Case Studies in Multi-Omics and Systems Biology

TCGA Pan-cancer

The Cancer Genome Atlas multi-omics integration

METABRIC

Molecular taxonomy of breast cancer

LINCS

Library of Integrated Network-based Cellular Signatures

HuBMAP

Human BioMolecular Atlas Program

Clinical Examples

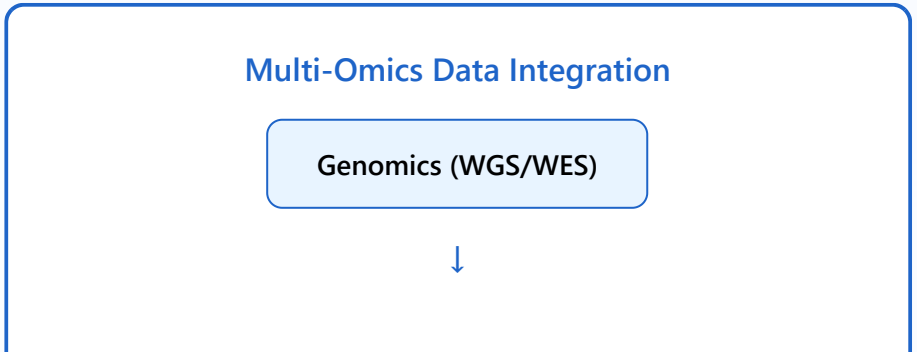
Real-world clinical integration

1 TCGA Pan-cancer Analysis

The Cancer Genome Atlas - Multi-Omics Integration

▶ Overview

The Cancer Genome Atlas (TCGA) represents one of the most comprehensive cancer genomics programs, analyzing over 33 different cancer types across more than 11,000 patients. The pan-cancer analysis integrates multiple omics



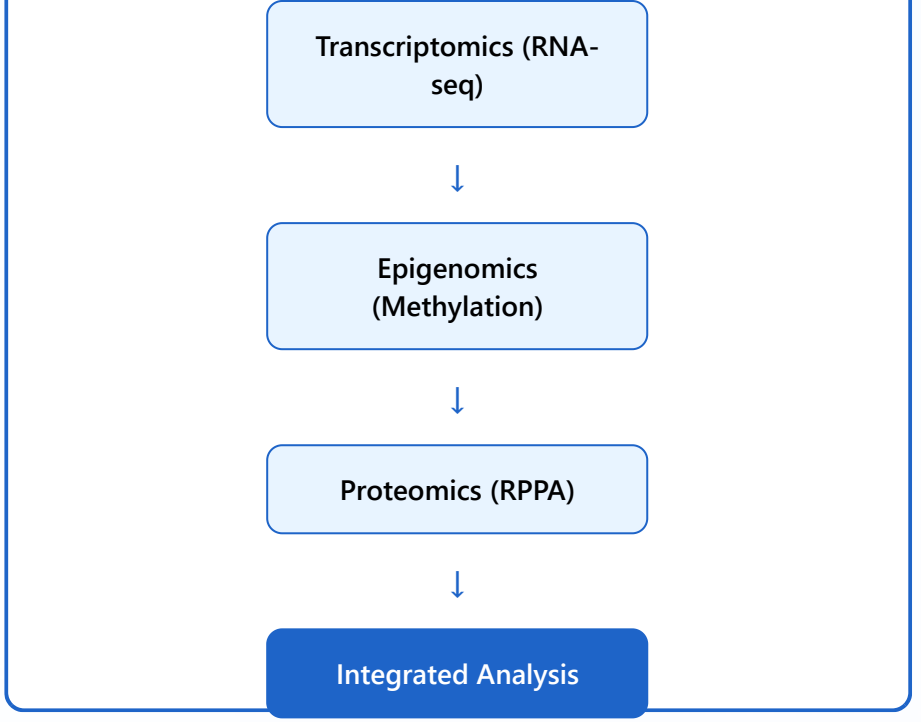
layers to identify common molecular features and driver events across cancer types.

