NIH LINCS PROGRAM

BD2K - LINCS
DATA COORDINATION AND INTEGRATION CENTER

Icahn School of Medicine at Mount Sinai

Integrating proteomics and transcriptomics across cell lines

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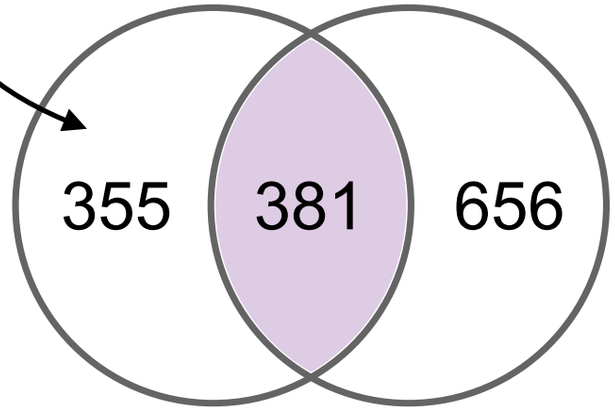
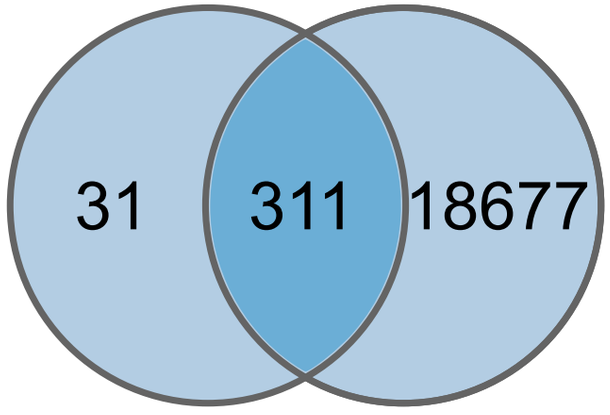
Mapping cancer cell line anti-body measurements (RPPA) to gene expression data (CCLE)

