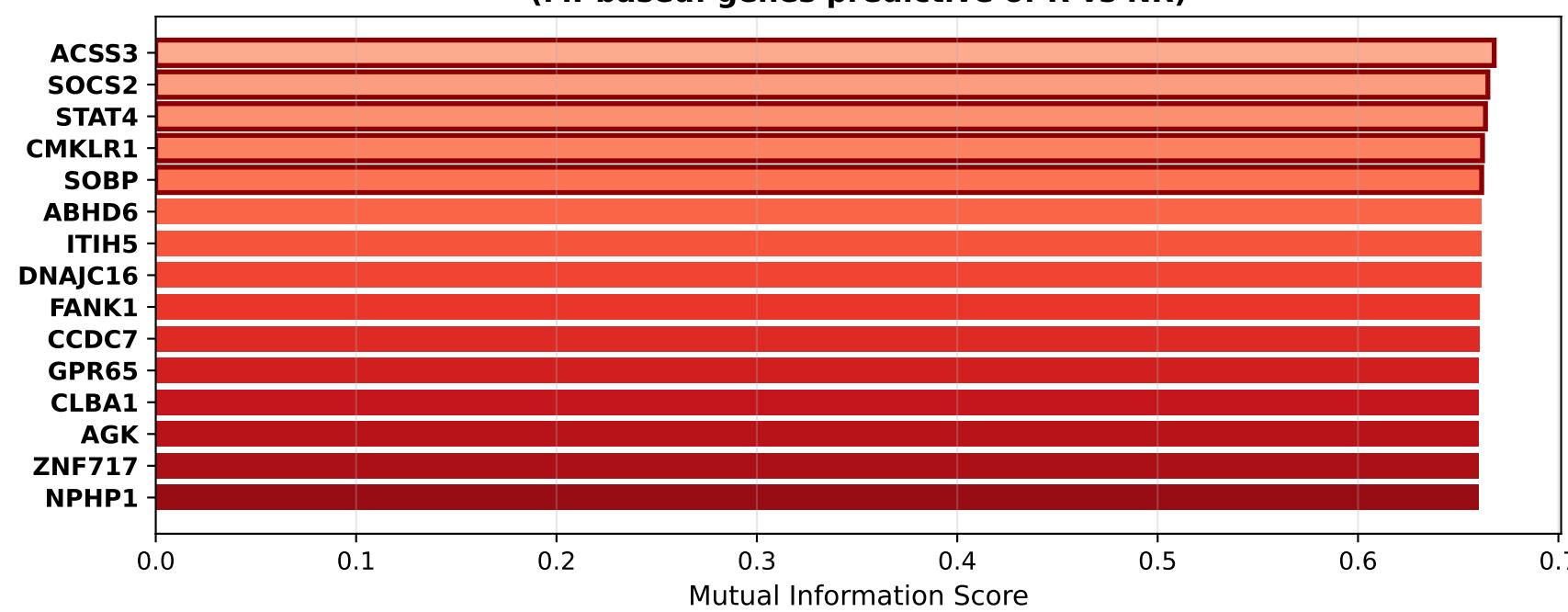
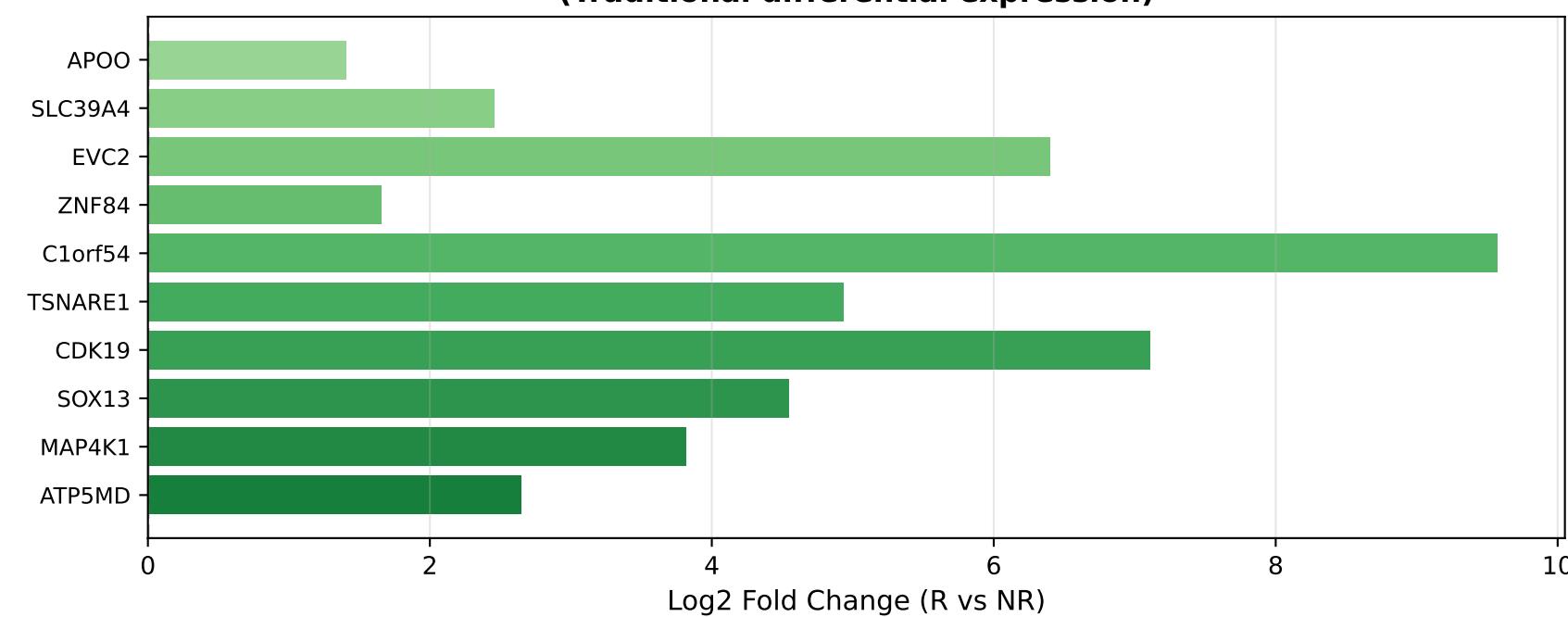