▶ Key Findings

- ✓ Identified 299 cancer driver genes across all tumor types
- ✓ Discovered shared molecular pathways across different cancers
- ✓ Characterized tumor microenvironment signatures
- ✓ Established molecular subtypes for precision medicine
- ✓ Created comprehensive mutation and expression landscapes

Impact on Precision Medicine

TCGA data has enabled the development of tumor-agnostic therapies, where treatment is based on molecular features rather than tissue of origin, revolutionizing cancer treatment approaches.



TCGA Statistics

33 Cancer Types	**11,000+** Patients
299 Driver Genes	**2.5PB** Data Generated

2 METABRIC Study

Molecular Taxonomy of Breast Cancer

▶ Study Design

The Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) analyzed nearly 2,000 breast cancer patients, integrating genomic and transcriptomic data to refine breast cancer classification and improve prognostic accuracy beyond traditional clinical markers.

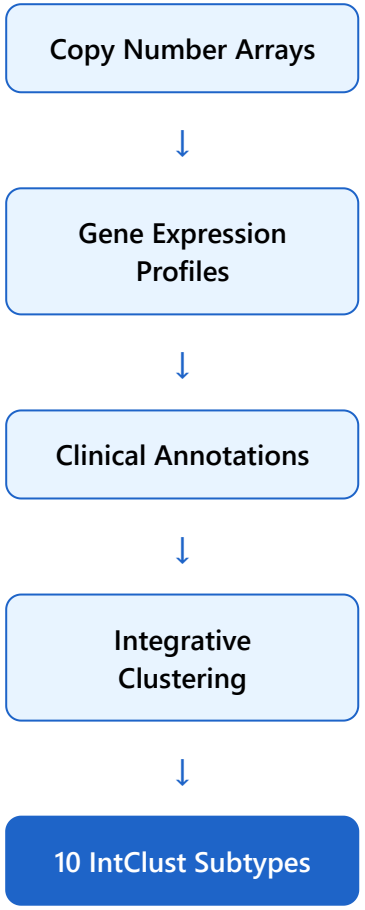
▶ Major Discoveries

- ✓ Identified 10 integrative molecular subtypes (IntClust 1-10)
- ✓ Refined PAM50 intrinsic subtypes with genomic data
- ✓ Discovered copy number-driven subtypes
- ✓ Identified novel driver alterations in specific subtypes
- ✓ Improved prognostic stratification for treatment decisions

Clinical Translation

METABRIC classifications are now used in clinical decision-making tools and have influenced the design of subtype-

METABRIC Analysis Pipeline



Study Metrics

1,980	10

specific clinical trials, particularly for triple-negative and HER2-positive breast cancers.

Patients

IntClust Subtypes

5
PAM50 Subtypes

15y
Follow-up Period

3 LINCS Program

Library of Integrated Network-based Cellular Signatures

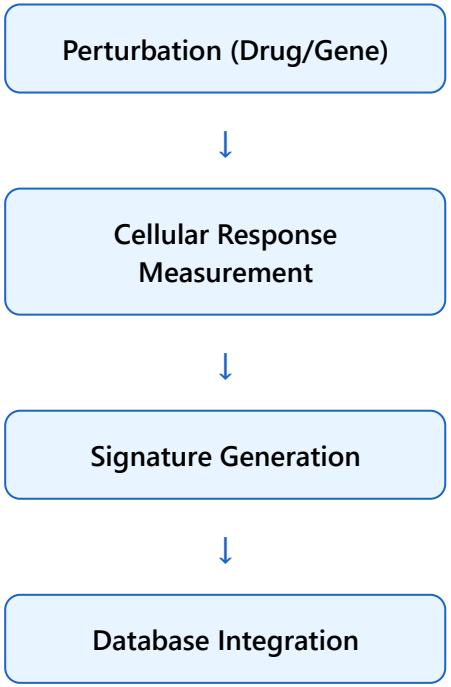
▶ Program Goals

The Library of Integrated Network-based Cellular Signatures (LINCS) is an NIH program that catalogs how cells respond to various perturbations including genetic manipulations and chemical compounds. The goal is to understand cellular pathways and discover new therapeutic targets.

