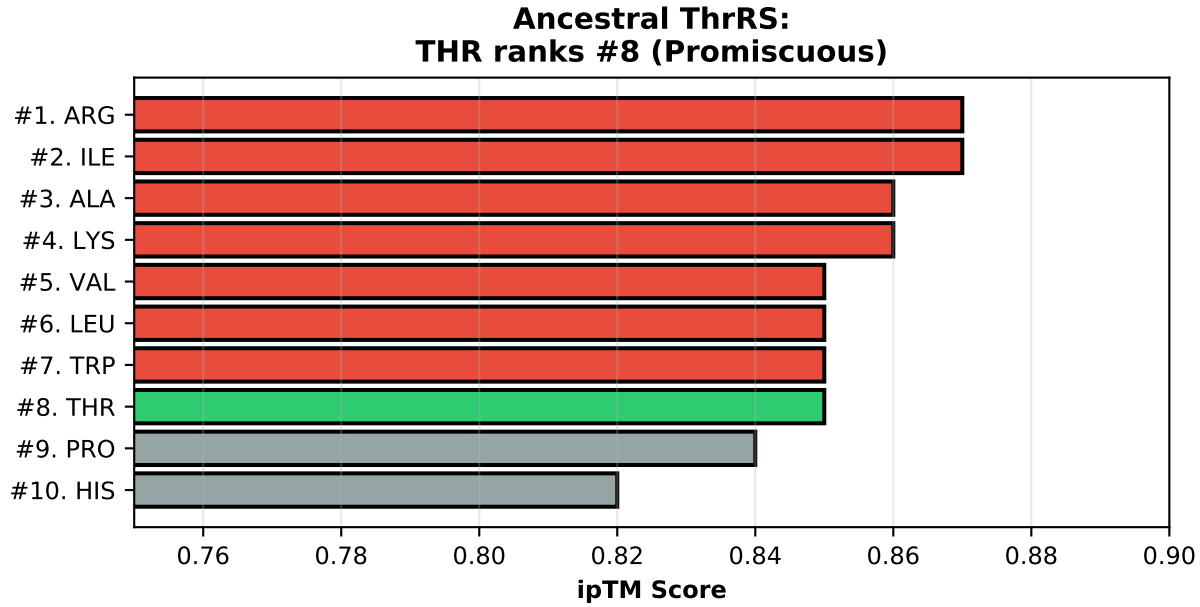
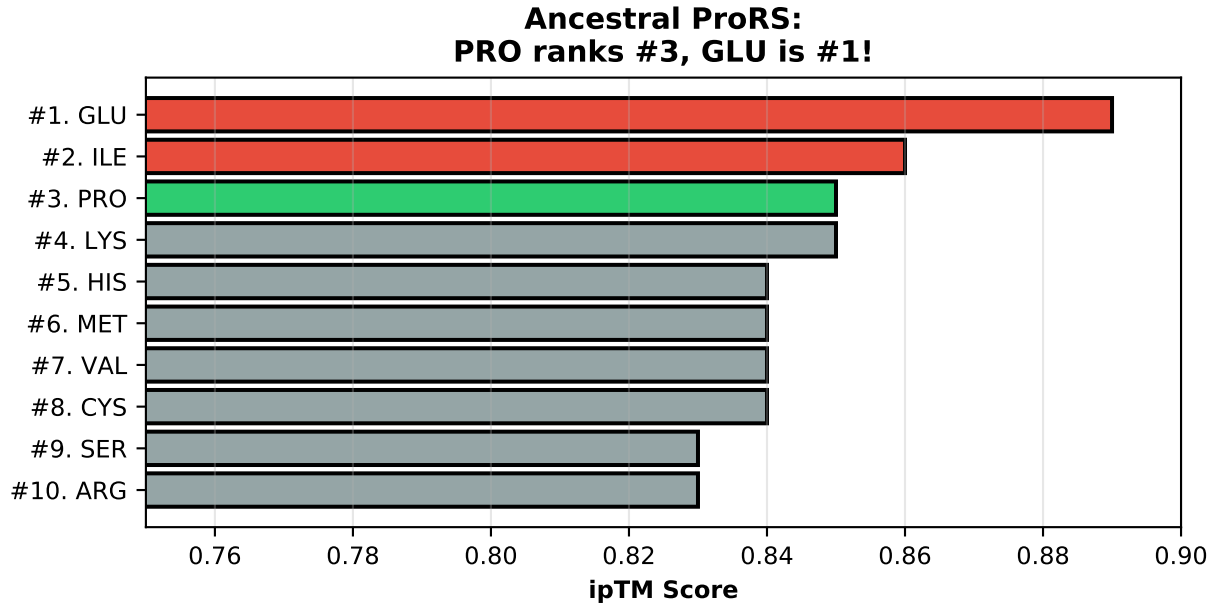
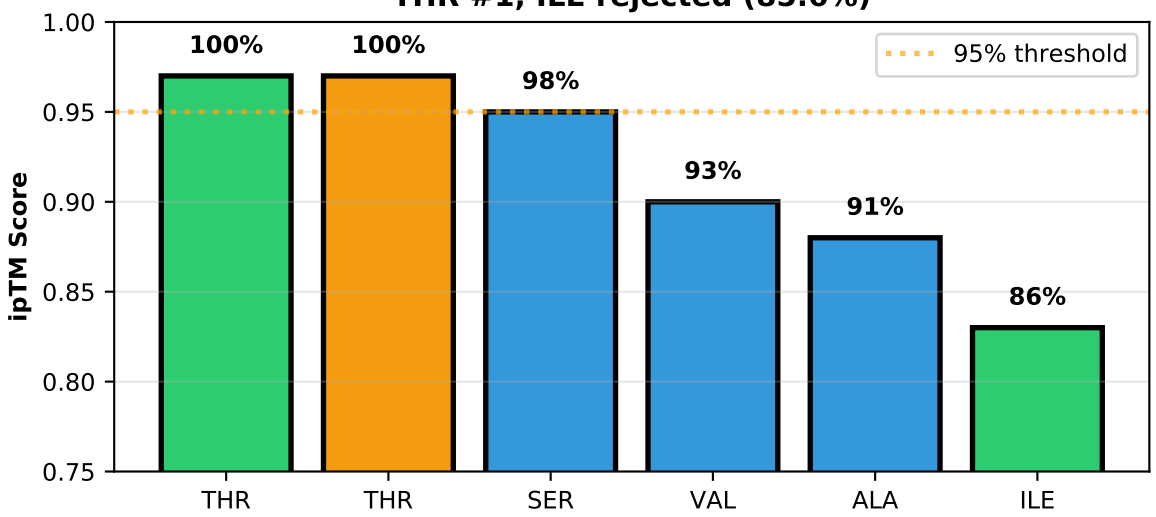
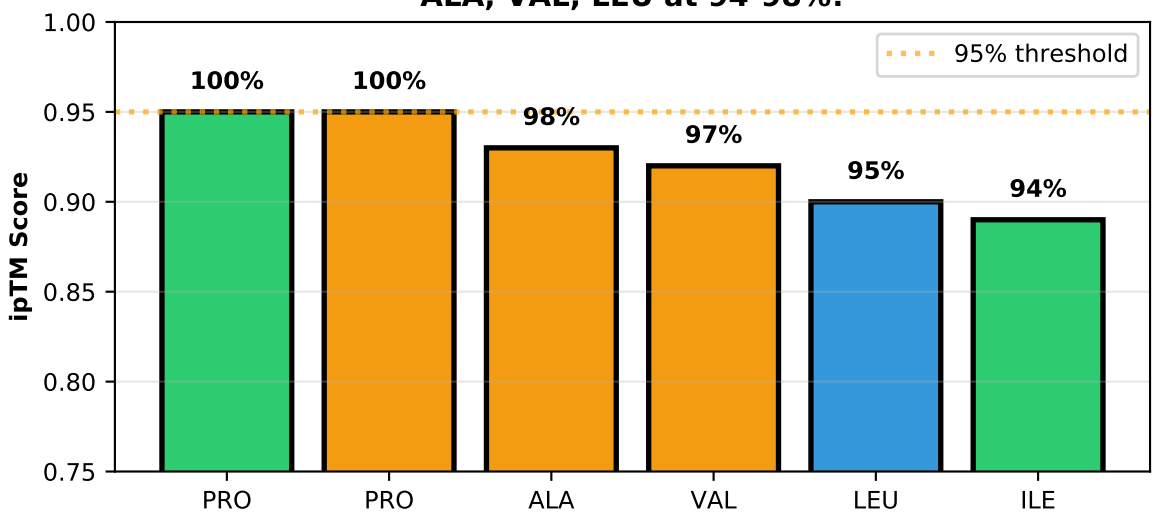
Figure 6: Evolutionary Synthesis - Two Solutions to Ancestral Promiscuity









	ThrRS Pathway	ProRS Pathway
Problem	Hydrophobic confusion (THR vs ILE/VAL)	Charge + size confusion (PRO vs GLU, ALA, VAL)
Ancestral State	THR ranks #8/20 (7 AAs bind better)	PRO ranks #3/20 (GLU binds 5% better)
Solution	STRUCTURAL Zn-mediated filter	KINETIC Editing domain
Modern Catalytic	THR: 0.97 (#1) ILE: 0.83 (#15) ✓	PRO: 0.95 (#1) ALA: 0.93 (98%) ✗ VAL: 0.92 (97%) ✗
Discrimination	THR/ILE: 1.17x THR/SER: 1.02x (LEAK!)	PRO/ALA: 1.02x PRO/VAL: 1.03x
Editing Role	SECONDARY (only for SER)	PRIMARY (essential for ALL)
Chemical Constraint	Hydrophobics can't coordinate Zn	No simple structural solution for charge