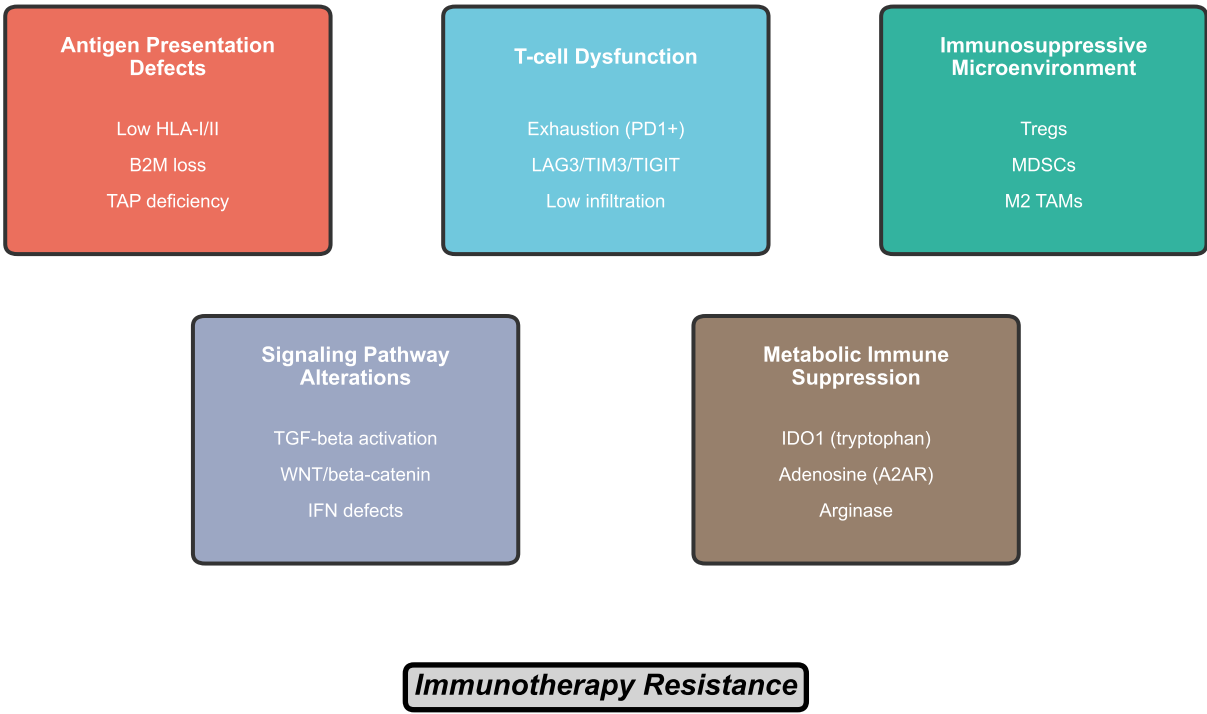
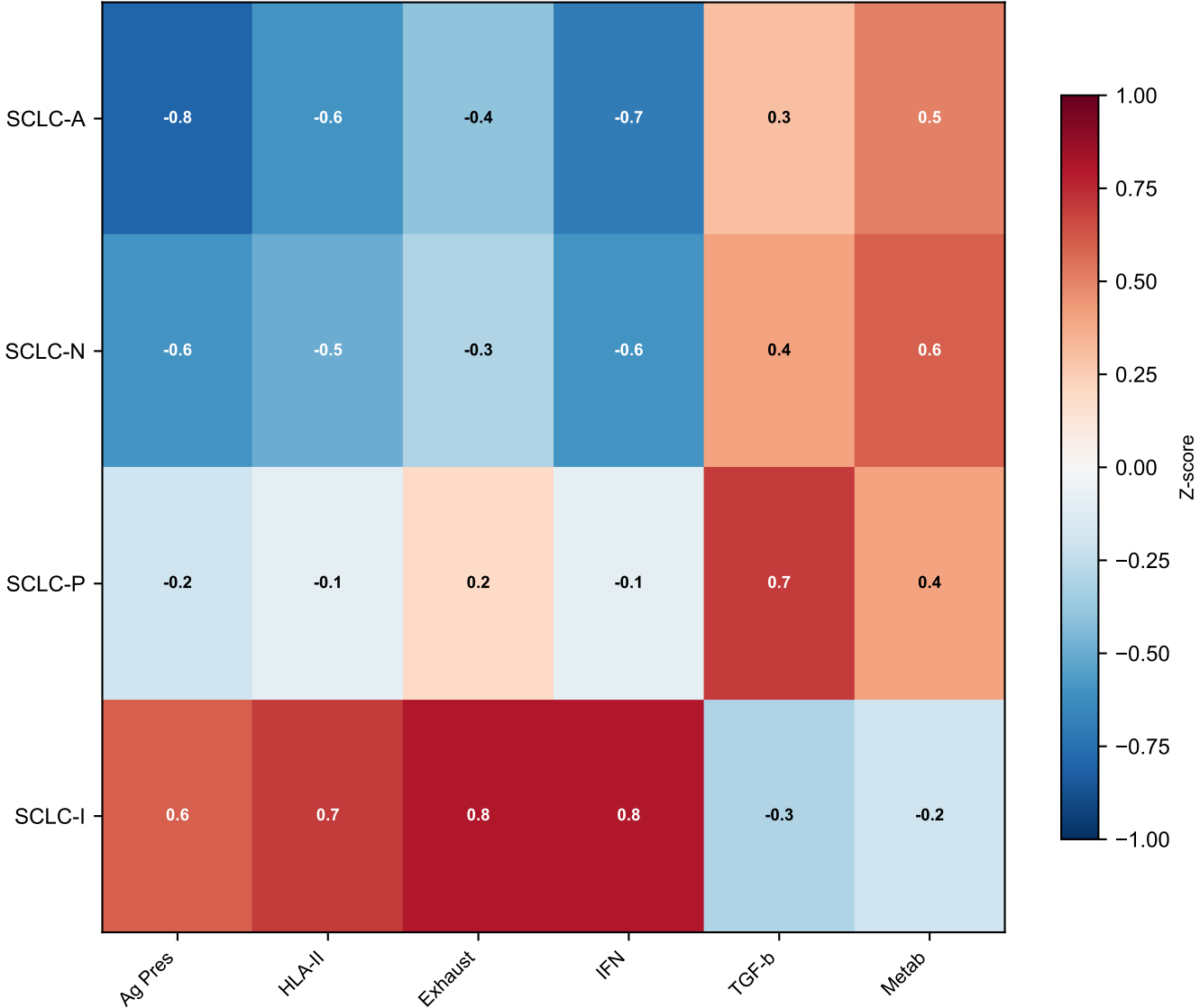


