# Analyzing Tumor Atlas Datasets from the NCI HTAN Network with the Galaxy Computational Platform
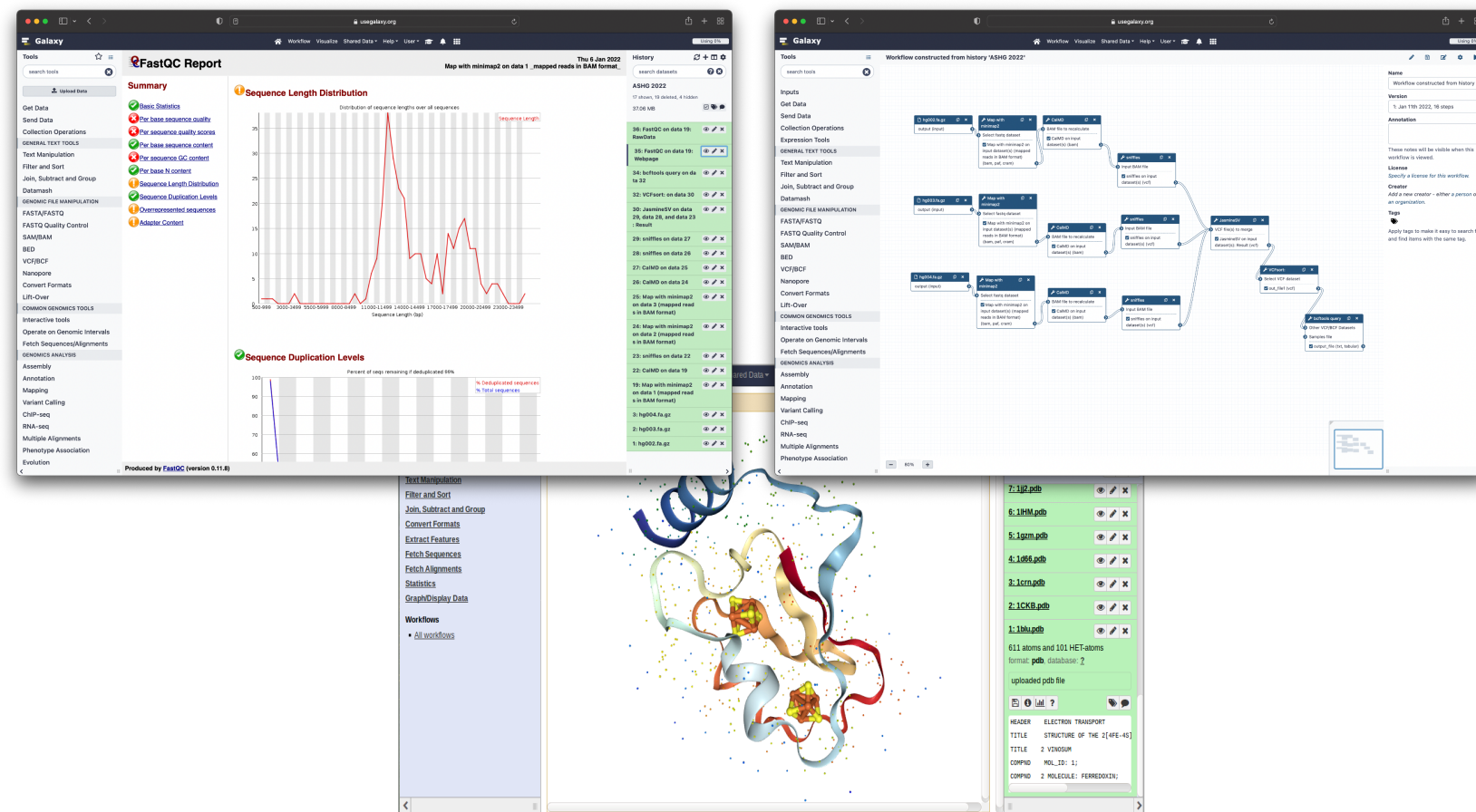
Luke Sargent[1], Allison Creason[1], Qiang Gu[1], Daniel Persson[1], Enis Afgan[2], Michael Schatz[2], and Jeremy Goecks[1]

