Integrative Genomics to Nominate Candidate Genes in AD GWAS Loci

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ADGC 10th Anniversary Symposium, Philadelphia, PA

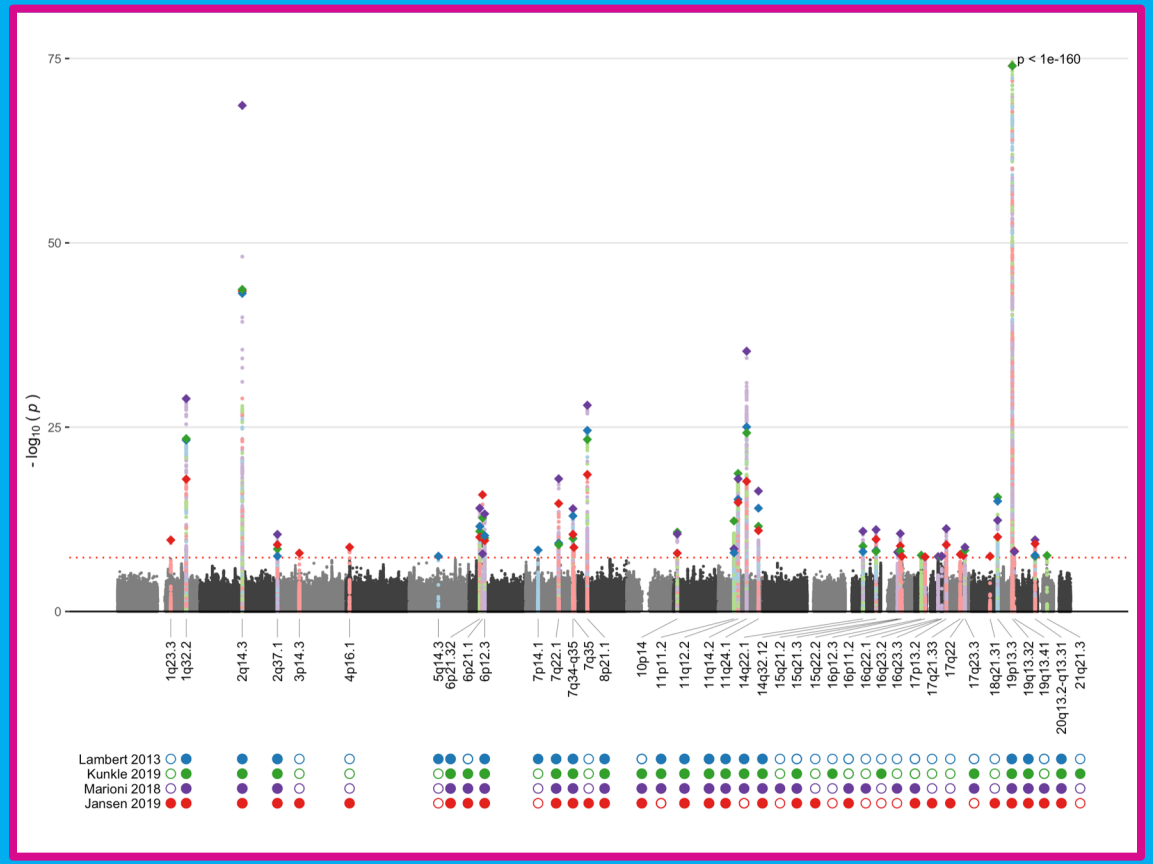
November 12, 2019

Icahn School of Medicine at Mount Sinai

Disclosure: Alison Goate, D.Phil.

