significant p -values by single variant tests

Bayesian Genome-wide TWAS

- Apply to study AD
- Identified significant gene *ZC3H12B* (p-value=1E-12) on chromosome X driven by trans-eQTL, with ~4K individual-level GWAS data

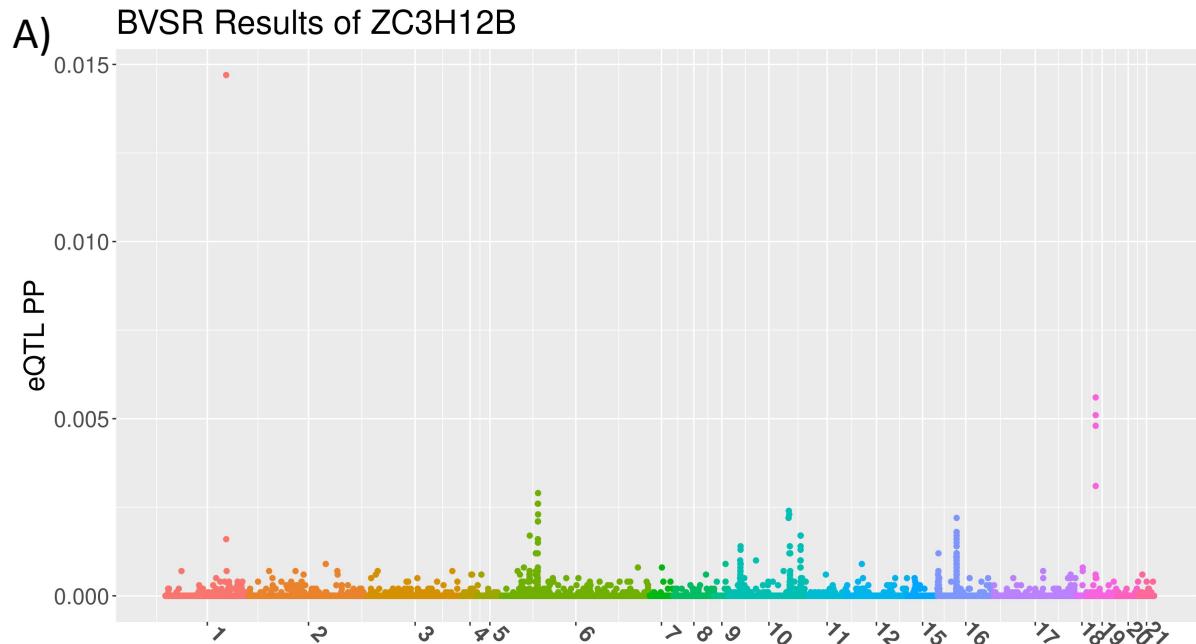


Table 2. Trans-eQTL with top five PP > 0.003 for gene ZC3H12B.

CHR	POS	rsID	Function	MAF	PP	w	p-value
1	159,135,282	rs3026946	Intergenic	0.213	0.0147	-0.071	6.25×10^{-7}
19	45,422,160	rs12721051	3' UTR (APOC1)	0.161	0.0031	0.071	3.94×10^{-6}
19	45,422,846	rs56131196	Downstream (APOC1)	0.173	0.0048	0.069	1.75×10^{-6}
19	45,422,946	rs4420638	Downstream (APOC1)	0.173	0.0051	0.068	1.77×10^{-6}
19	45,424,514	rs157592	Regulatory Region (APOC1)	0.181	0.0056	0.075	1.43×10^{-6}

