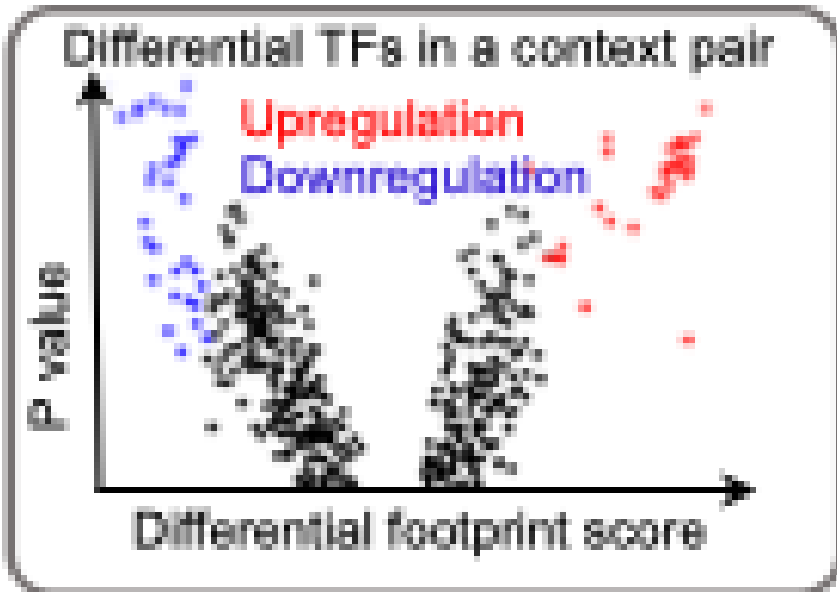
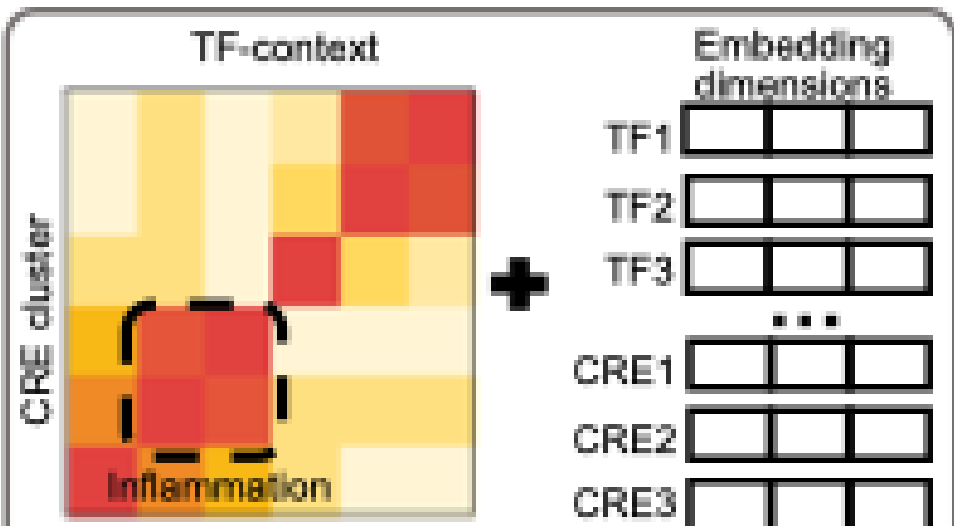
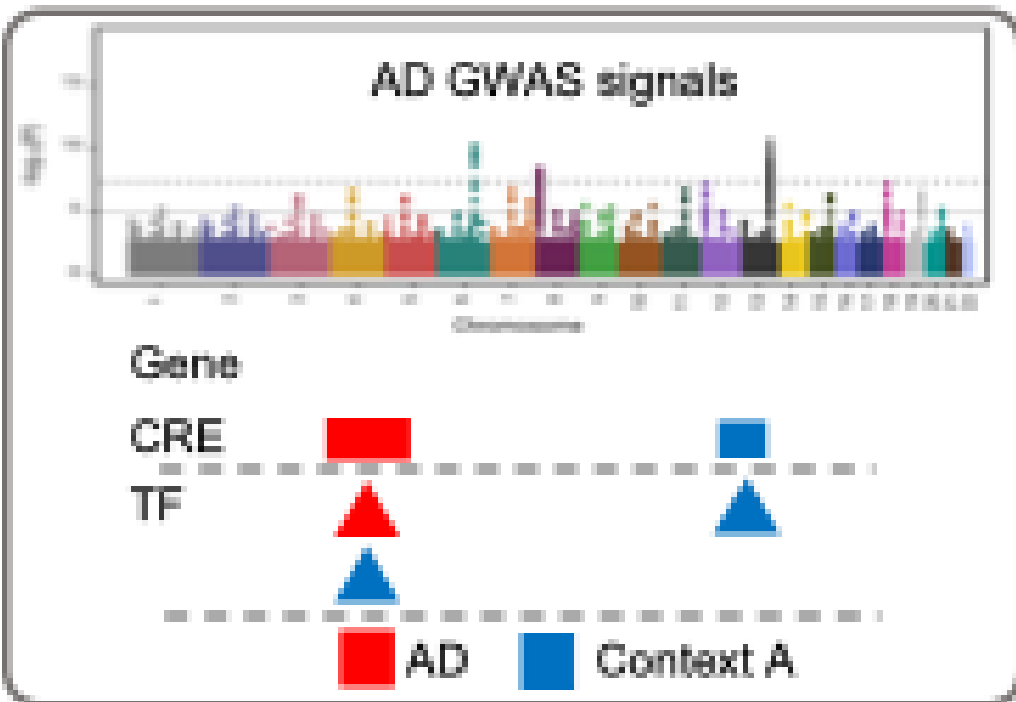
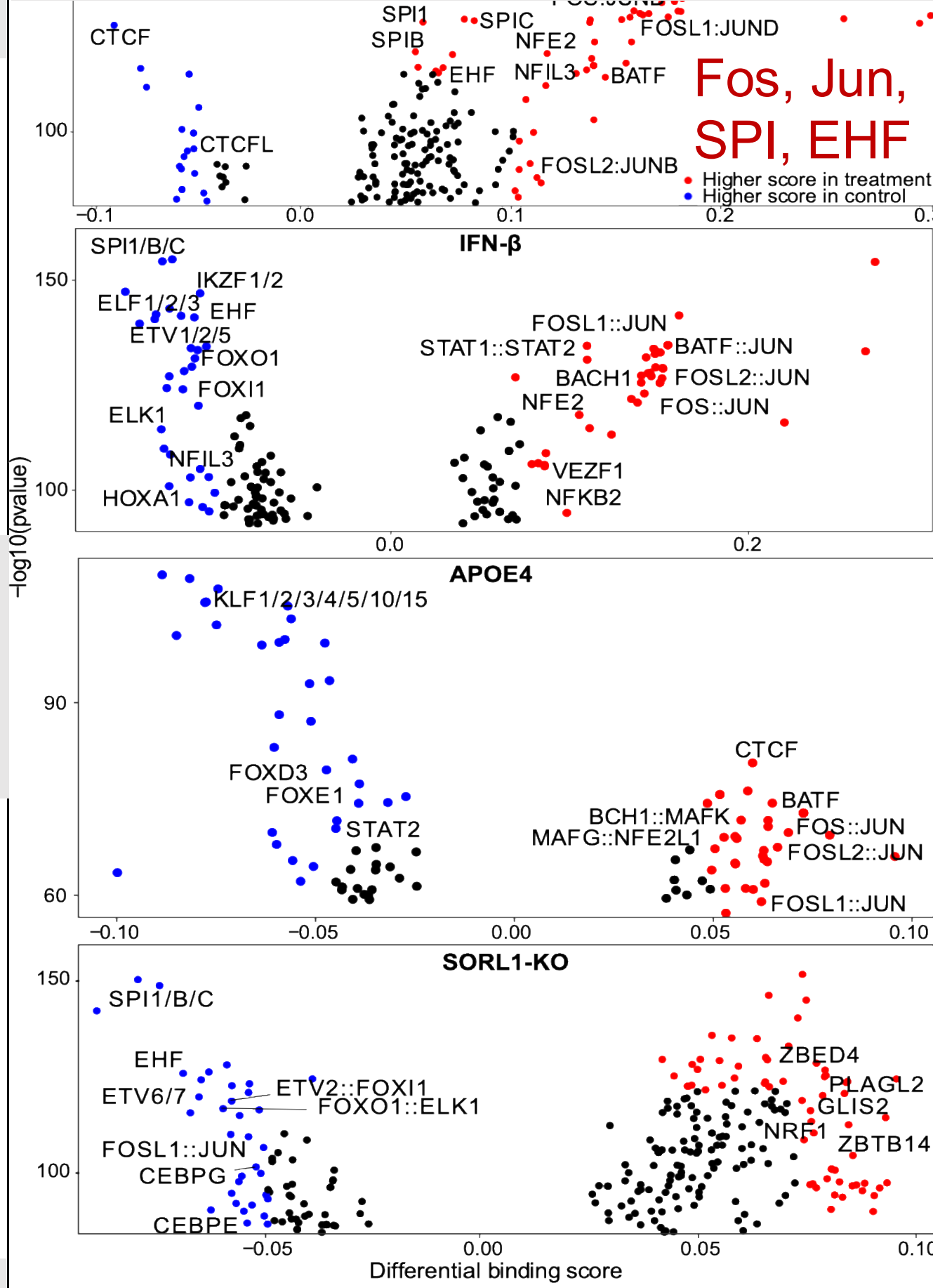
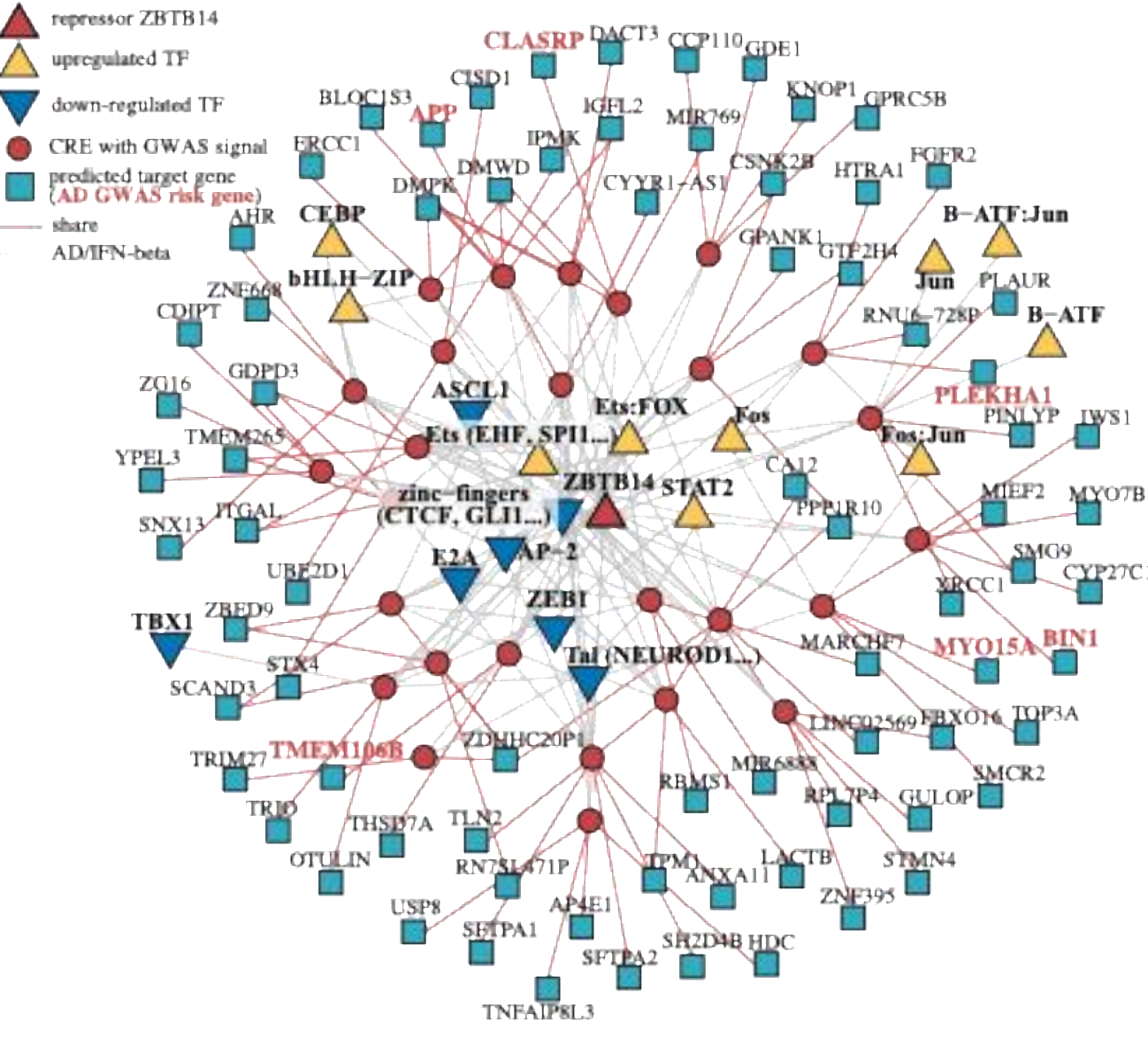


Context-dependent Epigenetic regulatory Networks (*cEpiNets*) in microglia reveals *cis*- and *trans*-regulatory programs in Alzheimer's disease (AD)

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INTRODUCTION	METHODS	RESULTS	CONCLUSIONS
Microglia play a pivotal role in AD pathogenesis. Recent snRNA-seq studies have systematically characterized the AD-associated transcriptional states and mapped cell-type-specific expression quantitative trait loci. However, it is not well understood how genetic susceptibility interacts with other risk factors, such as inflammation, to shape microglial regulatory programs in AD-associated cellular states.	2. Calculating differential TF footprint score for each perturbation conditions.  3. Prioritizing context-dependent TF-CRE links and predicting their target genes based on embeddings.  4. Investigating TF-CRE-gene networks of AD-associated microglial states, and tracking target genes of AD GWAS variants: 	1. Differential TF (dfTF) binding across contexts  2. Inflammatory TF ZBTB14 co-binds with AD dfTFs at AD GWAS variants, suggesting a key regulator.  3. <i>SORL1</i> variants disrupt AD dfTFs' binding, driving its expression change, and associate with the fraction of a microglial inflammatory state. 	We systematically charted context-dependent TF-CRE-gene networks for microglia under AD-related contexts. This provides a comprehensive resource to dissect functional AD risk variants and key regulators underlying gene-by-inflammation interaction. CONTACT HOU Group of Systems Genomics and Genetics (https://hougroup.xyz): Lei Hou, Assistant professor, Biomedical Genetics, Boston University, email: leihou@bu.edu; Ting-Ting Fu, Postdoctoral Associate, Biomedical Genetics, Boston University, email: tingtfu@bu.edu