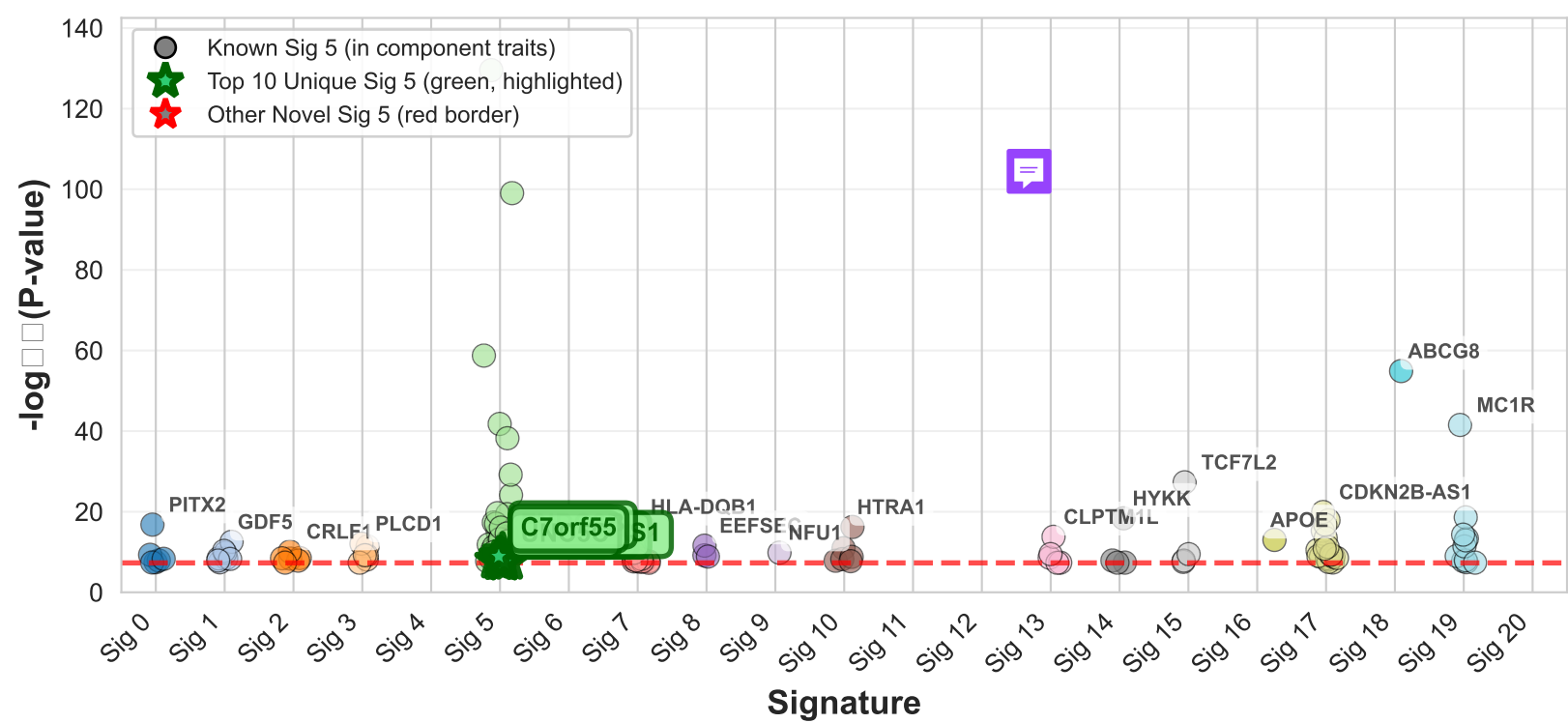
