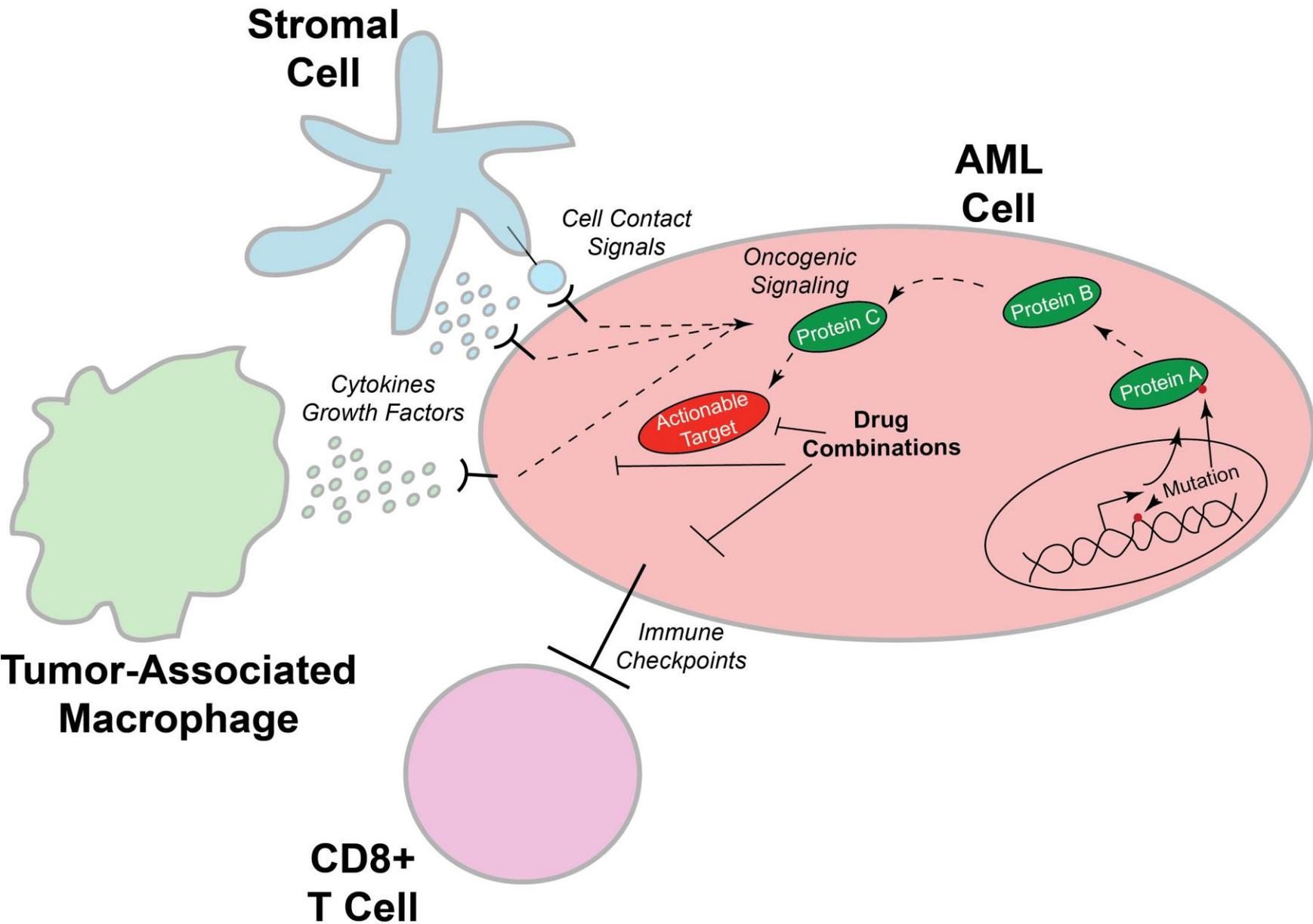




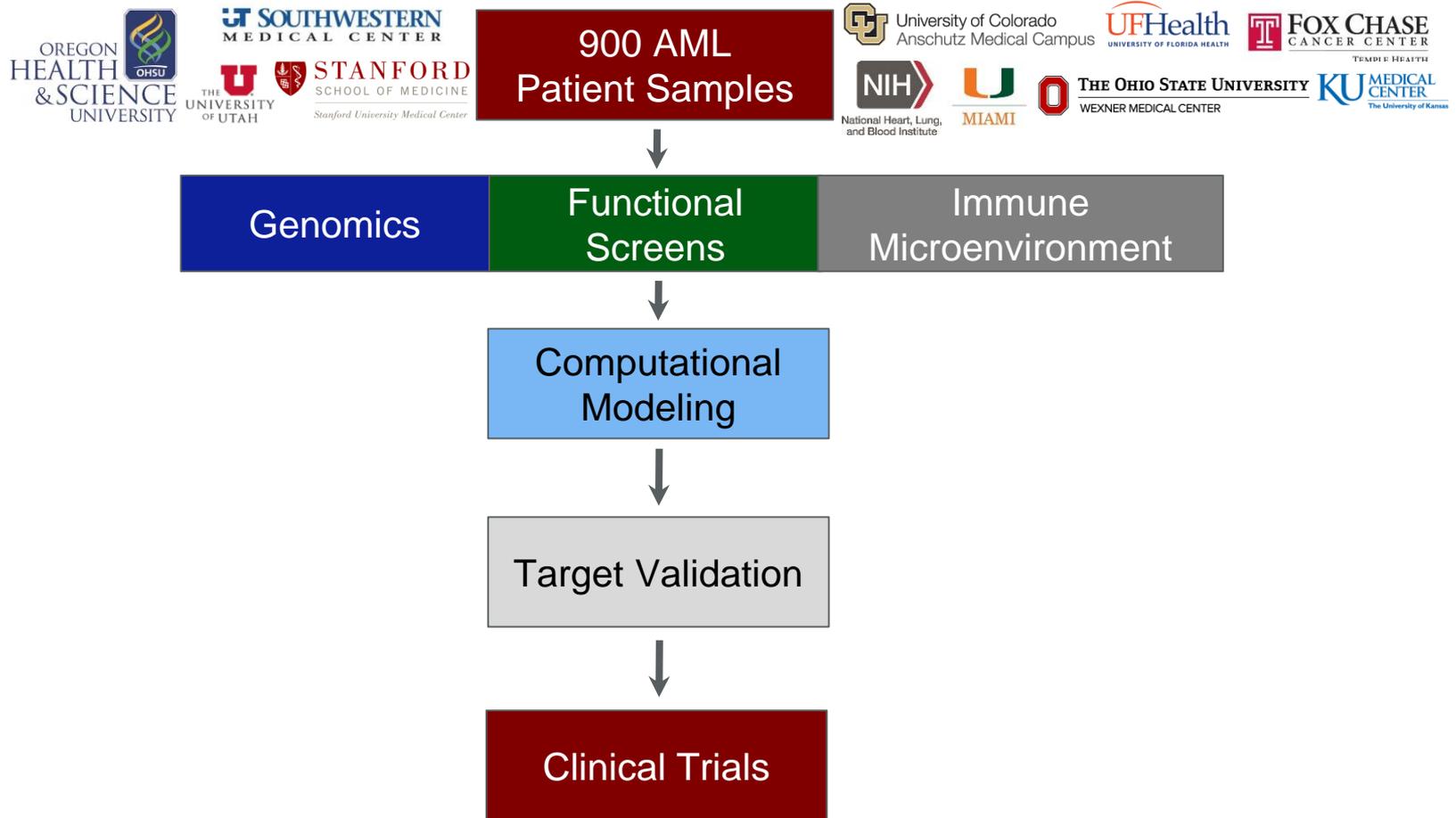
Oregon Health & Science University

Tumor intrinsic and microenvironmental mechanisms
driving drug combination efficacy and resistance in AML