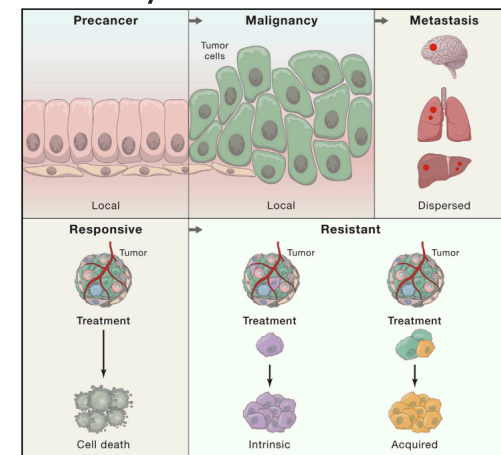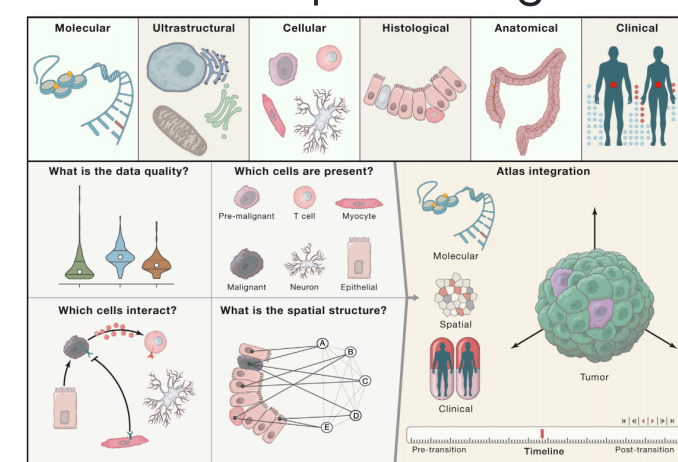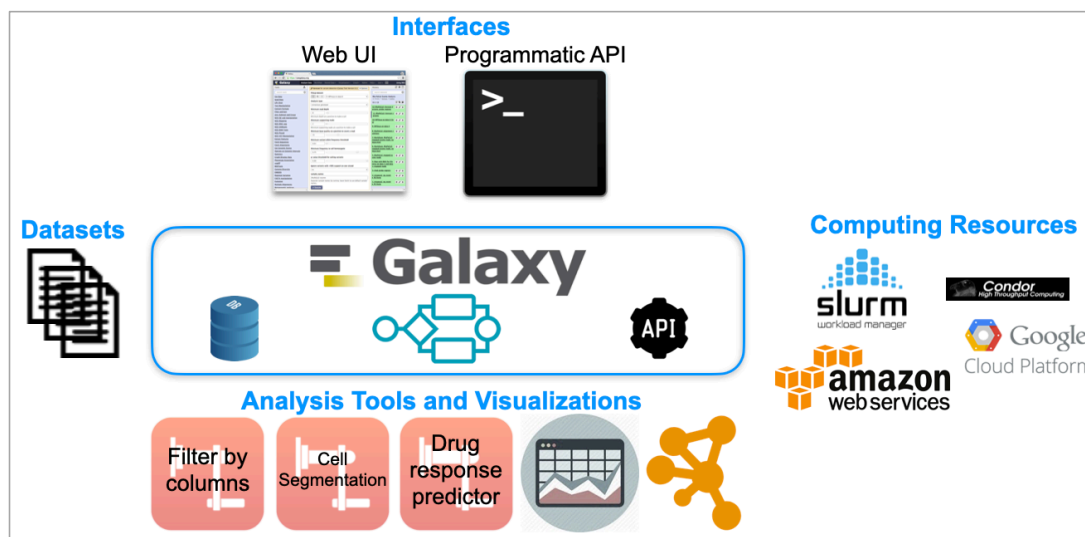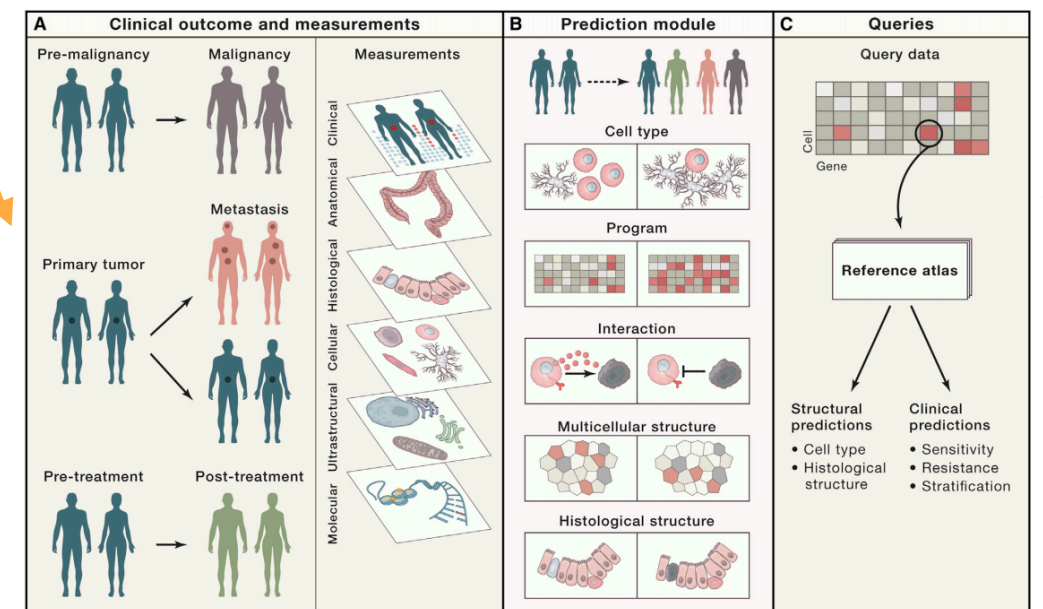[1]Oregon Health & Science University and [2]Johns Hopkins University