▶ Key Components

- ✓ L1000 gene expression signatures from perturbations
- ✓ Protein-protein interaction networks

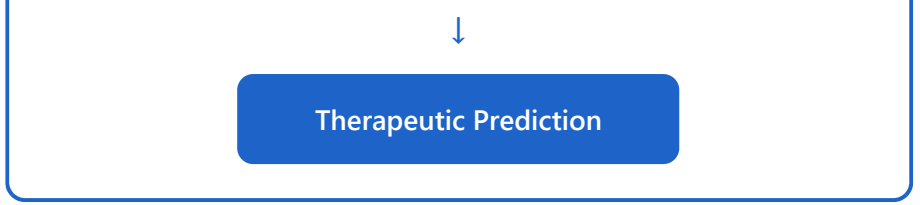
LINCS Workflow



- ✓ Cell morphology profiling (Cell Painting)
- ✓ Transcription factor binding data
- ✓ Drug repurposing and combination predictions

Applications in Drug Discovery

LINCS data enables systematic drug repurposing by identifying compounds with similar or opposite signatures to disease states, accelerating the discovery of new therapeutic applications for existing drugs.



LINCS Database Scale

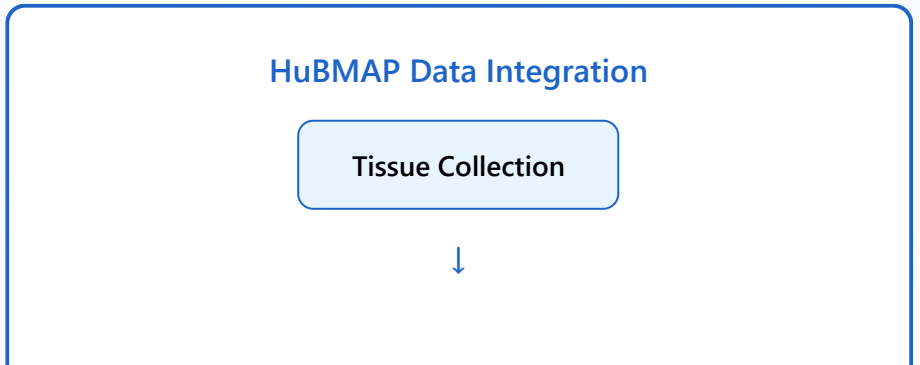
1.3M+ Perturbations	**25,000+** Compounds
70+ Cell Lines	**978** Landmark Genes

4 HuBMAP

Human BioMolecular Atlas Program

▶ Program Mission

The Human BioMolecular Atlas Program (HuBMAP) aims to create a comprehensive, high-resolution molecular atlas of the human body at single-cell resolution. This ambitious project integrates spatial transcriptomics, proteomics,



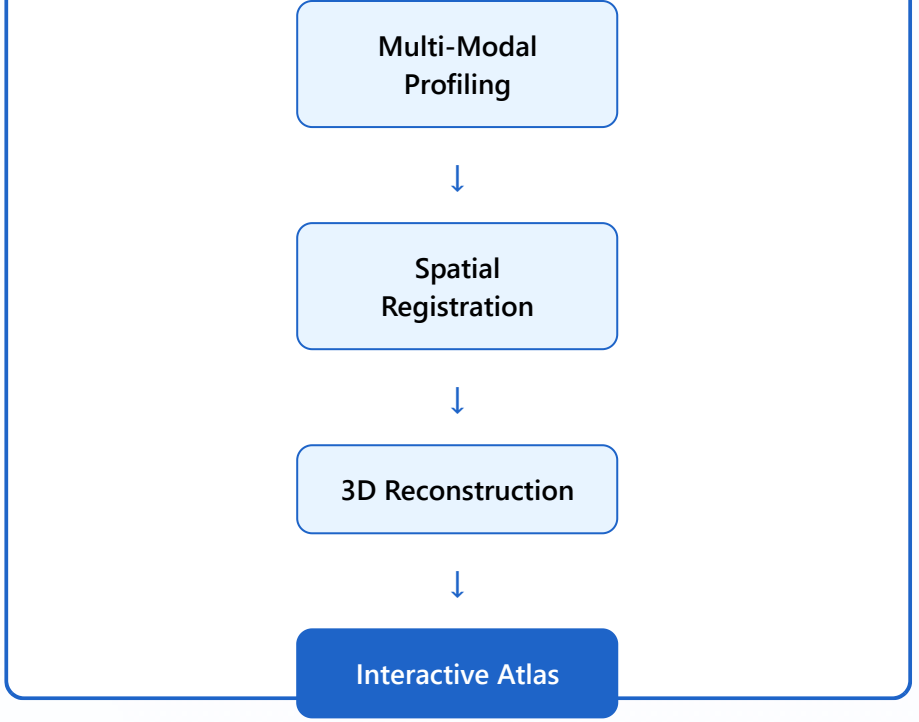
metabolomics, and imaging to map cellular architecture and function across organs.