A. IO Resistance Mechanisms Overview

Immunotherapy Resistance in SCLC



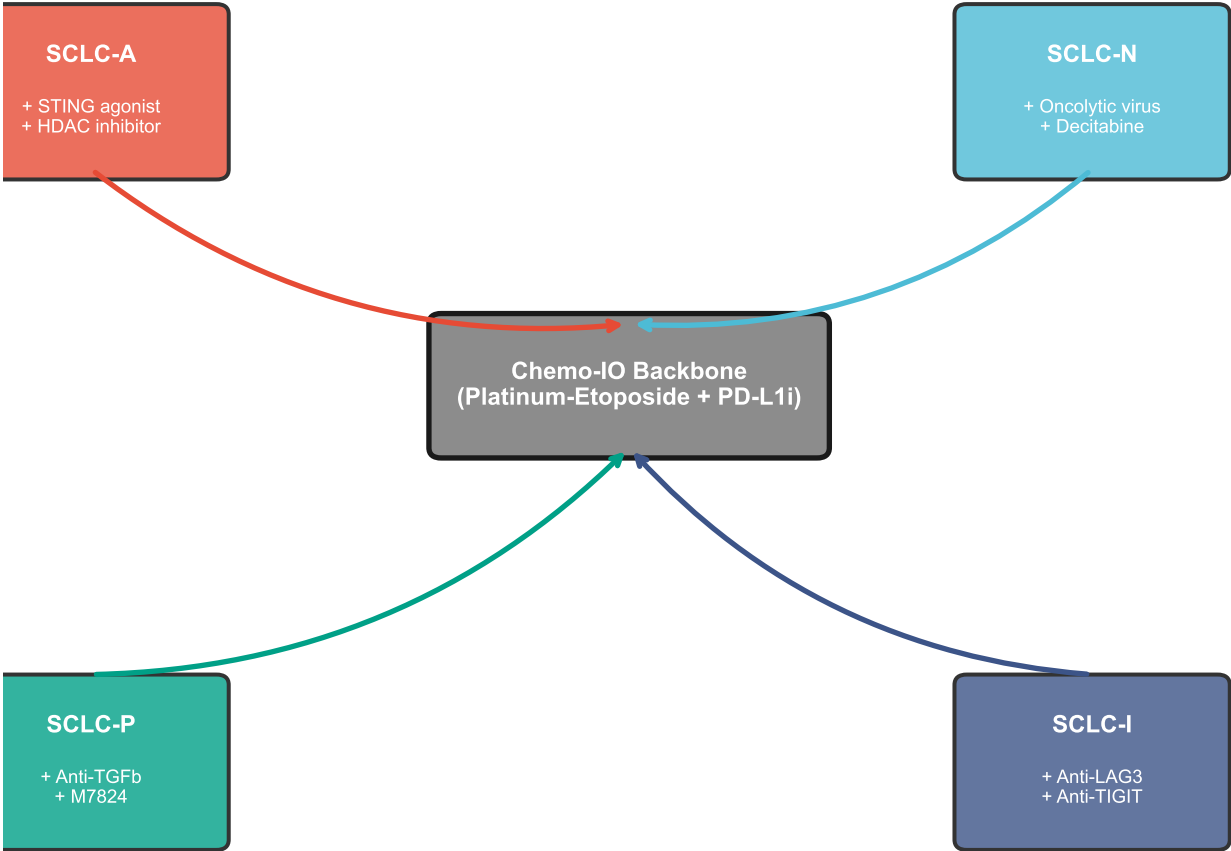
B. Resistance Signatures by Subtype



C. Therapeutic Strategies to Overcome Resistance

Subtype	Target	Drugs
SCLC-A/N (Low antigen)	Restore antigen presentation	HDAC inhibitors (entinostat) DNA methylation (decitabine)
SCLC-A/N (Low IFN)	Enhance IFN signaling	Oncolytic viruses STING agonists (ADU-S100)
SCLC-P (TGF-beta)	Block TGF-beta	Galunisertib Bintrafusp alfa
SCLC-I (Exhaustion)	Next-gen checkpoints	Anti-LAG3 (relatlimab) Anti-TIGIT (tiragolumab)

D. Subtype-Guided IO Combination Strategies



Goal: Overcome subtype-specific resistance to enhance IO response