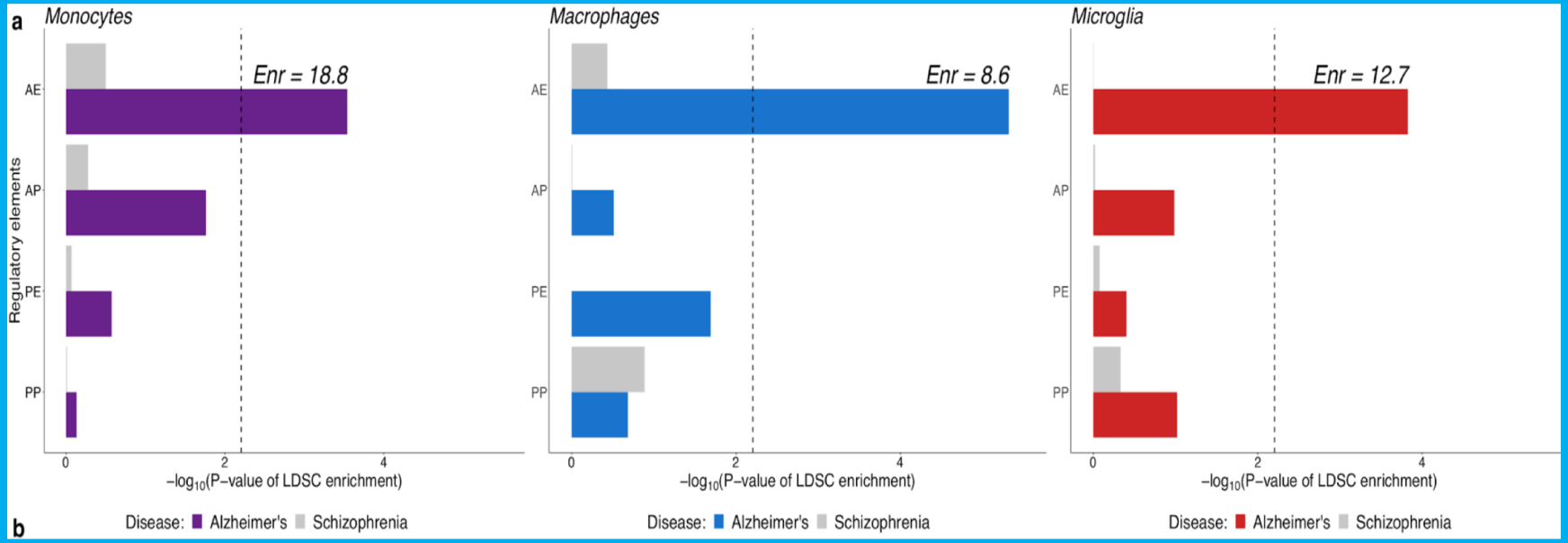
Research Support / Grants	NIH-NIA, JPB Foundation, Rainwater Foundation, Robert & Renee Belfer Foundation
Stock/Equity	None
Consulting	Cognition Therapeutics, Denali Therapeutics, Biogen, Eisai, AbbVie, GSK, Pfizer
Royalties	Taconic, Athena Diagnostics