Our Motivation



Long-Standing Collaborative Team Focused on Targeted Therapies for AML



Our Beat AML Consortium



Drug Combinations to Circumvent Resistance (D2RC)-DSRC

**Project 1:
Genetics & Signaling**

CRISPR/Cas Profiling

Mining of Genomic Datasets

New Targets to Enhance/Restore Drug Sensitivity

**Project 2:
Inflammatory, Immune & Stromal Microenvironment**

Inflammatory & Stromal Cell Analyses

Immune Landscape Profiling

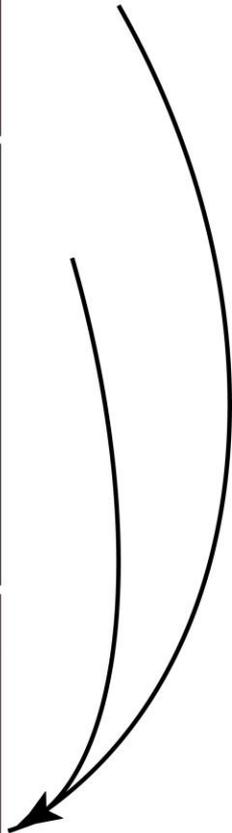
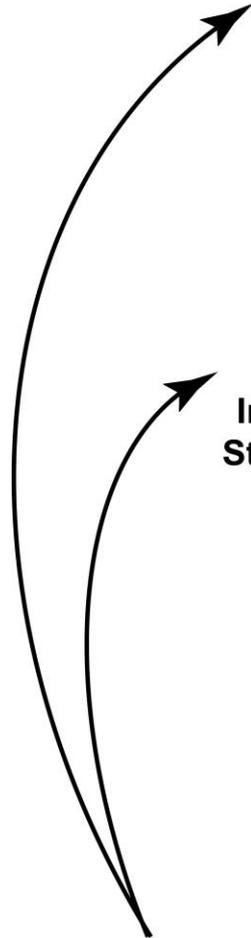
Microenvironmental Pathways to Synergize with Intrinsic Targets