Key Transitions

Deep Profiling

Systems Biology Understanding and Clinical Predictors

Galaxy

HTAN
HUMAN TUMOR ATLAS NETWORK

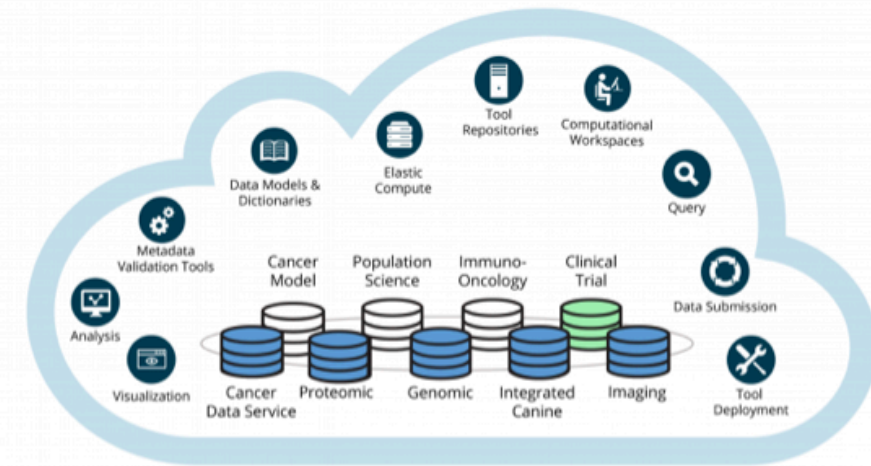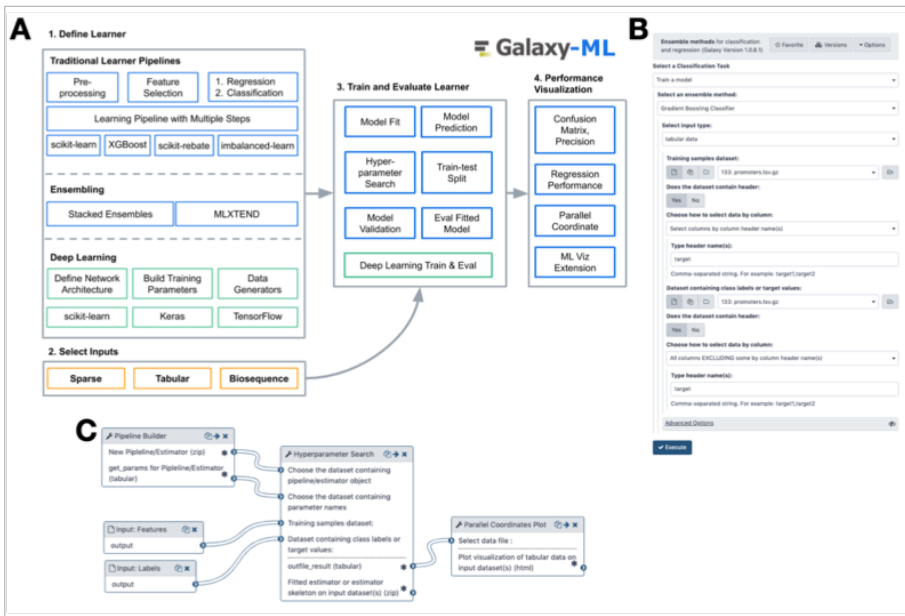Rozenblatt-Rosen et al., Cell 2020