Alzheimer's disease GWAS identify 40 risk loci



Shea Andrews & Brian Fulton-Howard

Active enhancers in myeloid cells are enriched for AD risk alleles



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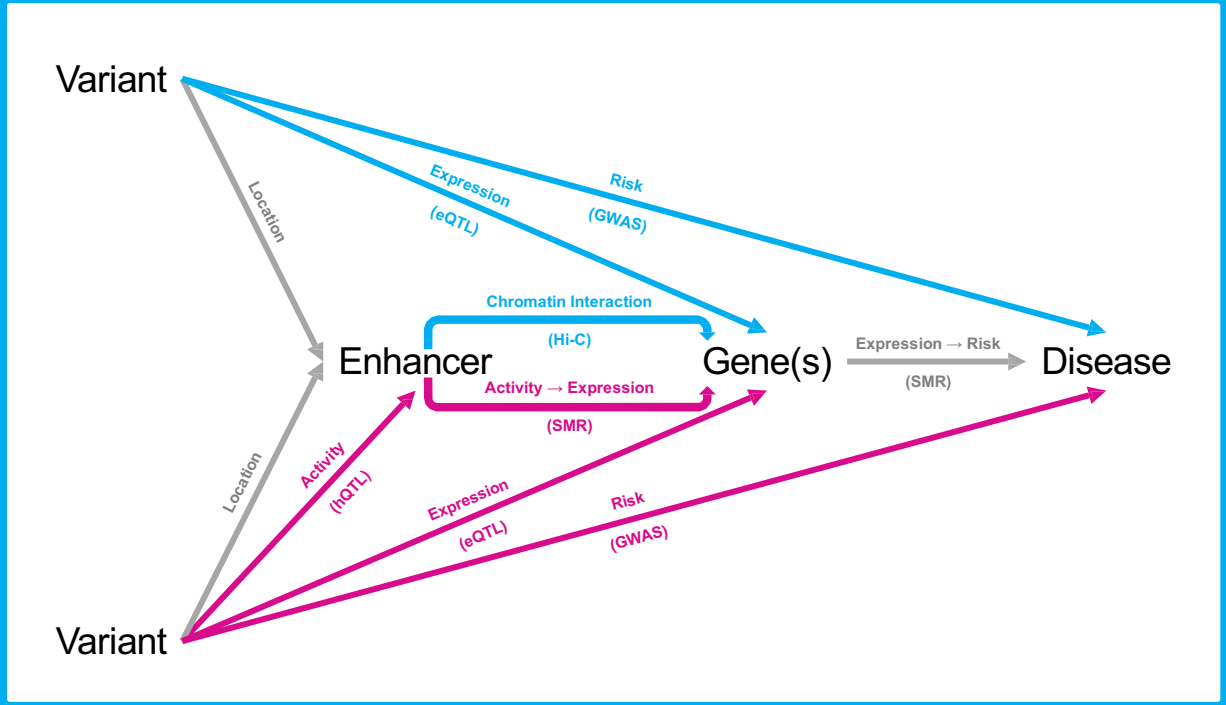
AD risk alleles are enriched in active enhancers, but how do we identify the genes these enhancers regulate?

Integrative analysis of GWAS, epigenomic, transcriptomic and chromatin data to discover of risk genes



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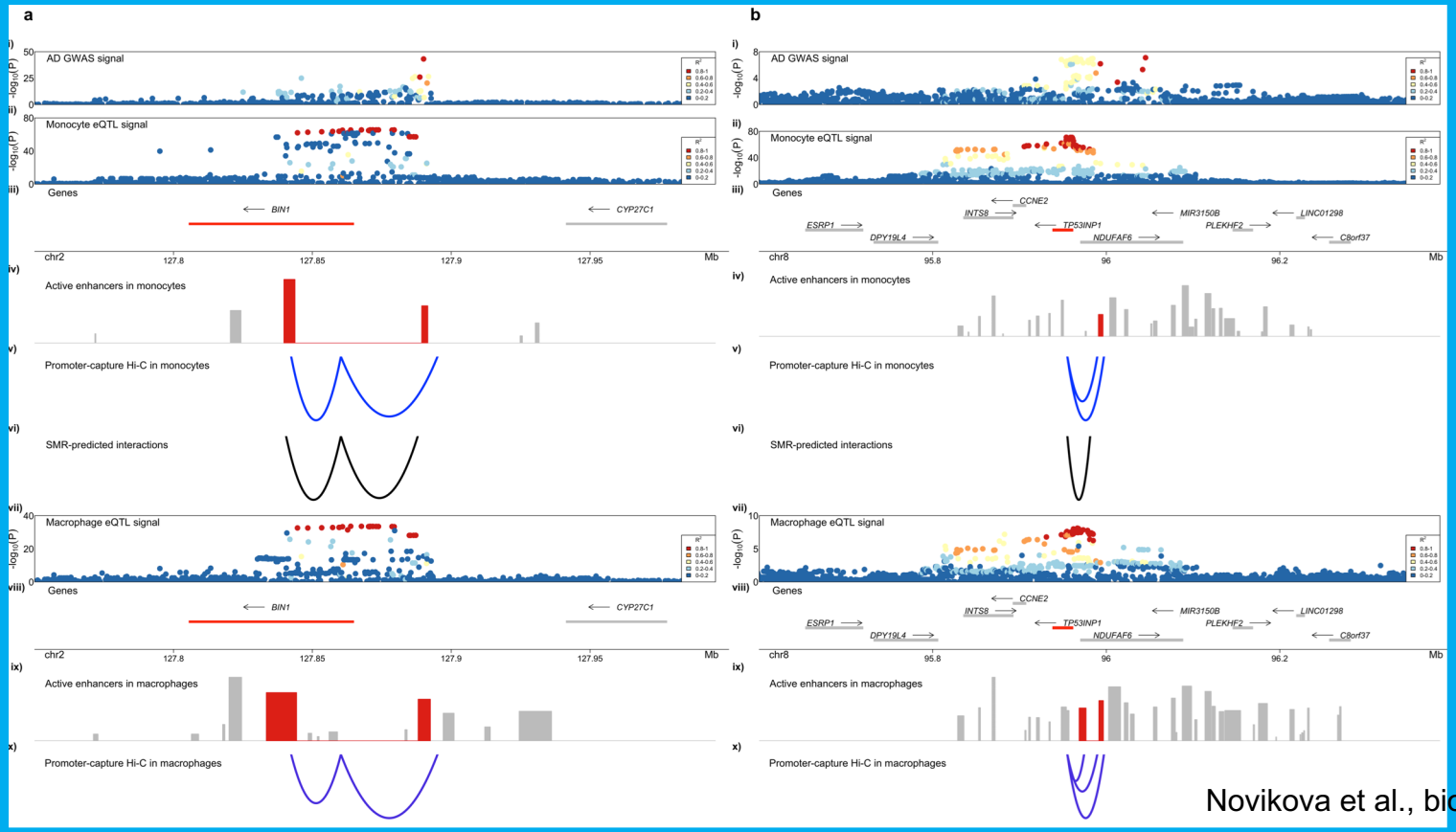
Data integration identifies *Bin1* and *TP53INP1* as candidate causal genes