**Project 3:
Drug Combinations**

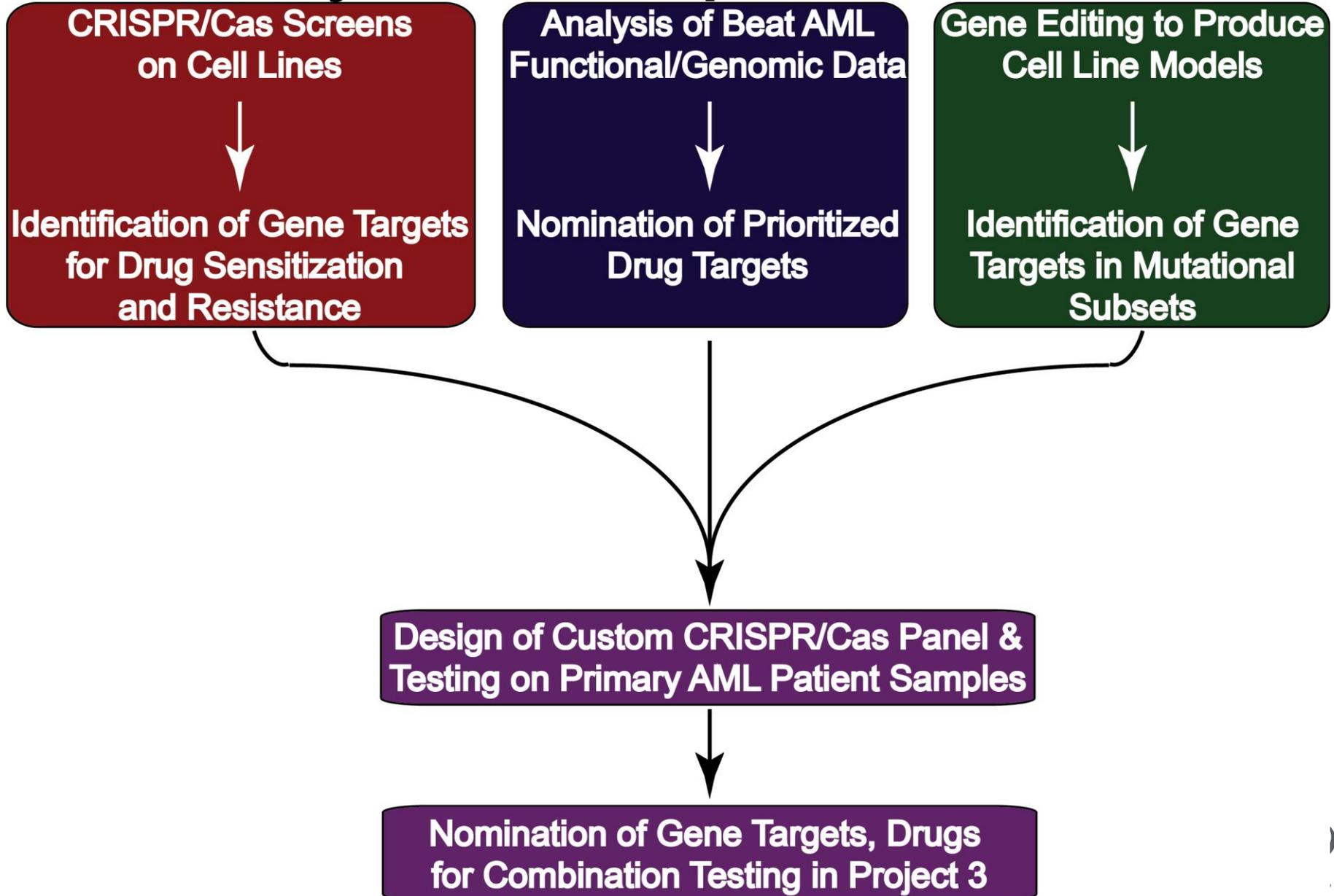
Small-Molecule Pair Testing