TREATMENT RESPONSE BIOMARKERS: Polymathic Discovery Pipeline

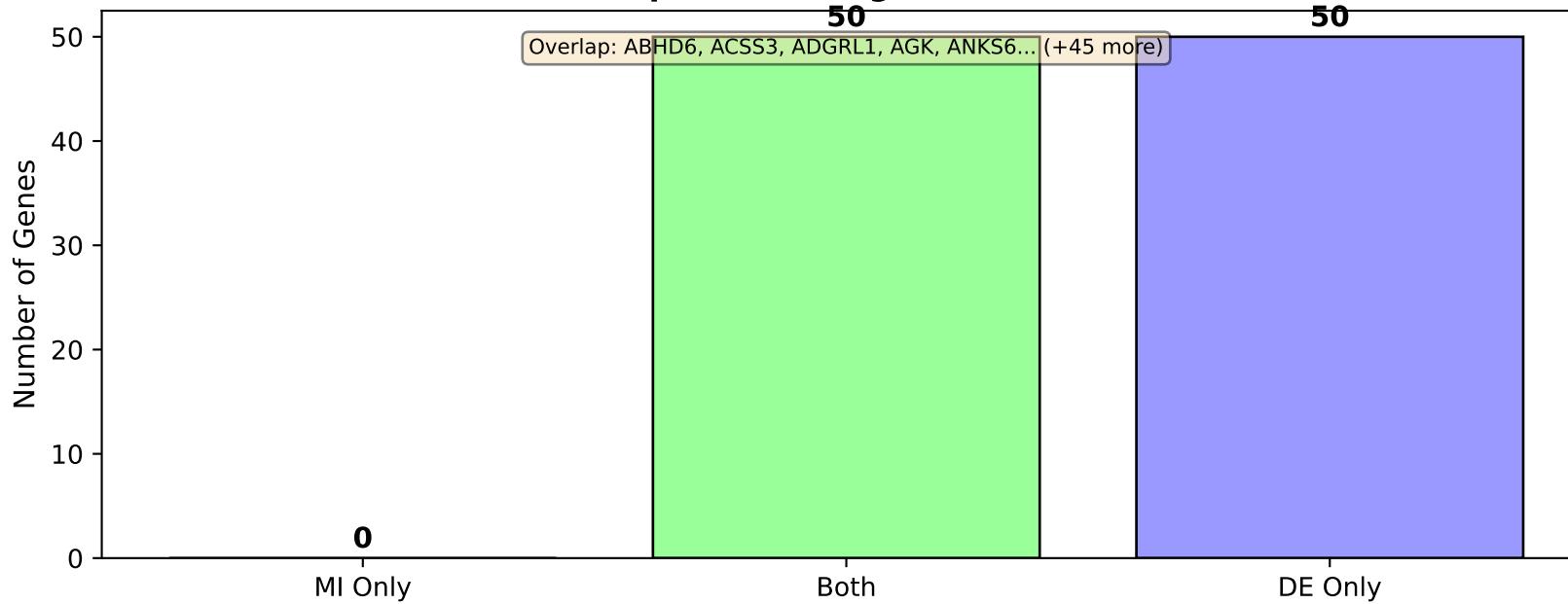
**Top 15 Treatment Response Biomarkers
(MI-based: genes predictive of R vs NR)**



**Top DE Genes Upregulated in Responders
(Traditional differential expression)**



**MI vs DE Gene Overlap
(Top 50 MI vs significant DE)**



BIOMARKER VALIDATION & INTERPRETATION

TOP MI BIOMARKERS (Novel Candidates):

- ACSS3: MI=0.668
- SOCS2: MI=0.665
- STAT4: MI=0.664
- CMKLR1: MI=0.662
- SOBP: MI=0.662

VALIDATION STATUS:

- ✓ STAT4: Known immune regulator
 - Th1 differentiation, IFN- γ signaling
 - Link to immunotherapy response
- ✓ SOCS2: Cytokine signaling regulator
 - JAK-STAT pathway suppressor
 - Tumor immune evasion role
- ? ACSS3: Acetyl-CoA synthetase
 - Metabolic gene (needs validation)
 - Potential tumor metabolism role

METHODS COMPARISON:

- MI: Information-theoretic (cross-domain)
- DE: Traditional statistics
- Overlap genes = highest confidence

NEXT STEPS:

- Validate in external PDAC cohorts
- Functional studies (KO/KD)
- Protein-level confirmation (IHC)