MCF10A

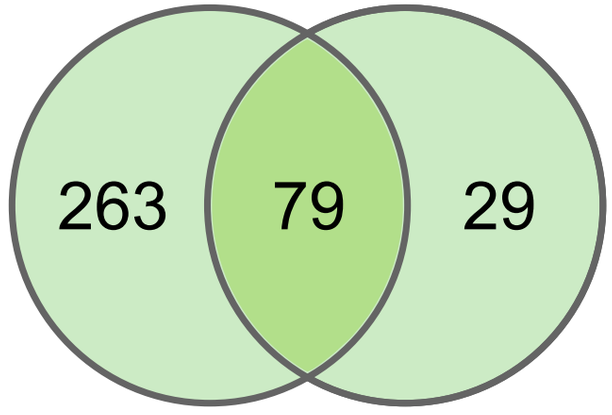
Cancer cell lines



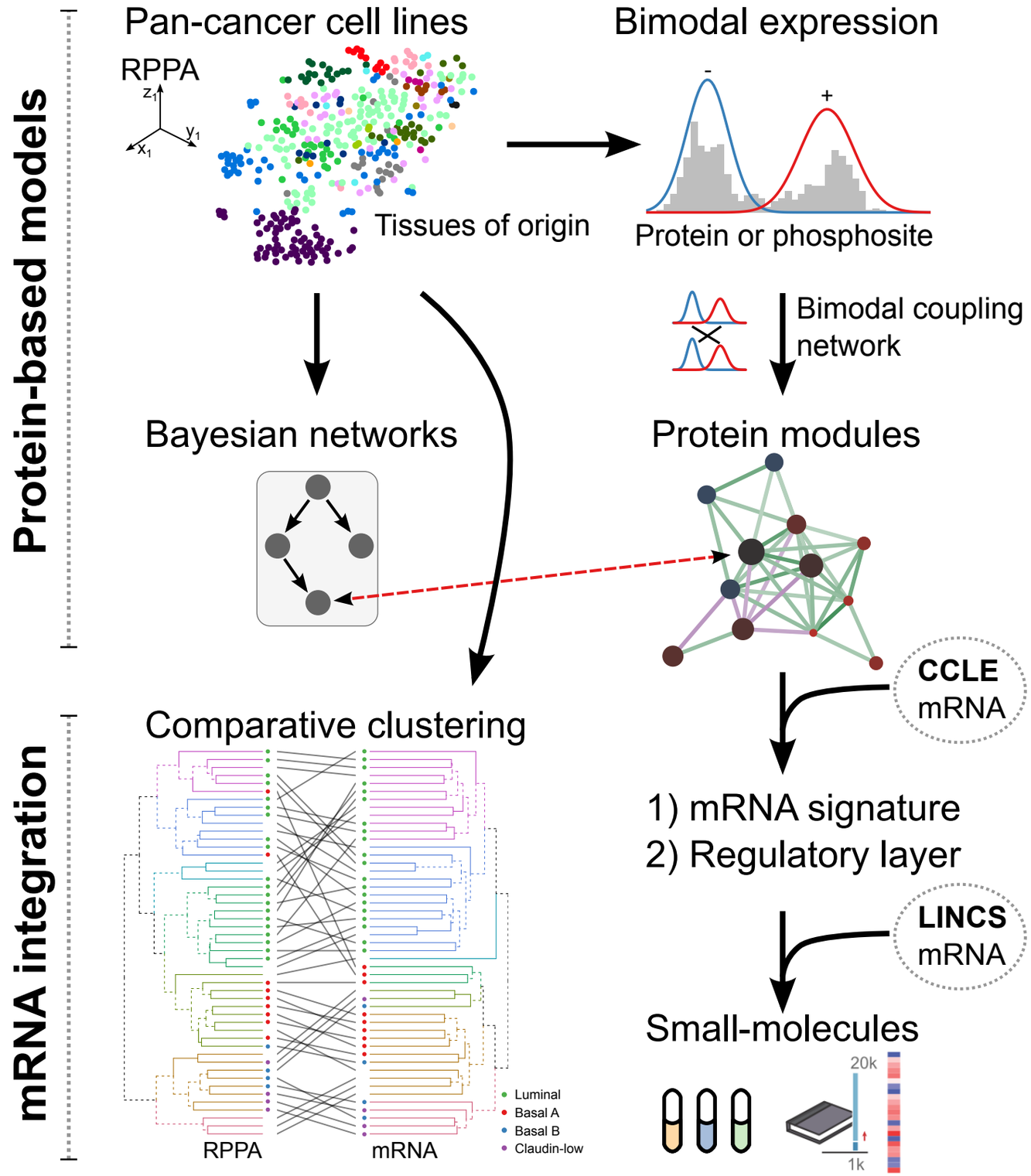
Genes: all considered