Significant TWAS Risk Genes of AD Dementia by BGW-TWAS with IGAP GWAS Data

Gene	CHR	Position	TWAS P-VALUE			
			BGW-TWAS	BVSR cis-eQTL	PrediXcan	TIGAR
<i>GPX1^a</i>	3	49,394,608	2.45×10^{-98}	2.45×10^{-98}	-	3.15×10^{-1}
<i>FAM86DP</i>	3	75,484,261	1.55×10^{-13}	4.81×10^{-1}	5.38×10^{-1}	9.63×10^{-1}
<i>BTN3A2^a</i>	6	26,378,546	1.59×10^{-26}	1.56×10^{-26}	3.17×10^{-1}	5.04×10^{-1}
<i>ZNF192^a</i>	6	28,124,089	1.26×10^{-32}	1.25×10^{-32}	8.56×10^{-2}	2.07×10^{-1}
<i>AL022393.7^a</i>	6	28,144,452	3.25×10^{-178}	2.24×10^{-178}	1.50×10^{-1}	8.36×10^{-2}
<i>HLA-DRB1^{ab}</i>	6	32,557,625	1.02×10^{-12}	8.99×10^{-13}	2.06×10^{-6}	-
<i>AEBP1</i>	7	44,154,161	5.55×10^{-220}	8.62×10^{-1}	6.69×10^{-1}	4.19×10^{-1}
<i>BUB3</i>	10	124,924,886	6.64×10^{-18}	1.05×10^{-2}	-	4.76×10^{-1}
<i>FBXO3</i>	11	33,796,089	1.48×10^{-9}	6.88×10^{-1}	-	1.13×10^{-1}
<i>CEACAM19^{abc}</i>	19	45,187,631	4.7×10^{-13}	2.54×10^{-13}	3.60×10^{-12}	2.83×10^{-16}
<i>APOC1^a</i>	19	45,422,606	8.9×10^{-11}	1.11×10^{-10}	3.18×10^{-6}	7.2×10^{-3}
<i>ZC3H12B</i>	X	64,727,767	2.08×10^{-37}	-	-	-
<i>CXorf56</i>	X	118,699,397	6.02×10^{-07}	-	-	-

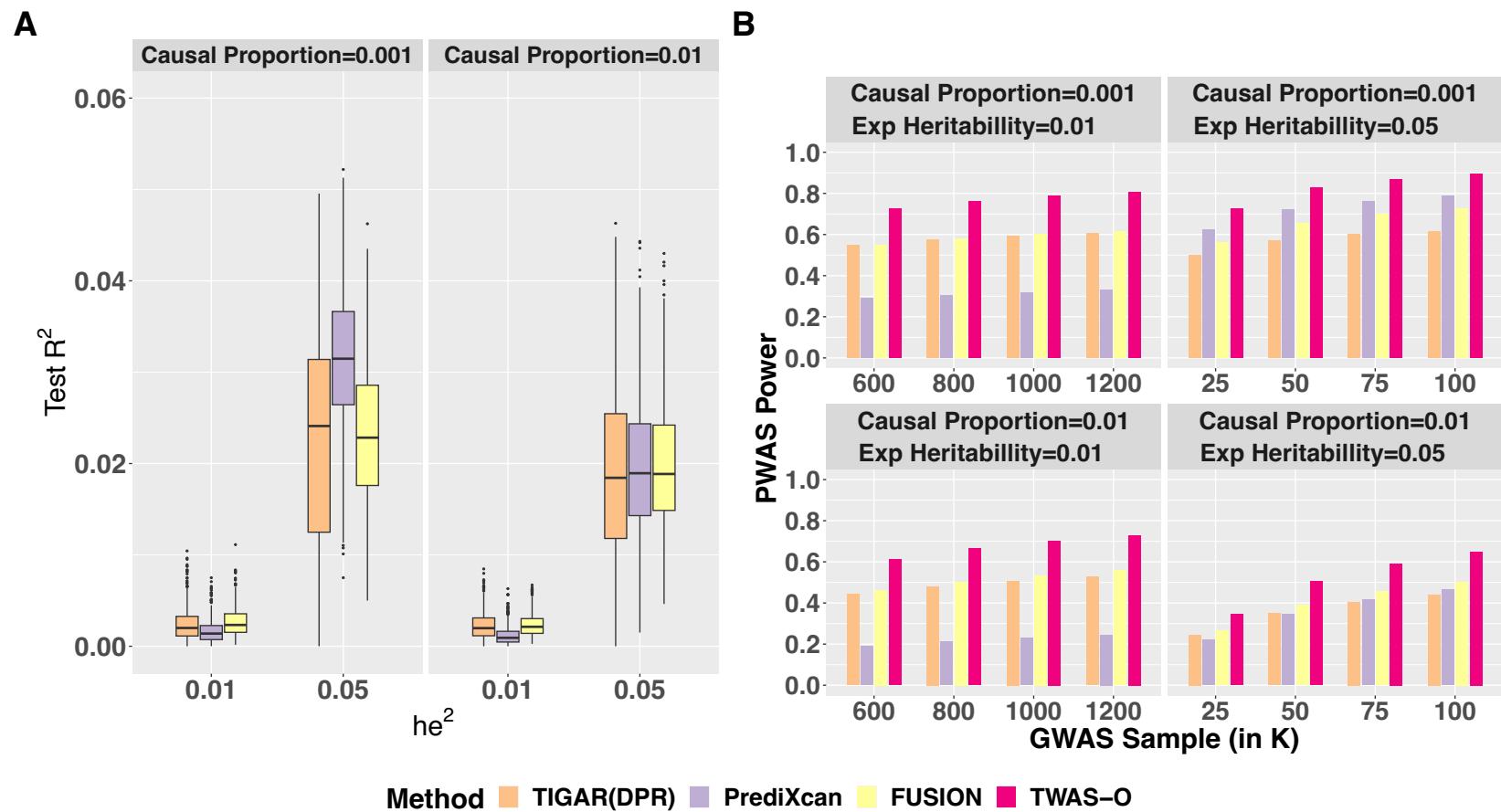
a. Genes that were also identified as significant by using BVSR cis-eQTL estimates.