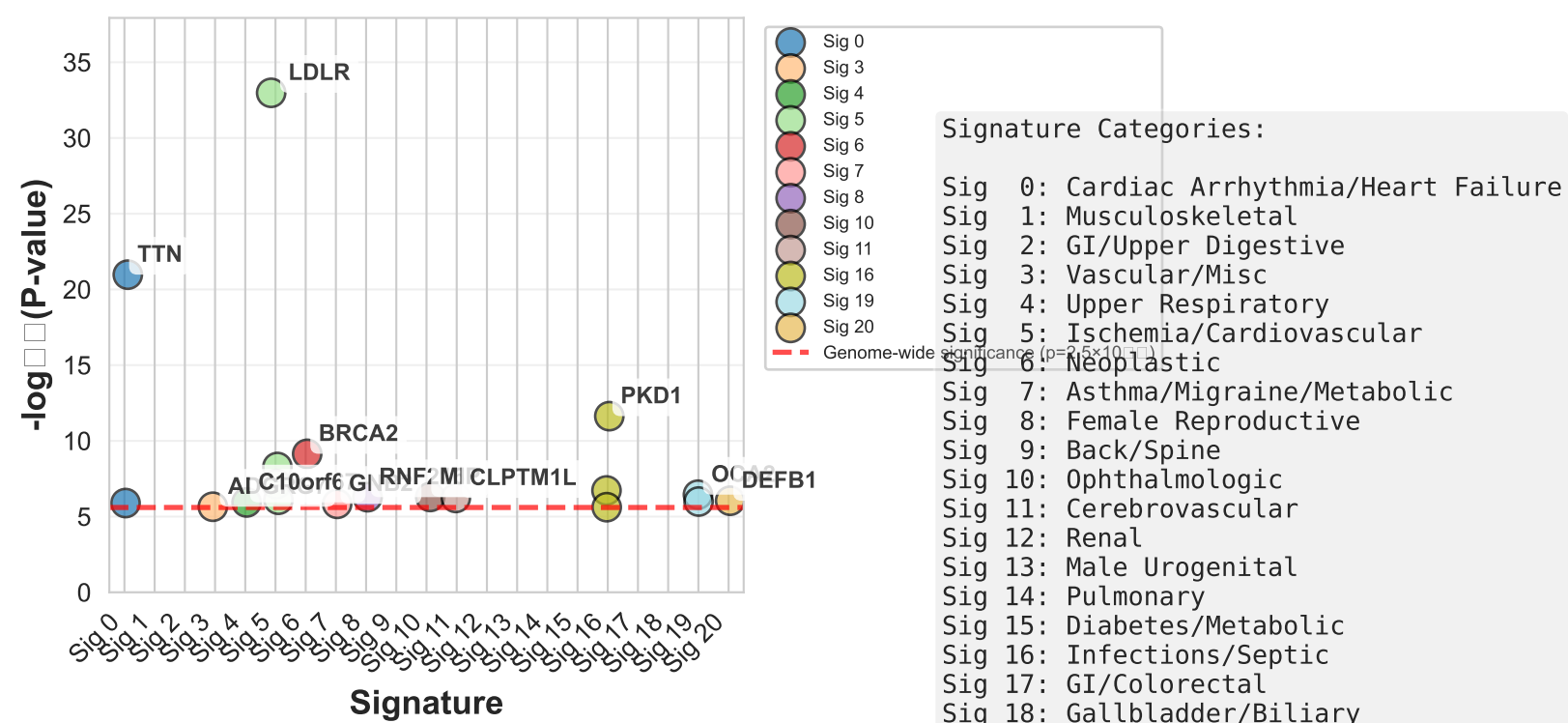