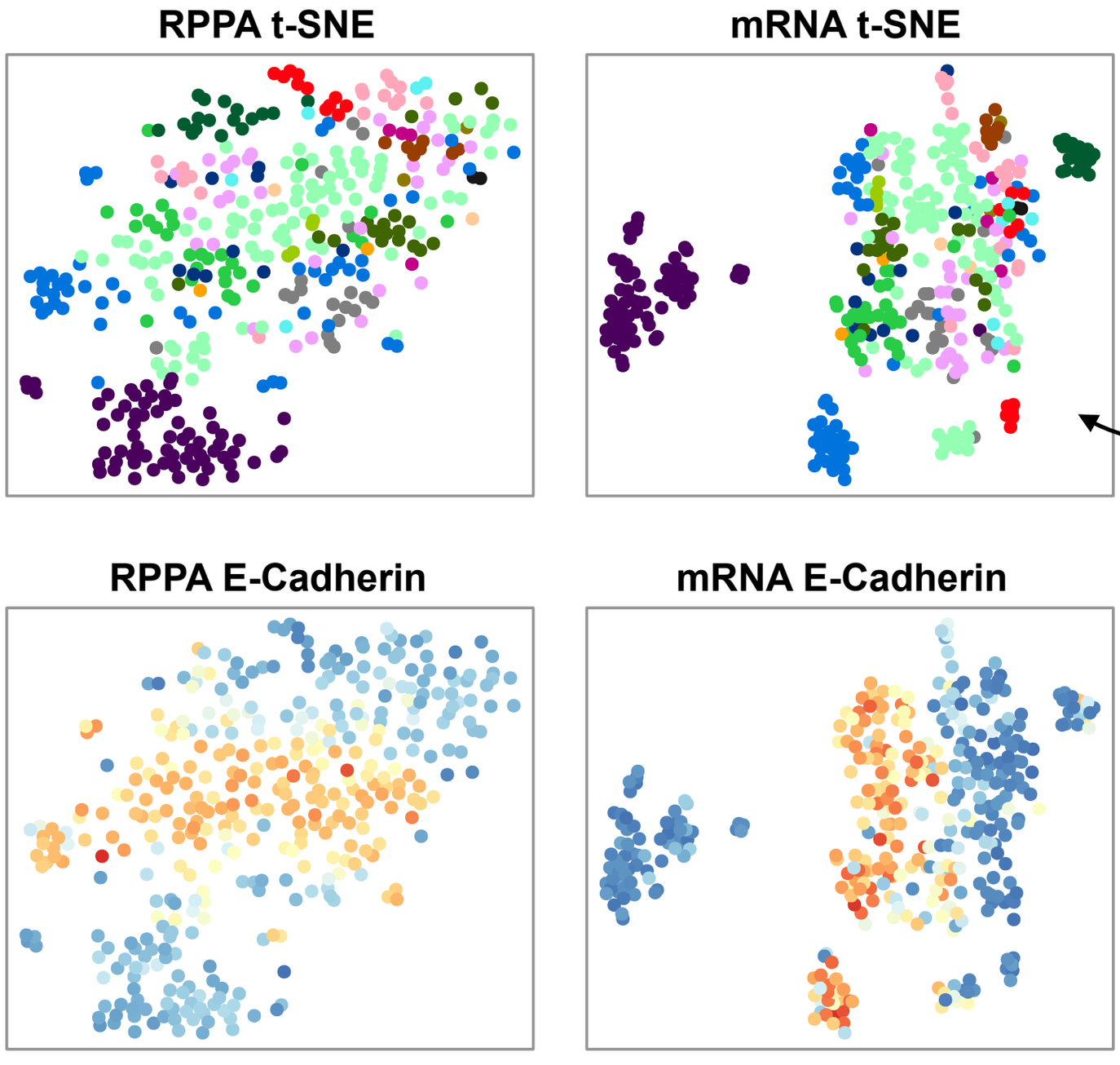
Antibody binding



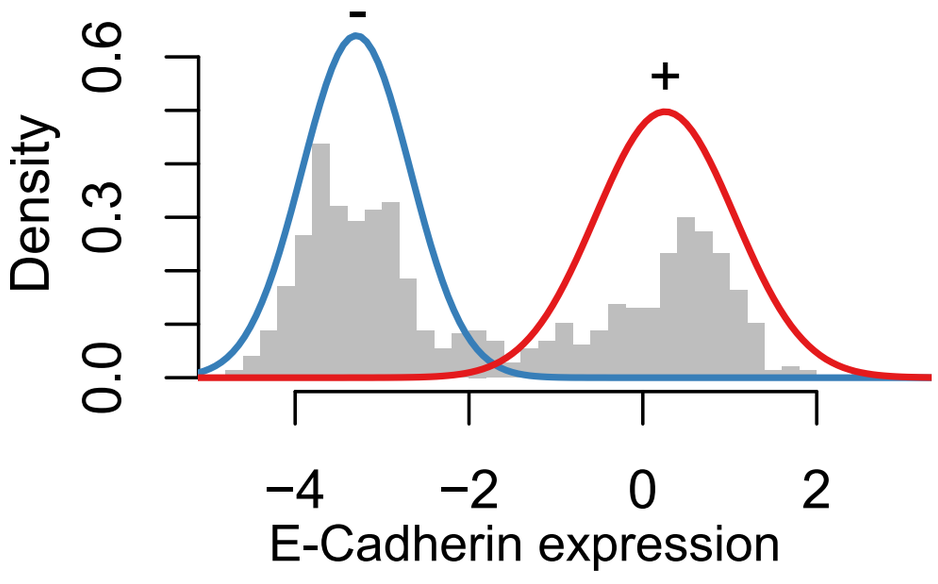
Analysis scheme