# Galaxy ITCR U24

‣ Integrate cancer tools—including many ITCR tools—into the Galaxy ecosystem

‣ Federated and data-local computing in Galaxy for large datasets

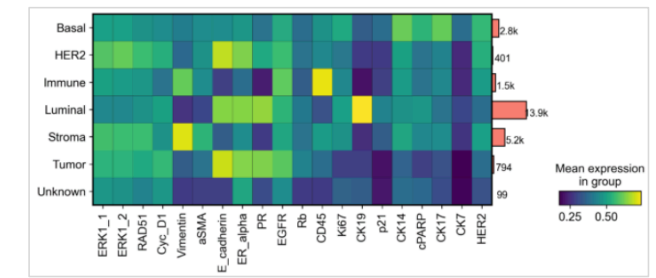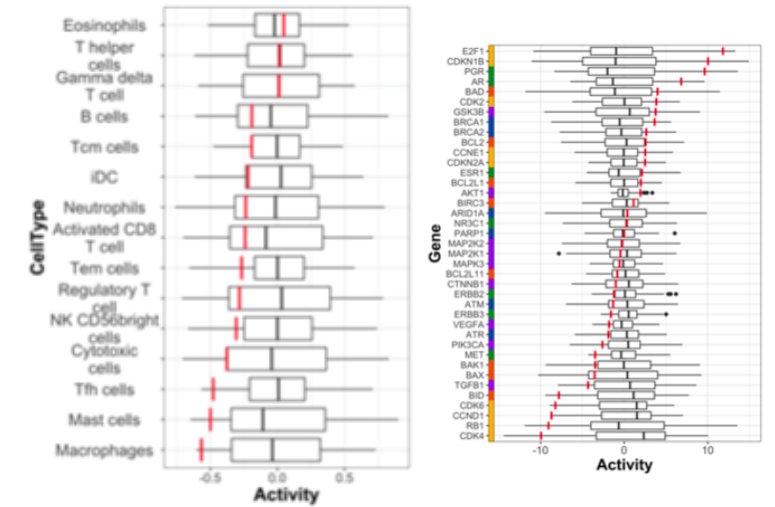‣ Precision oncology applications via multimodal analyses and machine learning

‣ https://cancer.usegalaxy.org/
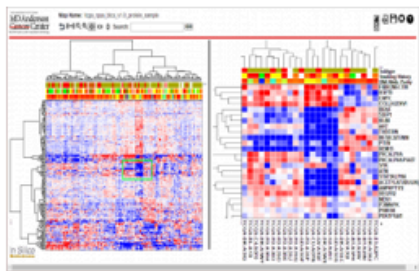
# Machine Learning