BIN1 locus ***TP53INP1 locus***



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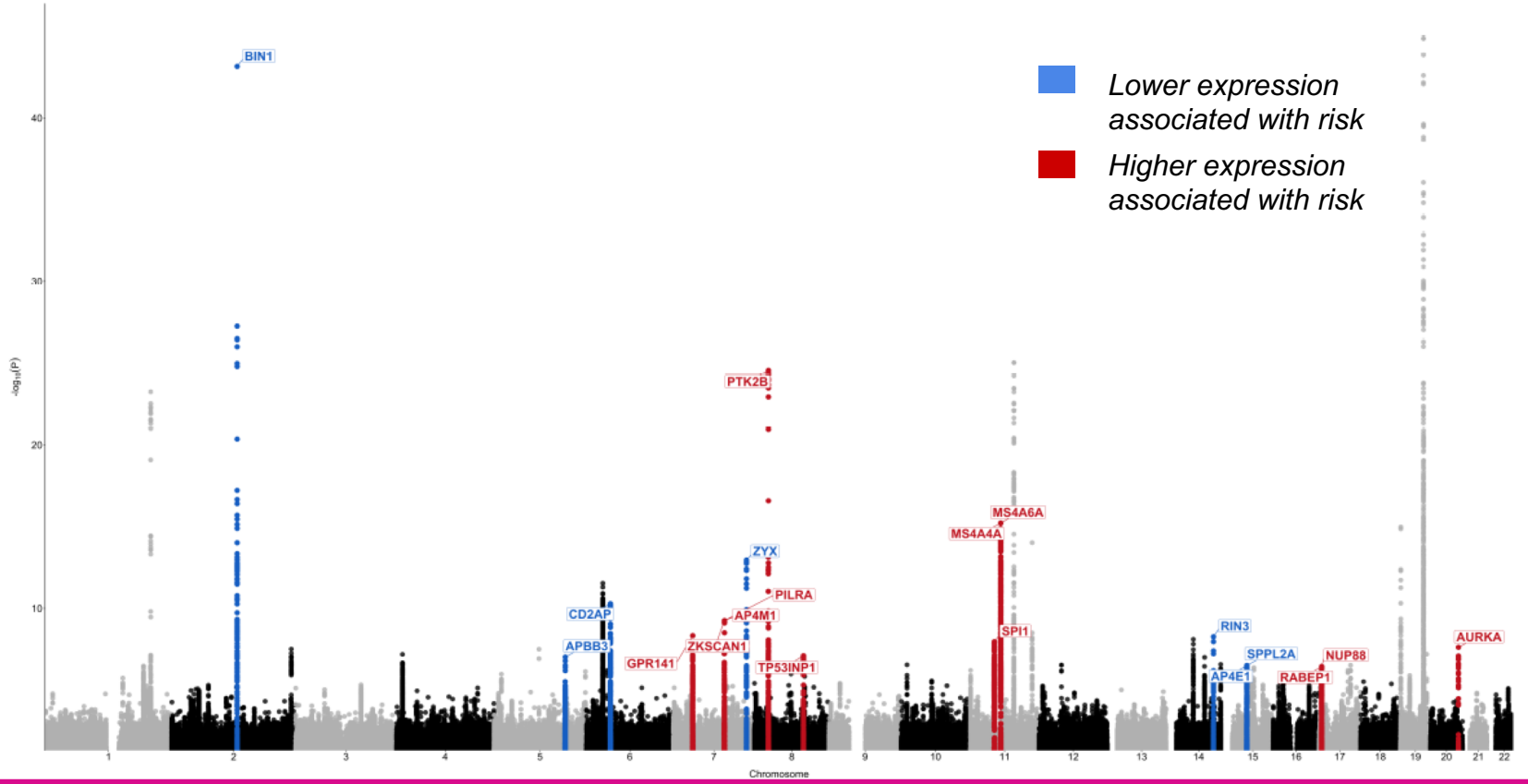
Twenty three AD candidate genes identified