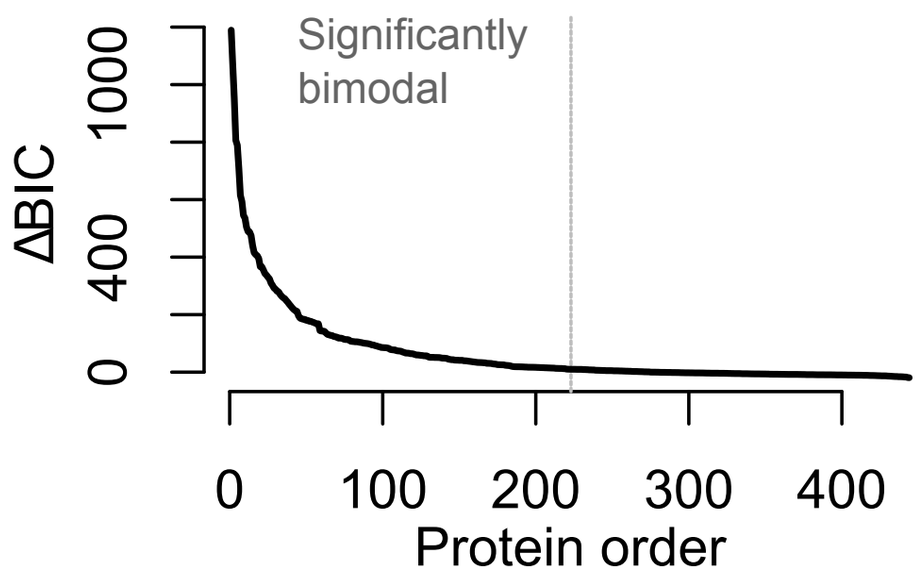


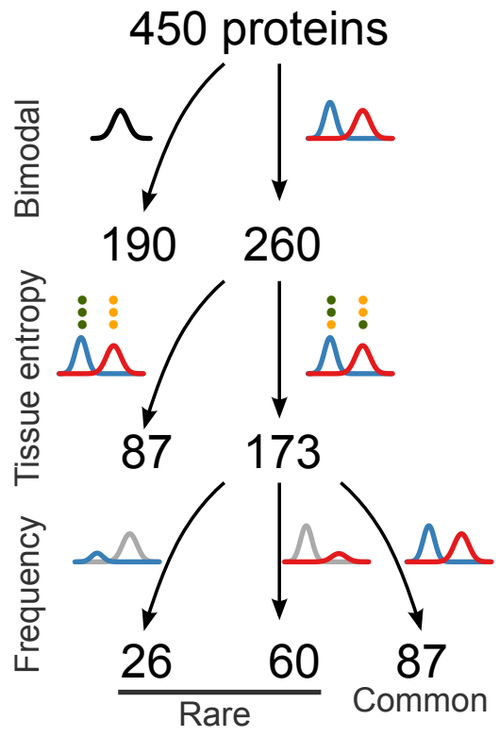
Cell lines are organized by tissue of origin and EMT