A. Lead Variants by Signature (GWAS)

□ = Novel Sig 5 loci; Green □ = Top 10 Unique Sig 5 discoveries



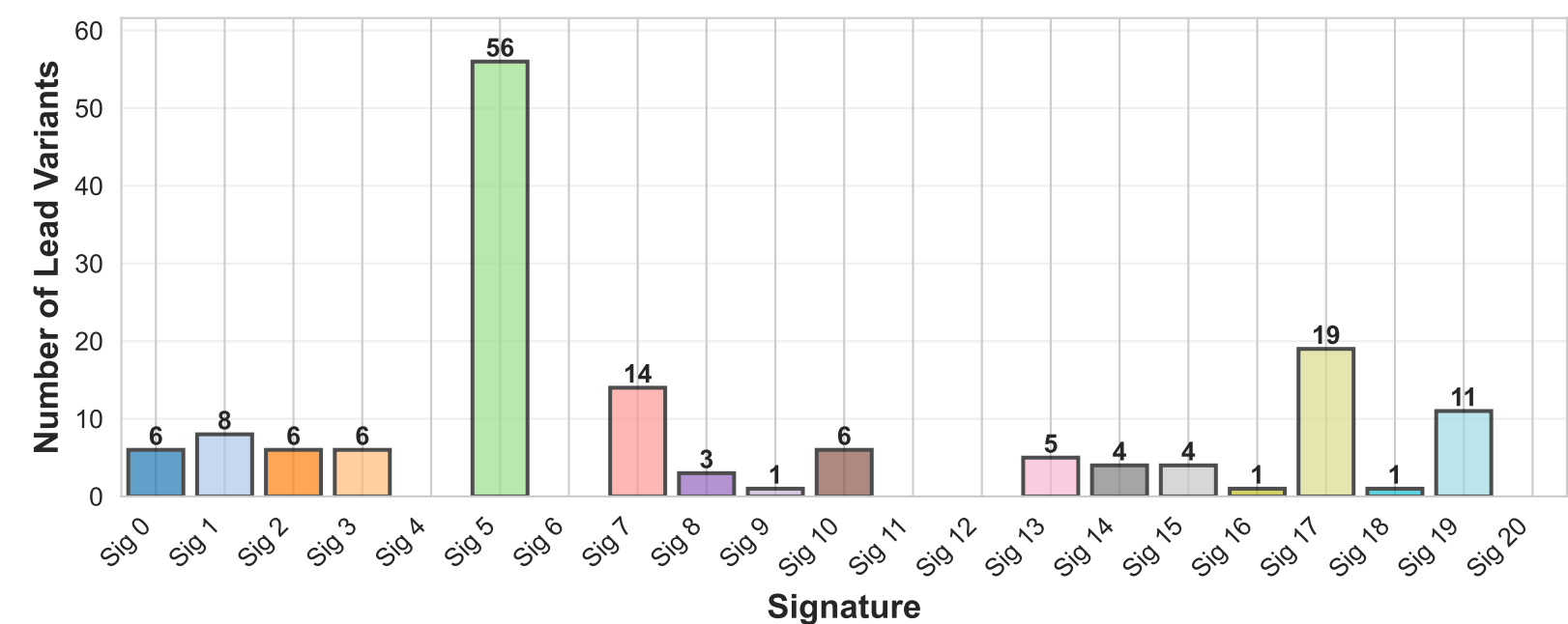
B. Significant Genes by Signature (mask3: LoF Variants)



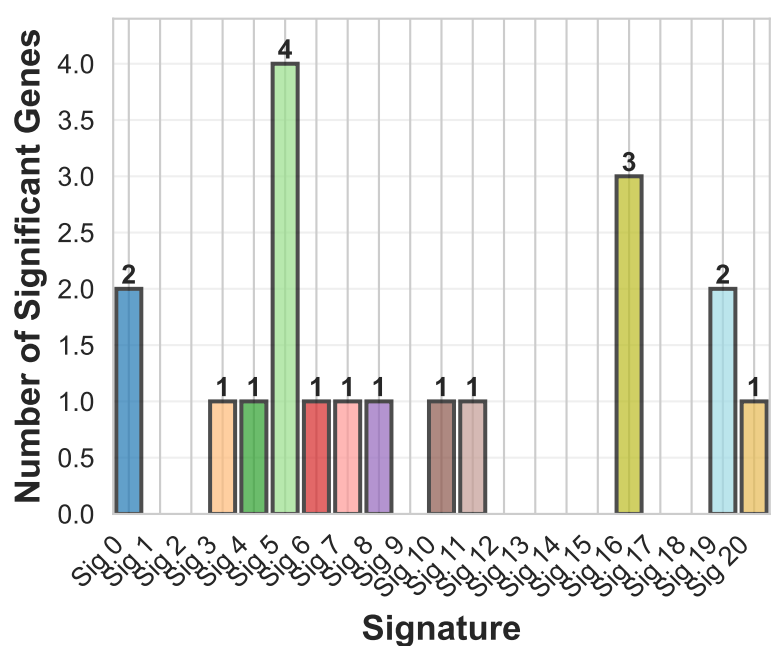
Signature Categories:

- Sig 0: Cardiac Arrhythmia/Heart Failure
- Sig 1: Musculoskeletal
- Sig 2: GI/Upper Digestive
- Sig 3: Vascular/Misc
- Sig 4: Upper Respiratory
- Sig 5: Ischemia/Cardiovascular
- Sig 6: Neoplastic
- Sig 7: Asthma/Migraine/Metabolic
- Sig 8: Female Reproductive
- Sig 9: Back/Spine
- Sig 10: Ophthalmologic
- Sig 11: Cerebrovascular
- Sig 12: Renal
- Sig 13: Male Urogenital
- Sig 14: Pulmonary
- Sig 15: Diabetes/Metabolic
- Sig 16: Infections/Septic
- Sig 17: GI/Colorectal
- Sig 18: Gallbladder/Biliary
- Sig 19: Skin/Kidney
- Sig 20: Healthy/Protective

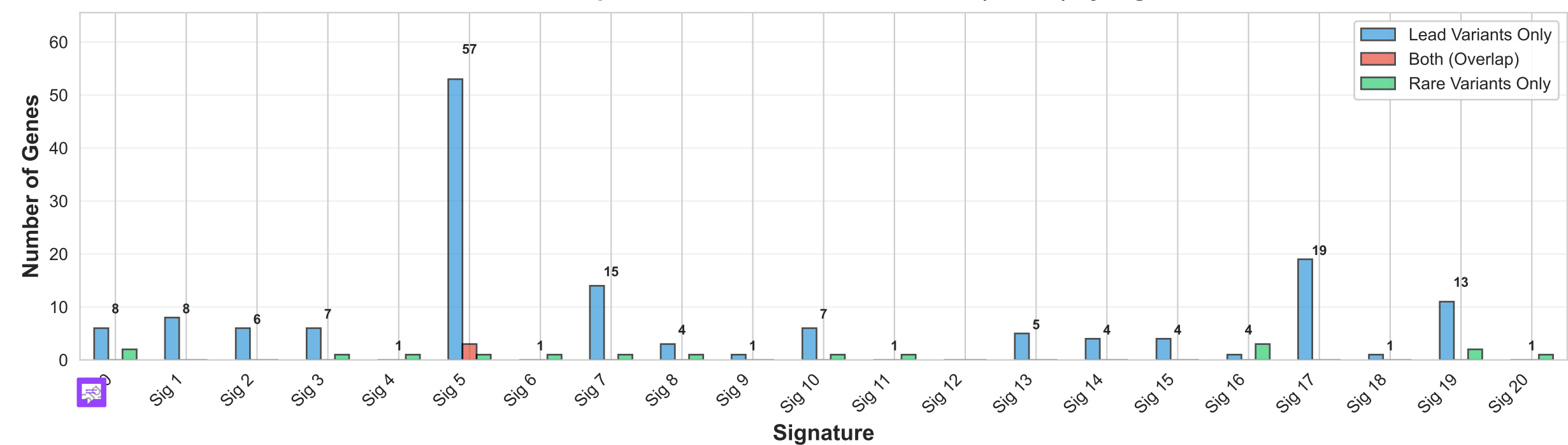
C. Number of Lead Variants per Signature



D. Number of Significant Genes per Signature (mask3)



E. Gene Overlap: Lead Variants vs Rare Variants (mask3) by Signature



Top 10 Unique Sig 5 Loci
(Not in component trait GWAS)

- FNDC3B (rs1499813)
Fibronectin domain, insulin signaling
- HYOU1 (rs2509121)
Hypoxia up-regulated protein, ER stress response
- C7orf55 (rs4732365)
Unknown function
- OPRL1 (rs8121509)
Opioid receptor, pain/stress signaling
- IL6R (rs6687726)
Interleukin-6 receptor, inflammatory pathway
- PLCG2 (rs35039495)
Phospholipase C gamma 2, platelet activation
- NR2F2-AS1 (rs7168222)
Nuclear receptor antisense RNA
- R3HDM2 (rs4760278)
RNA binding protein
- UNC5C (4:96088139_ATATG_A)
Netrin receptor, axon guidance
- ALDH1A2 (rs1532085)
Unknown function