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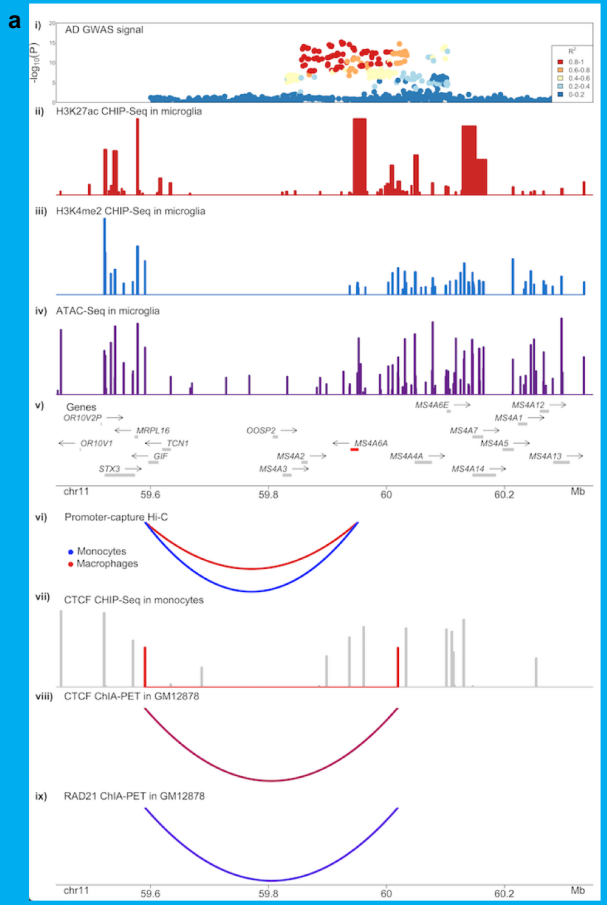
Candidate variant in *MS4A* locus disrupts CTCF binding site, alters chromatin activity and increases expression of *MS4A4A/6A*