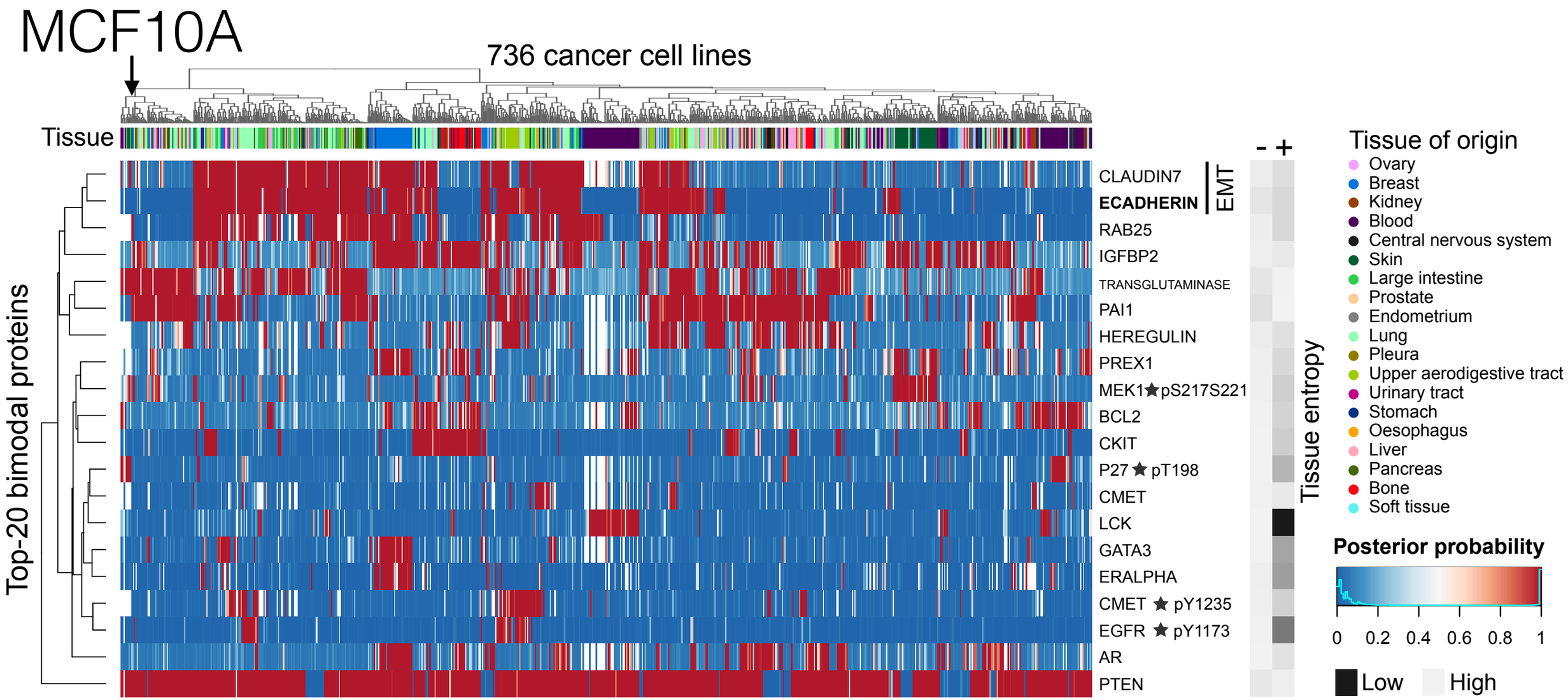
Bimodality of pan-cancer protein expression and phosphorylation



