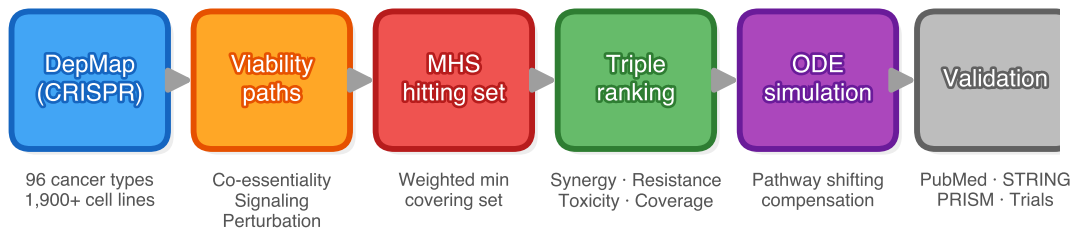# ALIN Framework Pipeline

A

DepMap (CRISPR)	→	Viability paths	→	MHS hitting set	→	Triple ranking	→	ODE simulation	→	Validation
96 cancer types 1,900+ cell lines		Co-essentiality Signaling Perturbation		Weighted min covering set		Synergy · Resistance Toxicity · Coverage		Pathway shifting compensation		PubMed · STRING PRISM · Trials

B

Intra-axial MHS: blocks 1–2 axes → resistance
Tri-axial combination: blocks all 3 axes → durable response

Compensatory pathway shifting

Upstream driver

KRAS · BRAF · EGFR

Downstream effector

CDK4 · CCND1 · CDK6

Orthogonal survival

STAT3 · MCL1 · FYN

BLOCK   BLOCK   BLOCK

Liaki et al., PNAS 2025: Tri-axial inhibition principle