# Research Tumor Board Reports



# Multiplex Tissue Imaging Analysis



# IO.BIO visualizations



https://iobio.io

# Omic and Multidimensional Spatial (OMS) Atlas
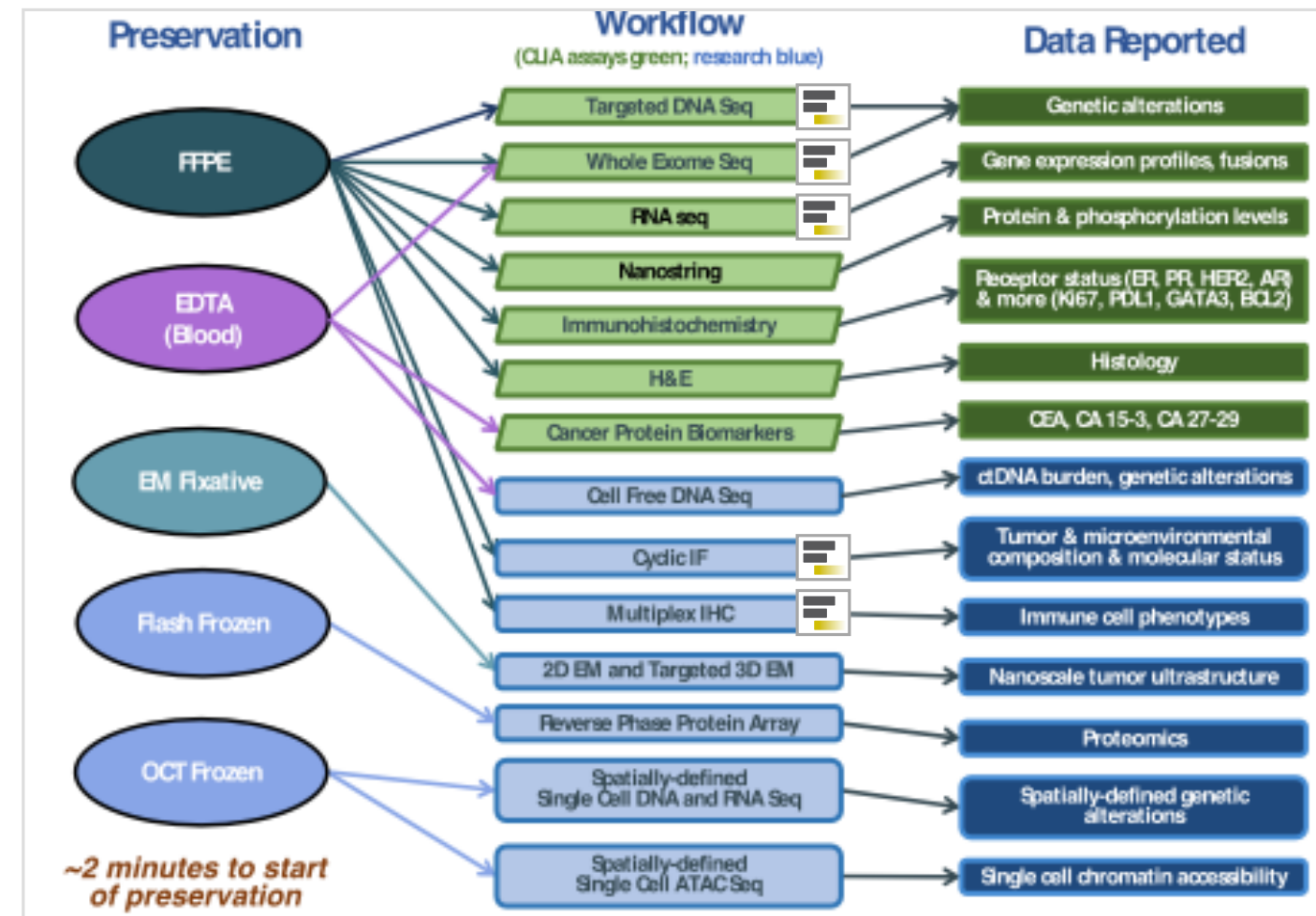
A cohort of matched biopsies from metastatic breast cancers
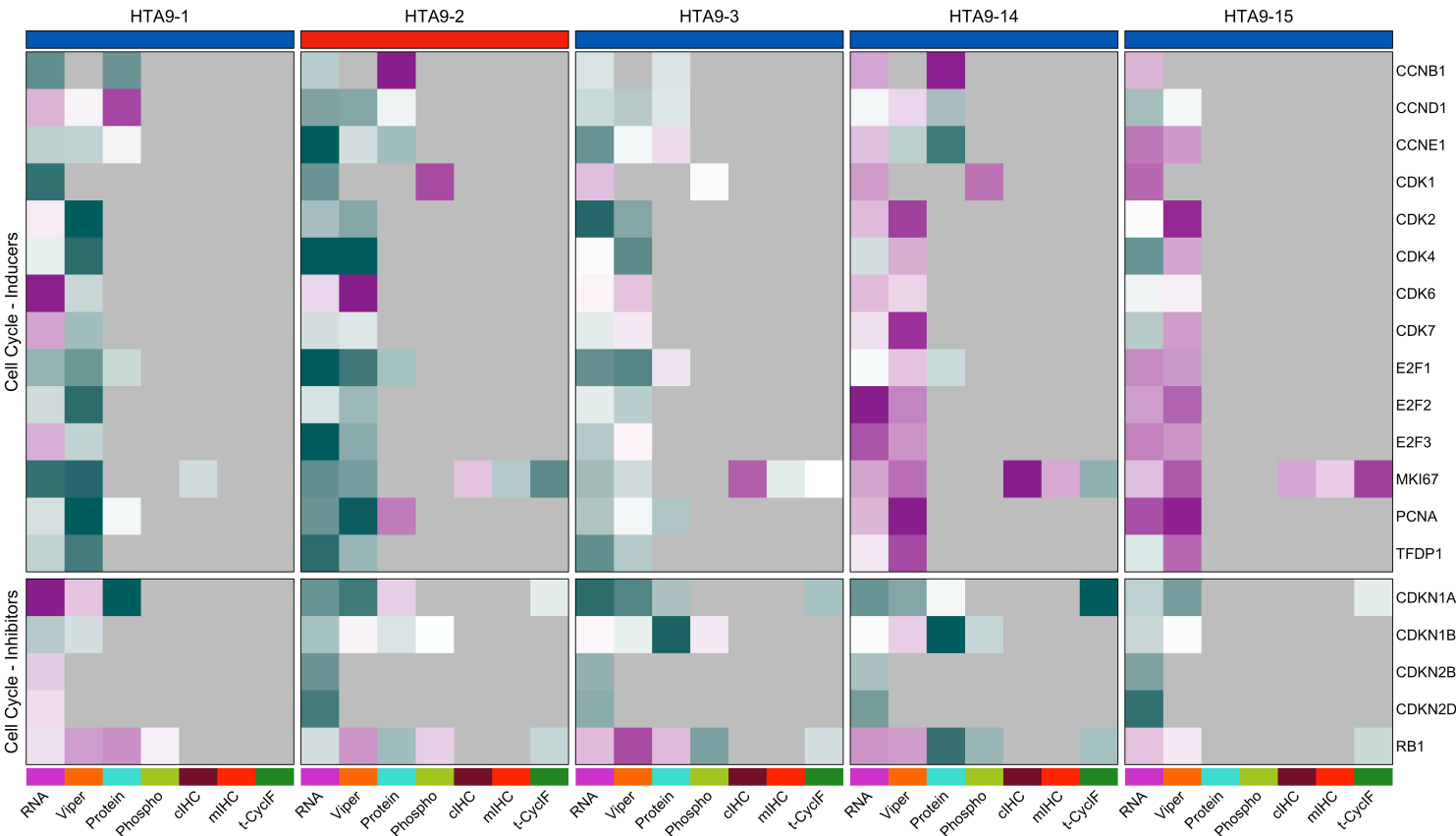‣ Same patients on CDK4/6i therapies