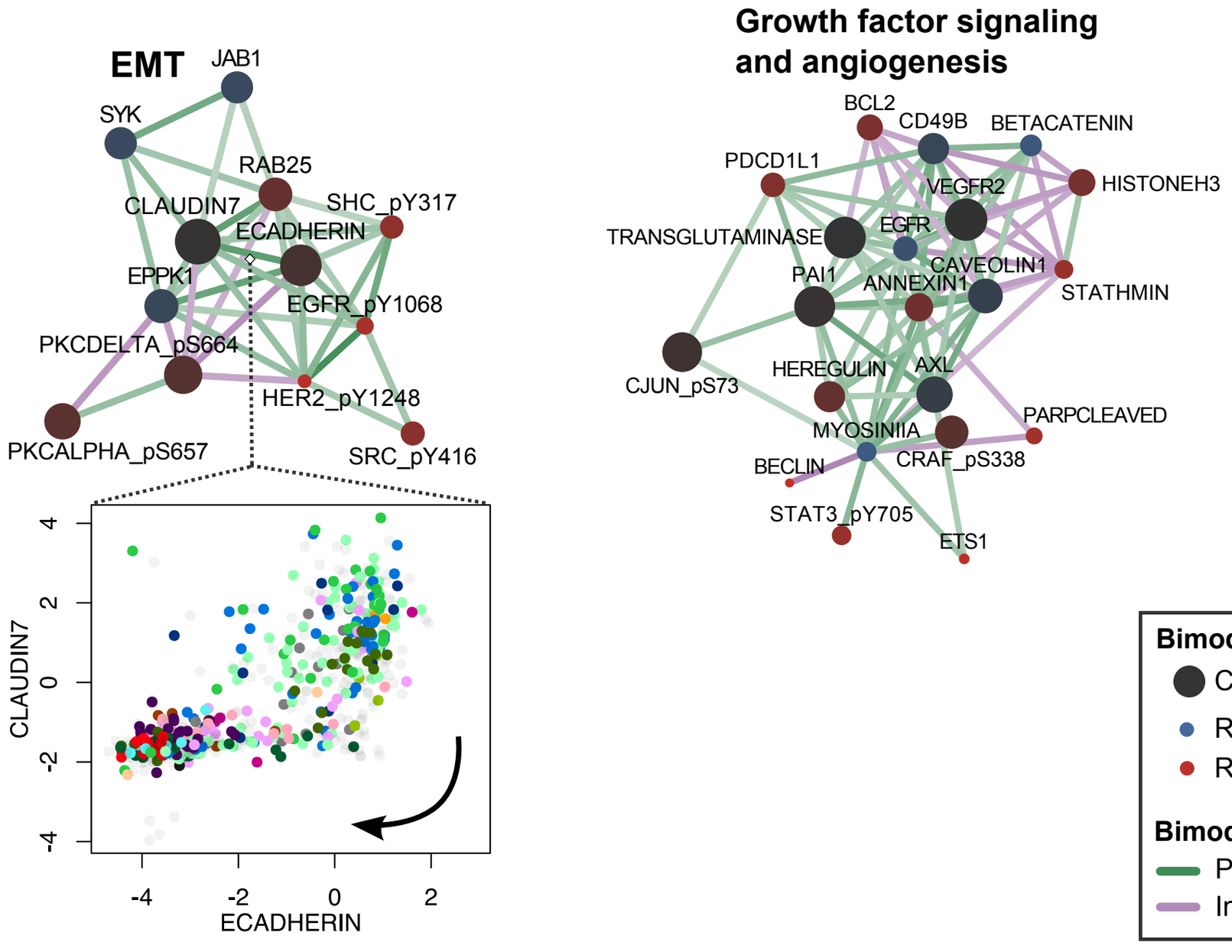




Top-20 most bimodal proteins and phosphosites cluster by EMT status



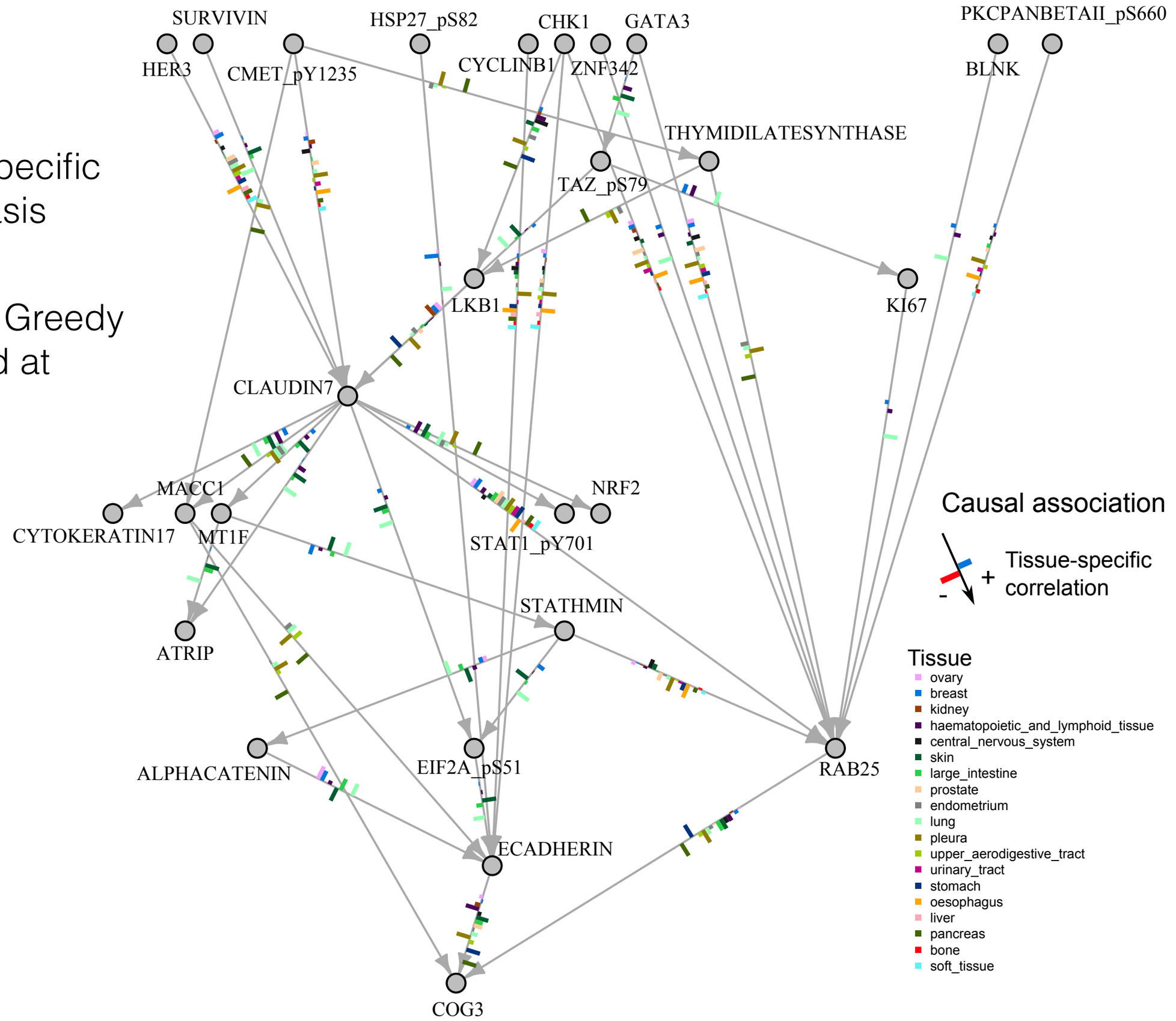
Bimodal coupling of proteins and phosphosites suggests core EMT module