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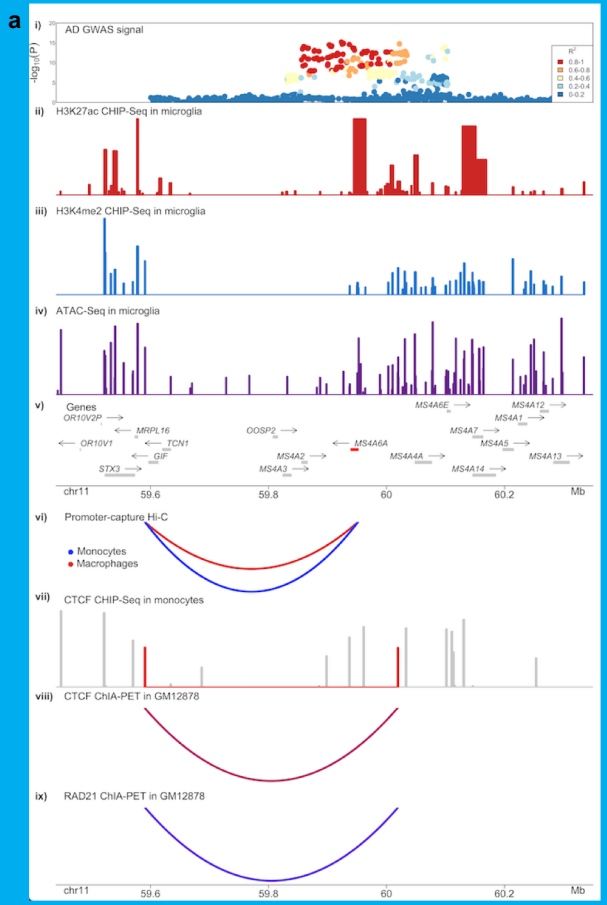

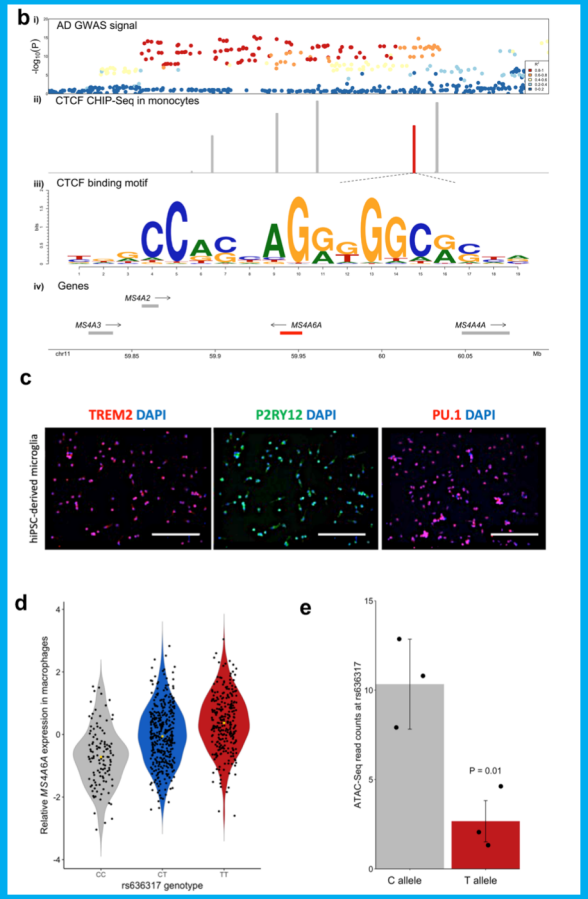

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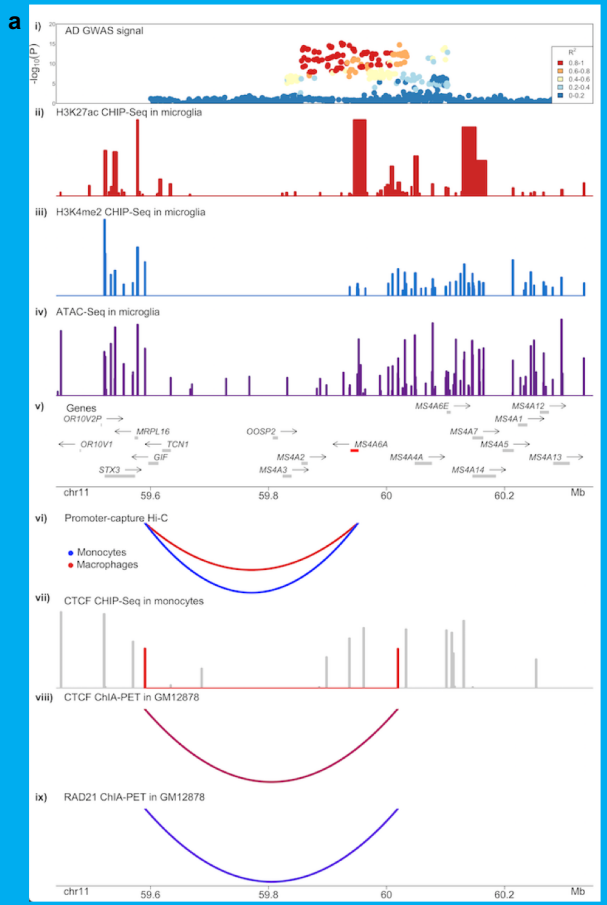