A large suite of omics and imaging assays is applied to each biopsy

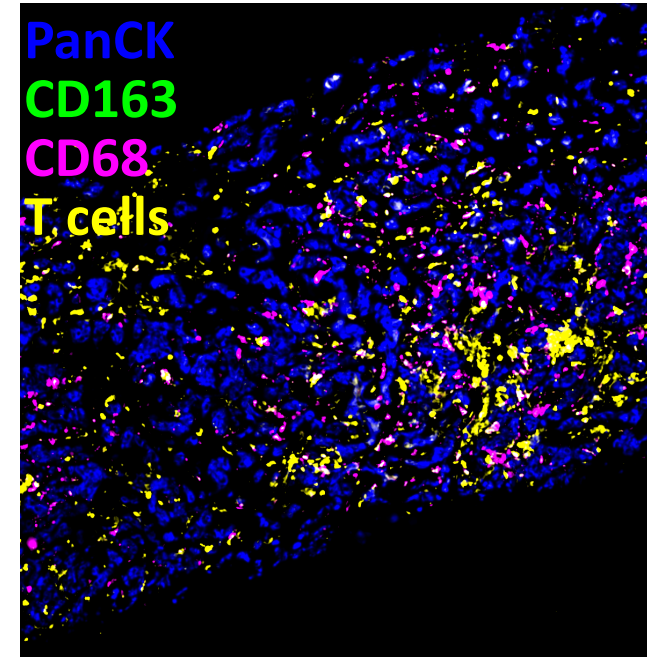Omics and imaging data is connected to clinical attributes to:
‣ Characterize how tumor is adapting to therapy
‣ Identify potential mechanisms of resistance to therapy
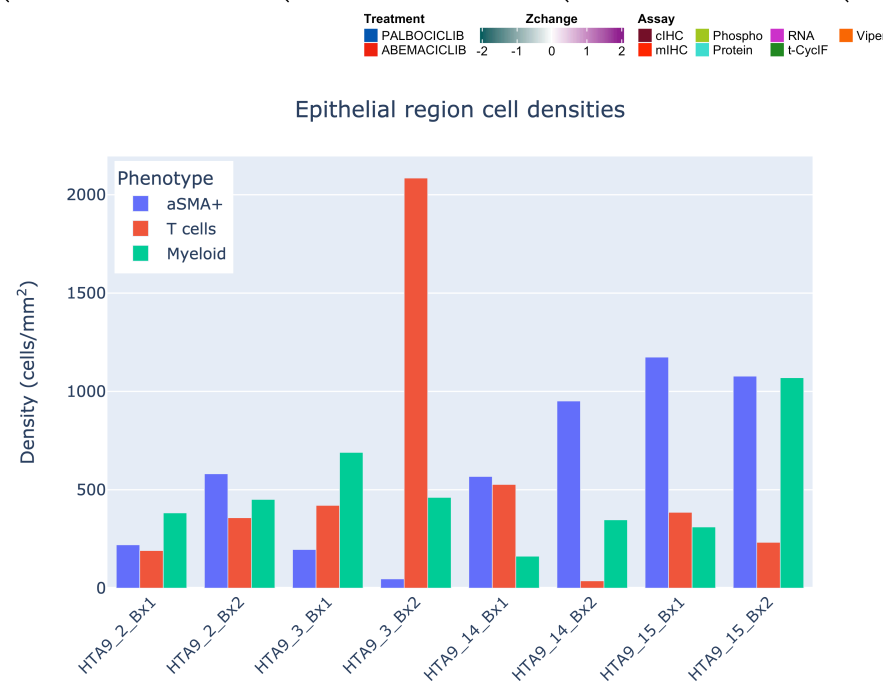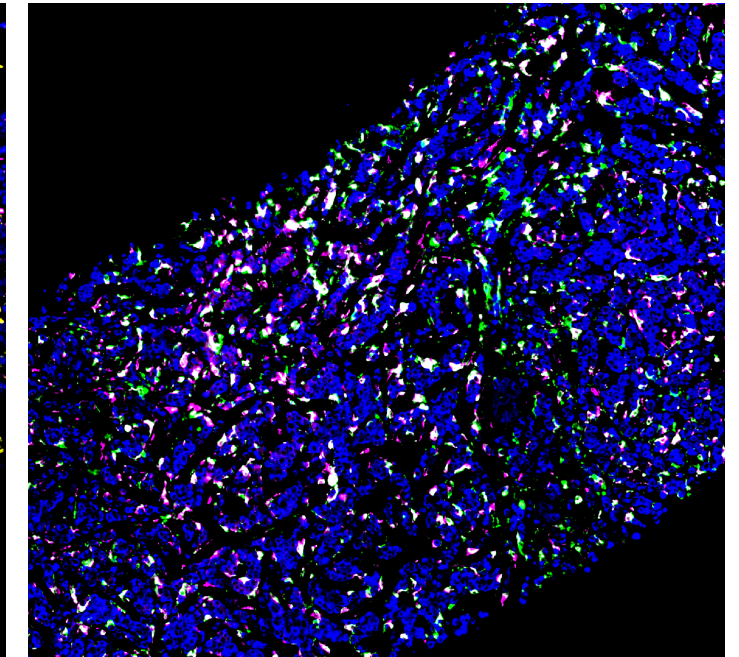‣ Develop actionable guidance for addressing therapeutic resistance