▶ Technical Approaches

- ✓ Single-cell and spatial transcriptomics (MERFISH, seqFISH)
- ✓ Multi-modal imaging (IMC, CODEX, MIBI)
- ✓ Tissue mapping and 3D reconstruction
- ✓ Integration of molecular and anatomical data
- ✓ Open-access data portal and visualization tools

Impact on Disease Understanding

By mapping healthy tissue architecture at unprecedented resolution, HuBMAP provides a reference atlas for understanding disease-related alterations in tissue organization, cellular composition, and molecular signaling.



Program Scope

80+ Organ Types	**10+** Assay Types
1000s Tissue Samples	**Single-cell** Resolution

Clinical Integration Examples

Precision Oncology Programs

Clinical implementation of multi-omics profiling has transformed cancer care through molecular tumor boards, where genomic, transcriptomic, and proteomic data inform treatment decisions. Programs like MSK-IMPACT and Foundation Medicine's comprehensive genomic profiling guide targeted therapy selection.

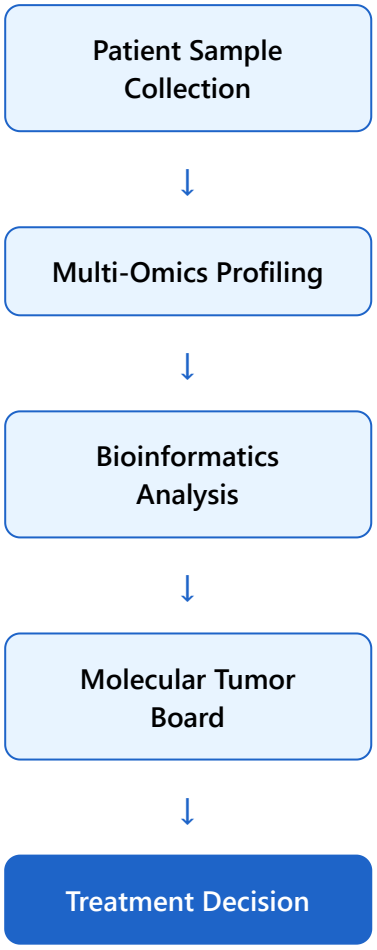
Clinical Success Stories

- ✓ NTRK fusion detection leading to tumor-agnostic larotrectinib approval
- ✓ Liquid biopsy for minimal residual disease monitoring
- ✓ Pharmacogenomics guiding drug dosing (CYP2D6, TPMT)
- ✓ Multi-omic subtyping in acute myeloid leukemia (AML)
- ✓ Immune profiling for immunotherapy patient selection

Future Directions

The integration of multi-omics data into electronic health records, real-time clinical decision support systems, and AI-

Clinical Workflow Integration



Clinical Impact Metrics

30-40%
Actionable Findings

15-20%
Treatment Changes

driven treatment recommendations represents the next frontier in precision medicine implementation.

10-15%
Clinical Trial Matches

2-4 weeks
Turnaround Time