1-Slide U54 summary received from the NCI

Architecture and Trajectory of Acquired Resistance to Therapy in AML

Architecture and Trajectory of Acquired Resistance to Therapy in AML

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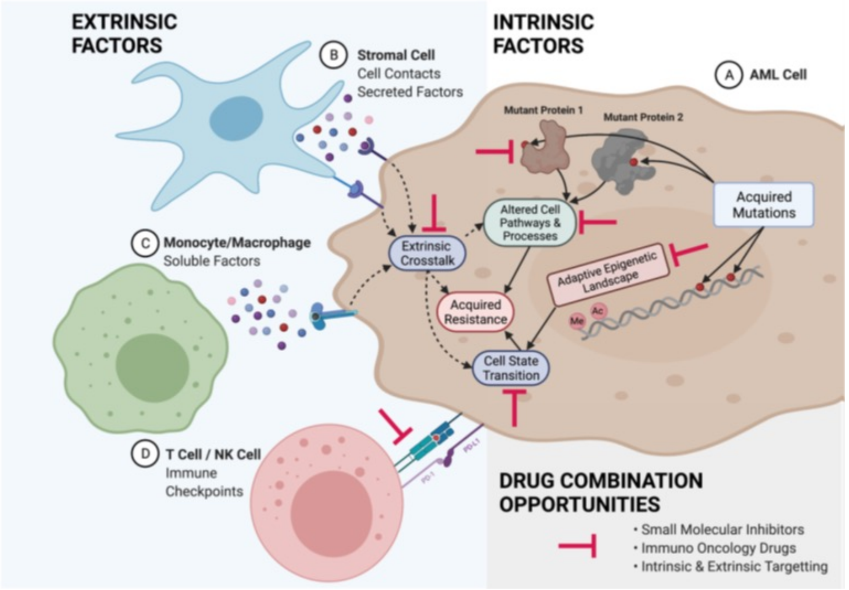
- Integrated Atlas
- Longitudinal TME/plasticity profiling
- Functional Genomics/Mut landscape
- SC transcriptomics/epigenomics



(AML)

- **P1 Trajectory and Architecture of Tumor Intrinsic Drug Resistance in AML**
  - ✓ *Perform next-generation genome-wide interrogation of key acquired resistance scenarios*
  - ✓ *Study epigenomic evolution of acquired resistance using single-cell analysis after drug exposures*
  - ✓ *Develop an Atlas of intrinsic mechanisms of acquired drug resistance in AML*
- **P2 Trajectory and Architecture of Microenvironment-Mediated Resistance in AML**
  - ✓ *Map immune/tumor/stromal cross-talk against clinical, genetic, and drug response features of AML*
  - ✓ *Functional profiling of stromal and monocyte-mediated pathways that govern drug response*
  - ✓ *Identify the mechanisms by which immune cells can sensitize drug resistant tumor cells to targeted therapy*
- **P3 Translating Improved Paring and timing of Drug Combination strategies**
  - ✓ *Evaluate signatures of resistance using primary AML samples in ex vivo assays with advanced AML models*
  - ✓ *Longitudinal evaluation of samples from patients receiving rational therapeutic regimens*
  - ✓ *Employ sensitive detection techniques to detect low levels of resistance in primary samples*

- **Functional Phenotyping Core**
  - ✓ *Biospecimen needs, standardized assays, centralized and validated workflows for data integration, analyses, and modeling*

- **Administrative Core**
  - ✓ *Oversight and support, data and resource sharing, help to coordinate the center*