Small-molecule Immune Checkpoint Testing

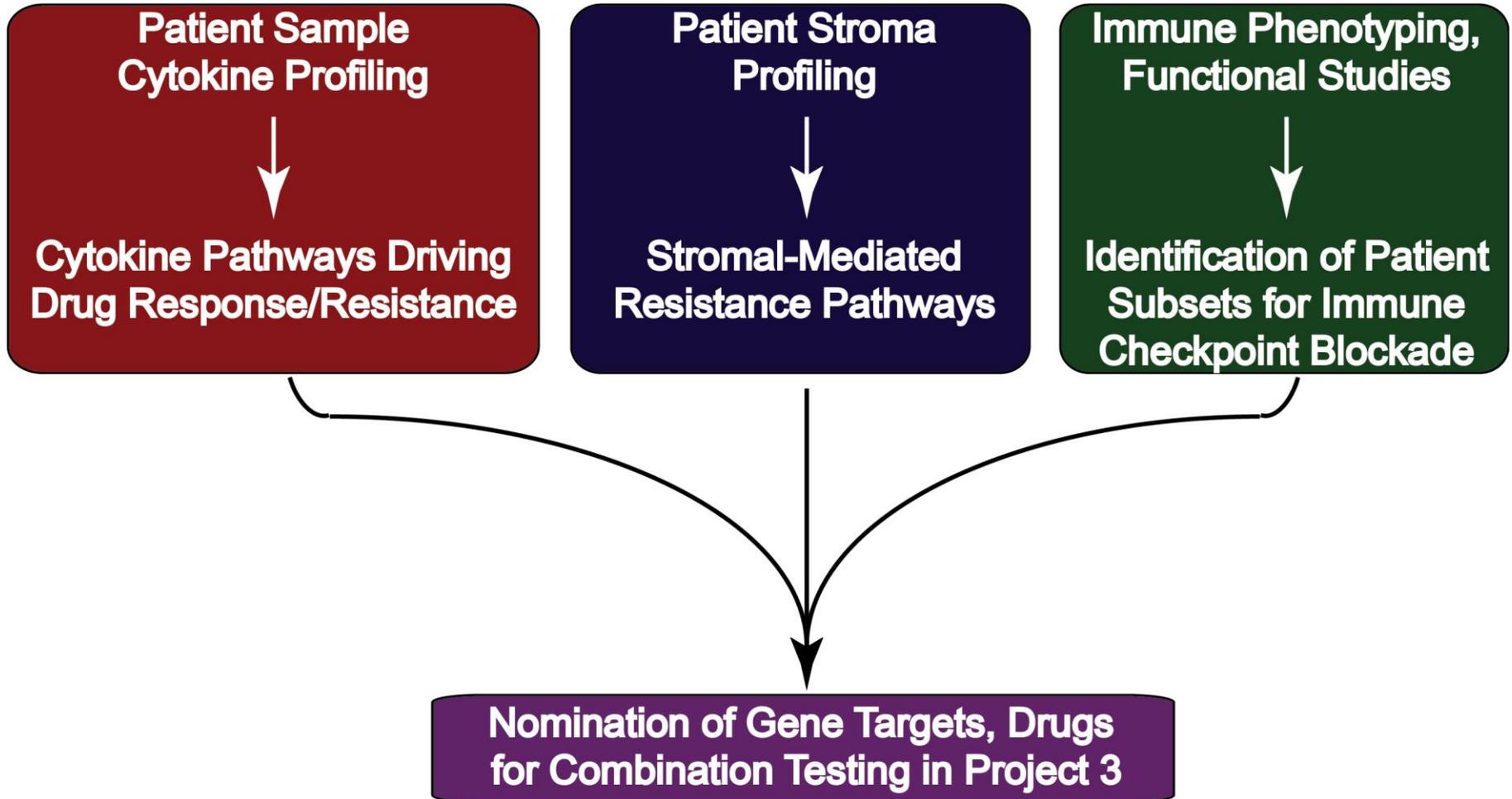
In vivo Xenograft Validation for PK/PD and Efficacy