Pre-treatment biopsy — CDK4/6i Therapy — Paired biopsy on treatment or progression



| Preservation | Workflow (CLIA assays green; research blue) | Data Reported |
|---|---|---|
| FFPE | Targeted DNA Seq | Genetic alterations |
| | Whole Exome Seq | Gene expression profiles, fusions |
| | RNA seq | Protein & phosphorylation levels |
| | Nanostring | Receptor status (ER, PR, HER2, AR) & more (Ki67, PDL1, GATA3, BCL2) |
| EDTA (Blood) | Immunohistochemistry | |
| | H&E | Histology |
| | Cancer Protein Biomarkers | CEA, CA 15-3, CA 27-29 |
| EM Fixative | Cell Free DNA Seq | ctDNA burden, genetic alterations |
| | Cyclic IF | Tumor & microenvironmental composition & molecular status |
| | Multiplex IHC | Immune cell phenotypes |
| Flash Frozen | 2D EM and Targeted 3D EM | Nanoscale tumor ultrastructure |
| | Reverse Phase Protein Array | Proteomics |
| OCT Frozen | Spatially-defined Single Cell DNA and RNA Seq | Spatially-defined genetic alterations |
| | Spatially-defined Single Cell ATAC Seq | Single cell chromatin accessibility |

~2 minutes to start of preservation

# Diverse Patient Changes Observed



Epithelial region cell densities

| Mechanisms | Cases | Observations |
|---|---|---|
| Mitogenic signals, Cell Cycle Entry | HTA9-1, HTA9-14, HTA9-15 | Increased E2F, CDK2, CDK6, CCNE1 |
| Cell Cycle Checkpoint Bypass | HTA9-14, HTA9-15 | Increased Ki67, PCNA, CCNB1, G2M Checkpoint |
| Immunoreactive | HTA9-1, HTA9-3, HTA9-15 | Increased interferon, Jak/Stat, immune density, T cell density |
| Immunosuppressive | HTA9-3, HTA9-15 | Elevated FOXP3 (Treg), CTLA4, PD-L1 Elevated Myeloid density |
| Immune Cold | HTA9-2, HTA9-14 | Low immune infiltrate in both Bxs, Minimal change or reduction in immune cells |

# Acknowledgements: The Galaxy Community



Galaxy

All things Galaxy:
https://galaxyproject.org/

Public Galaxy servers:
https://galaxyproject.org/use/

Download and run Galaxy locally:
https://getgalaxy.org

Galaxy training network:
https://training.galaxyproject.org/

GCC2019 in Freiburg

# Acknowledgements: SMMART and HTAN