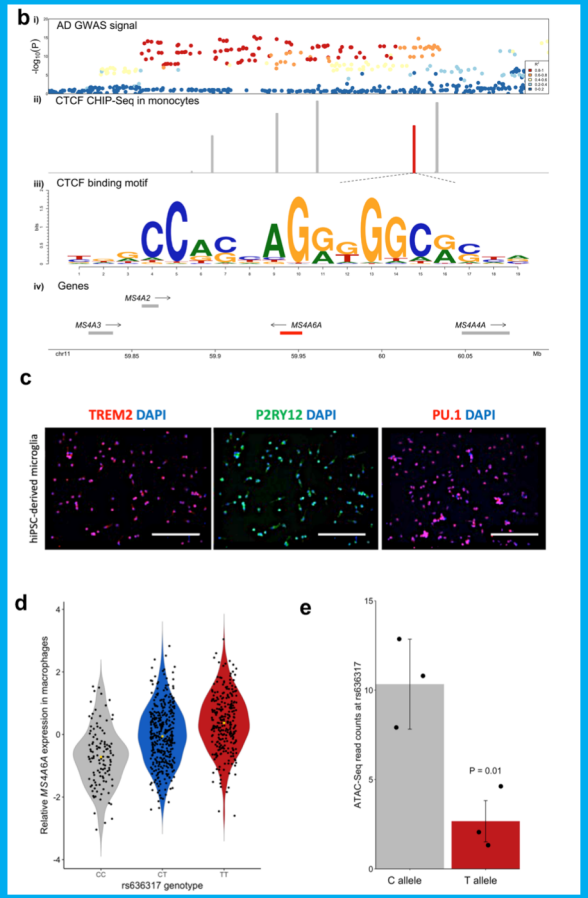

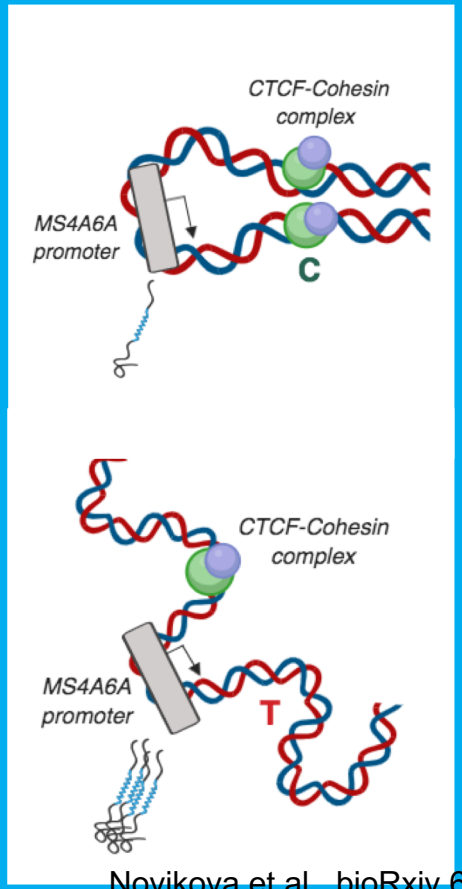

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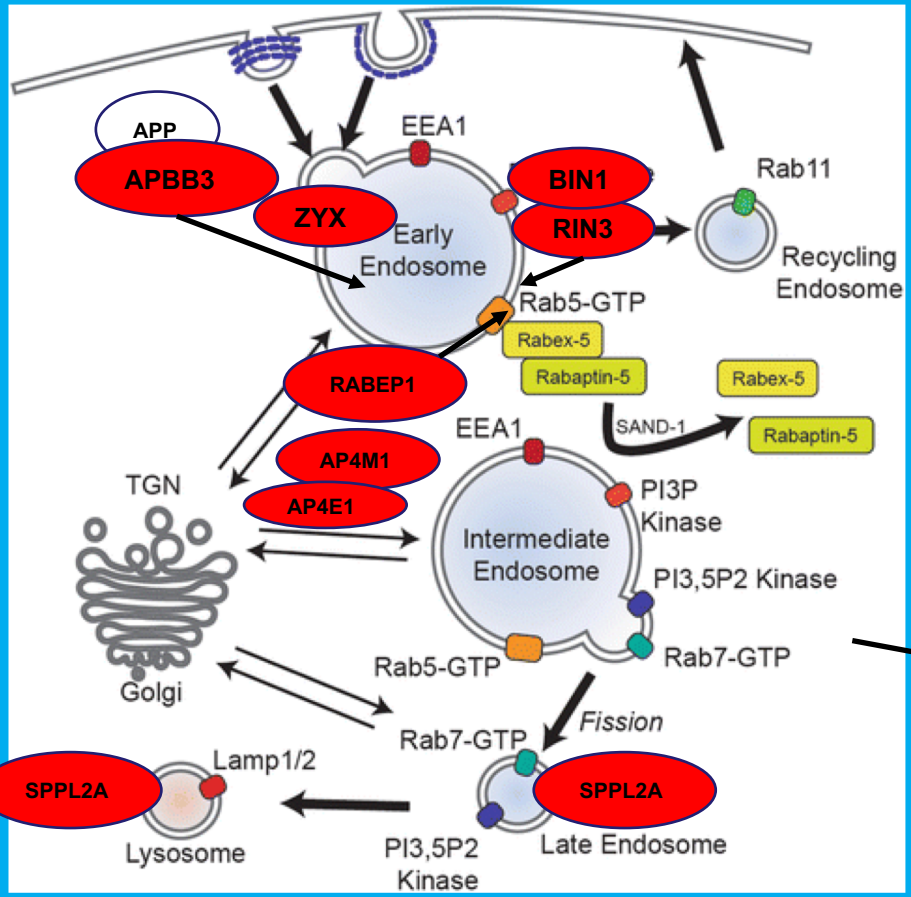
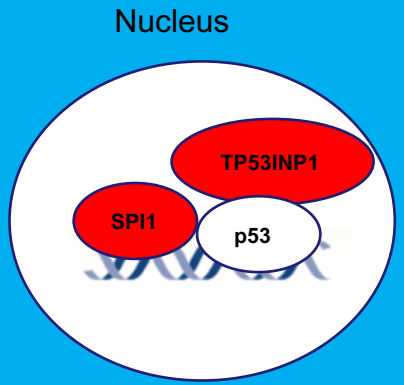
Genes coalesce around endolysosomal pathway





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Summary

- 40 common AD risk loci are enriched in myeloid enhancers
- Integration of GWAS with myeloid cell genomic/epigenomic data nominates 23 candidate genes
- Candidate genes implicate endolysosomal system in myeloid cells

Acknowledgements

Collaborators:
MSSM: Ke Hao, Bin Zhang, Towfique Raj, Anne Schaefer, Pinar Ayata, Panos Roussos, Paul O'Reilly

Washington University: Carlos Cruchaga, Oscar Harari, Celeste Karch

IGAP Consortium: ADGC/GERAD/CHARGE/EADI

Funding:
NIA, JPB Foundation
Rainwater Foundation,
Neurodegeneration Consortium

Gloriia Novikova, Edoardo Marcora, Manav Kapoor, Julia TCW, Anastasia Efthymiou, Kuan-lin Huang,

IGAP

INTERNATIONAL

GENOMICS OF ALZHEIMER'S PROJECT

ADGC/GERAD/IGAP/ADSP investigators