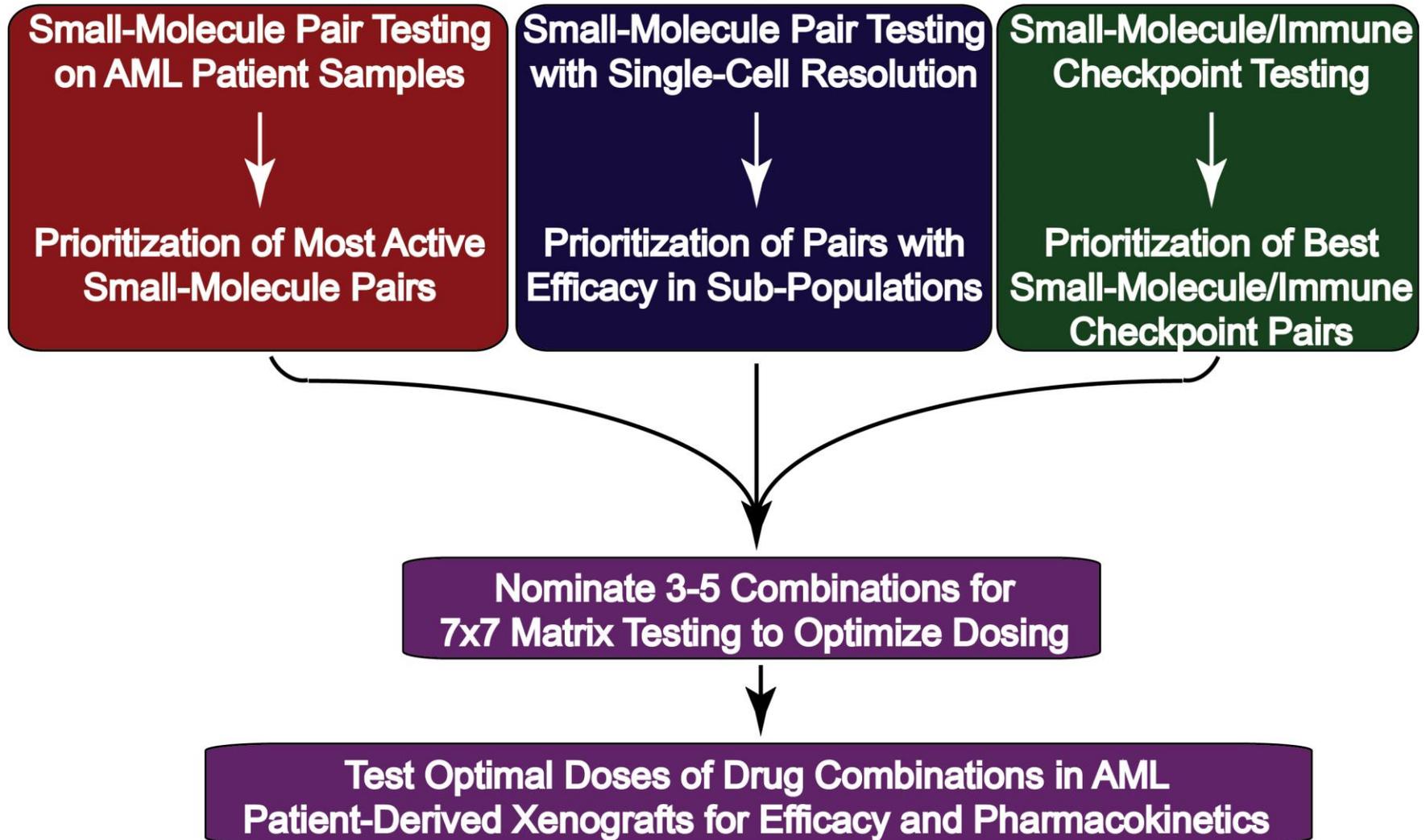
Project 1 Concept & Workflow



Project 2 Concept & Workflow



Project 3 Concept & Workflow



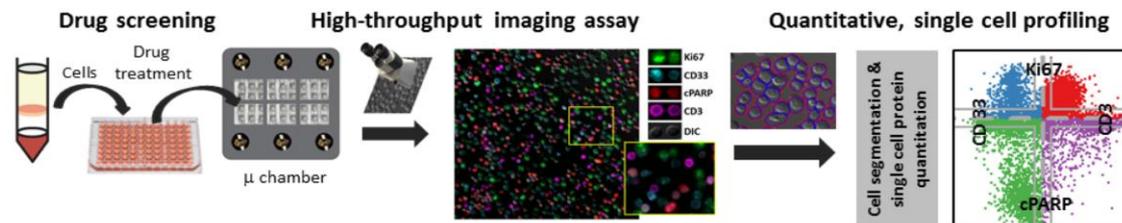
Center Resources & Collaborative Opportunities

Biospecimen Resources

- Primary AML patient samples (prospective and banked)
- Xenografted AML patient sample material
- Novel drug-resistant cell lines

Cutting-Edge Technical Expertise

- CRISPR-Cas screening capabilities (genome-wide and custom sgRNA panels)
- CyTOF panels as well as technical and computational expertise with CyTOF data
- Small-molecule libraries and drug screening capabilities
- Imaging-based assay for synergy of small-molecule + immune checkpoint drug pairs



Problem Driven Methodology

- HitWalker2 Prioritization Framework
- Cancer Targetome
- Modeling Tools integrated w/ Reactome Knowledgebase