b. Genes that were also identified by PrediXcan.

c. Genes that were also identified by TIGAR.

Omnibus TWAS

- Performance by individual TWAS tools based on different statistical models vary according to the underlying genetic architecture of gene expression
- Omnibus TWAS?
- Combining TWAS p-values by individual TWAS tools?



Aggregated Cauchy Association Test (ACAT)

- p_k : TWAS p-value using the k^{th} TWAS tool:

An average of “correlated” Cauchy variables is approximated by a Cauchy distribution, under the NULL hypothesis

$$T_{ACAT} = \frac{1}{K} \sum_{k=1}^K \tan\{(0.5 - p_k)\pi\}$$
$$p_{ACAT} \approx \frac{1}{2} - \frac{\{\arctan(T_{ACAT})\}}{\pi}$$

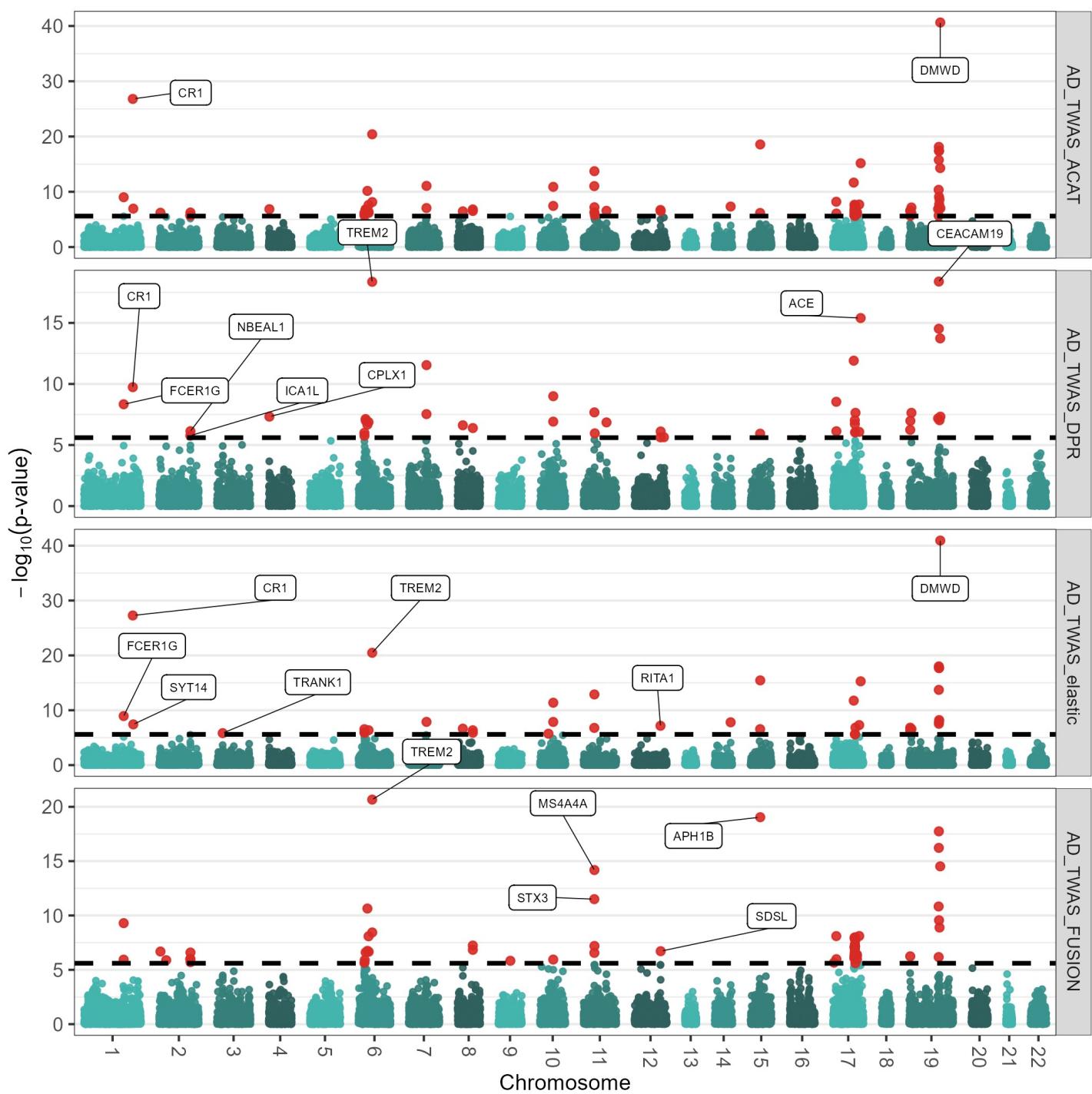
Cauchy transformed p-values: Cauchy distributed under null hypothesis

- Transformed p values increase quickly as the p value approaches 0, T_{ACAT} is essentially dominated by the components with very small p values;
- **If one of the TWAS tools give very small p-value, p_{ACAT} will also be very small.**
- Thus, ACAT can combine the strength of multiple TWAS tools and perform an omnibus test.

Omnibus TWAS of AD Dementia



Qiang (Leo) Liu



Web Resources

- MetaXcan (PrediXcan, S-PrediXcan, MultiXcan, S-MultiXcan)
 - <https://github.com/hakyimlab/MetaXcan>
- FUSION
 - <http://gusevlab.org/projects/fusion/>
- TIGAR/DPR/EN/VC-TWAS
 - <https://github.com/yanglab-emory/TIGAR>
- BGW-TWAS
 - <https://github.com/yanglab-emory/BGW-TWAS>
- Omnibus TWAS/PWAS Pipeline
 - <https://github.com/tingyhu45/PWAS-O>