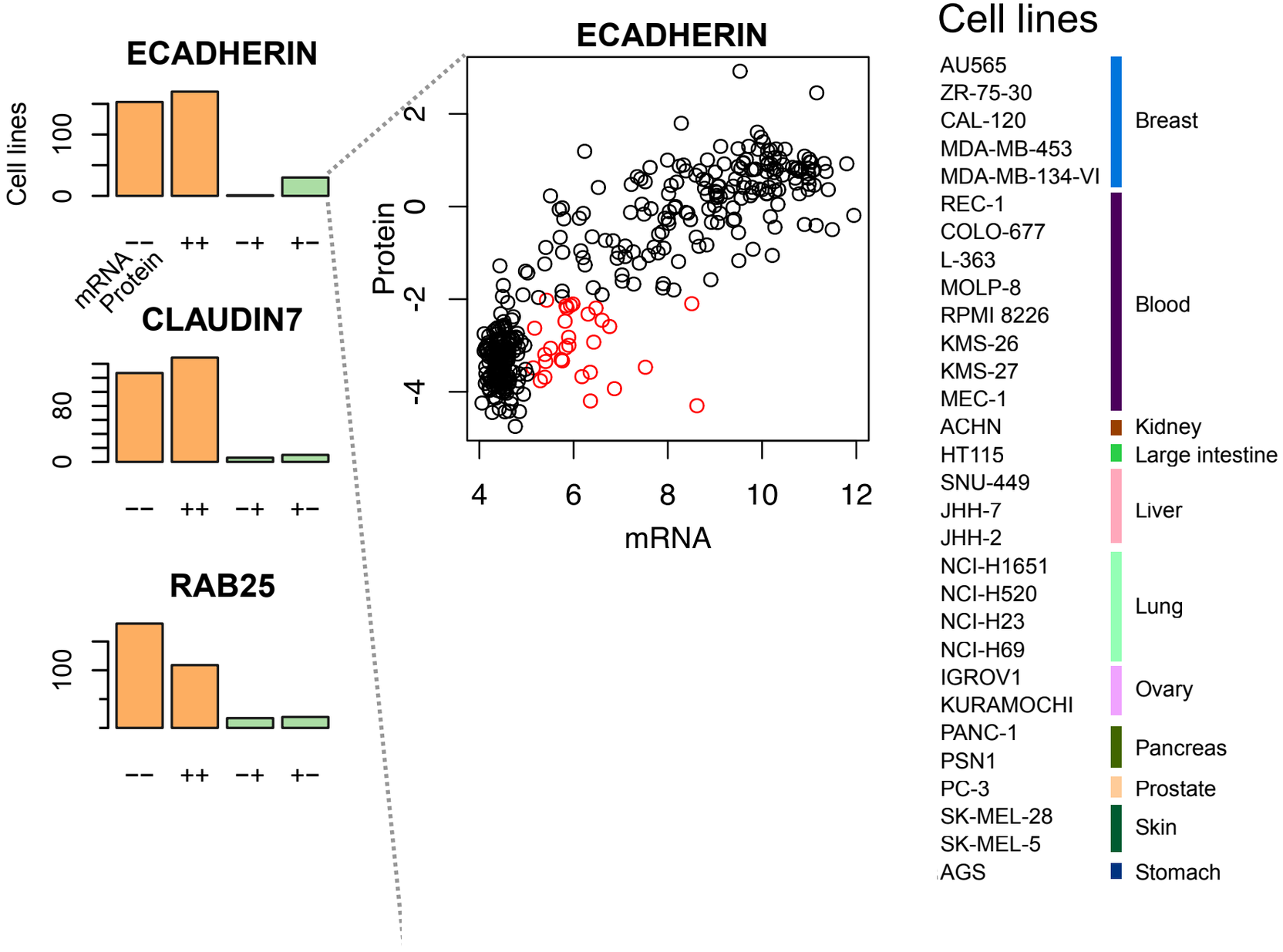
Causal RPPA neighborhood of core EMT proteins

- Tissue-of-origin-specific drivers of metastasis
- Inference by Fast Greedy Search developed at BD2K:

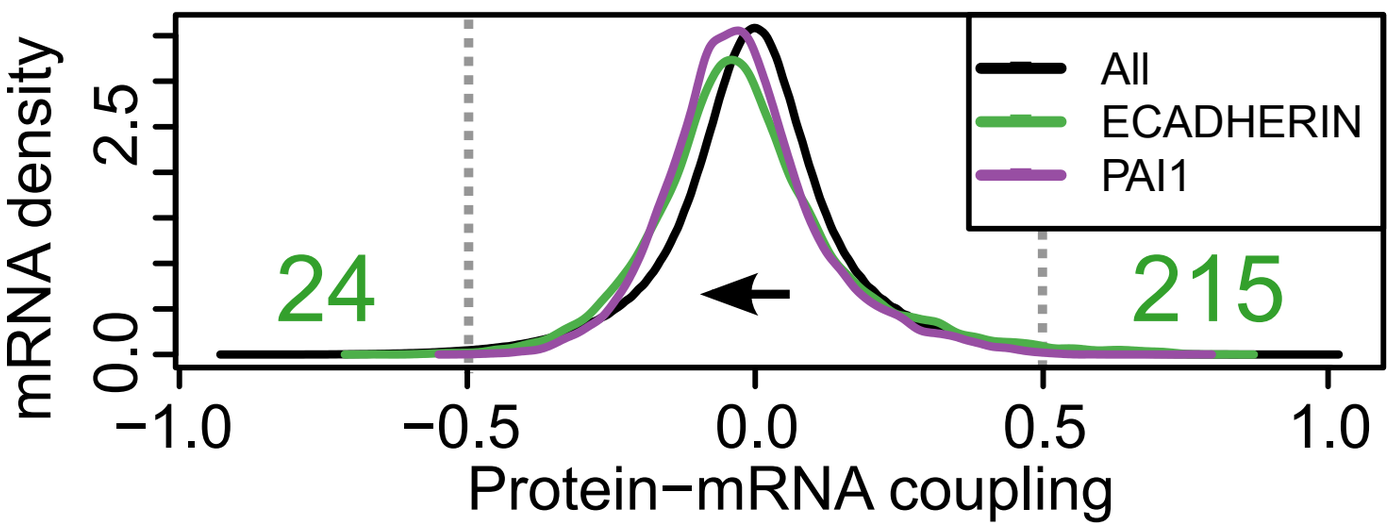
Center for Causal Discovery

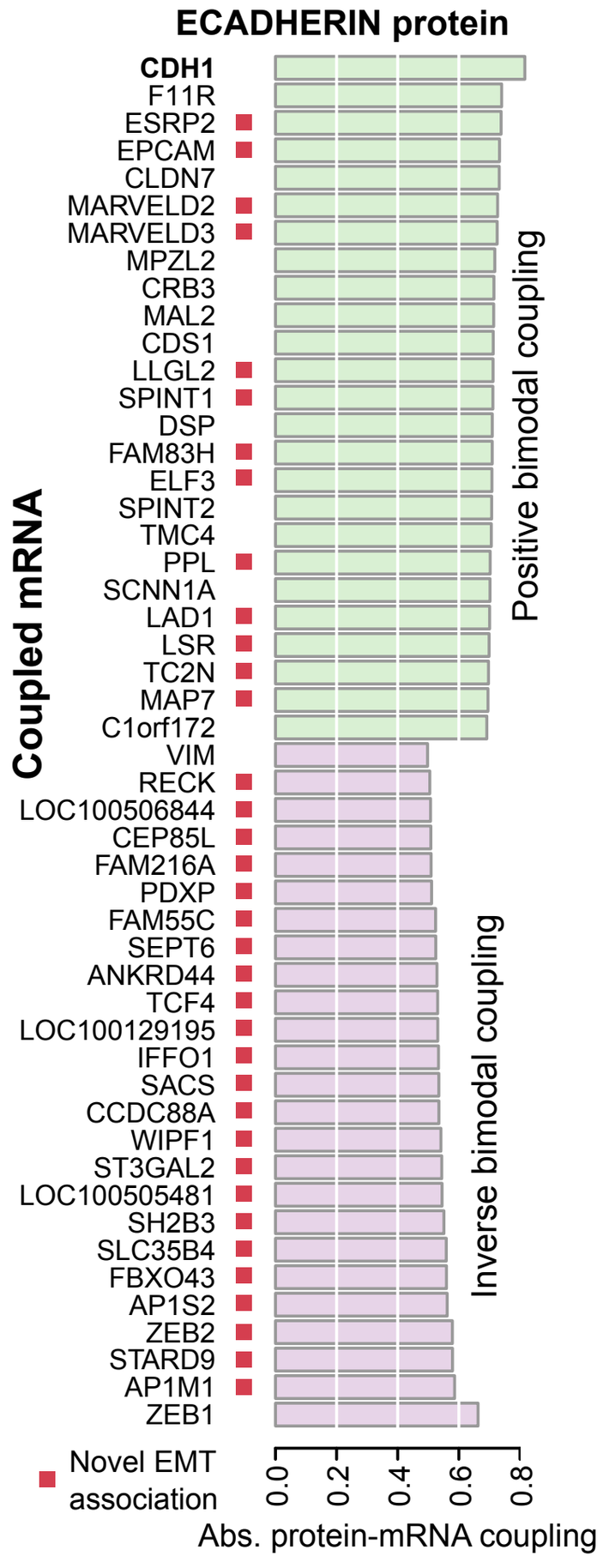


Bimodal coupling of E-cadherin mRNA and protein

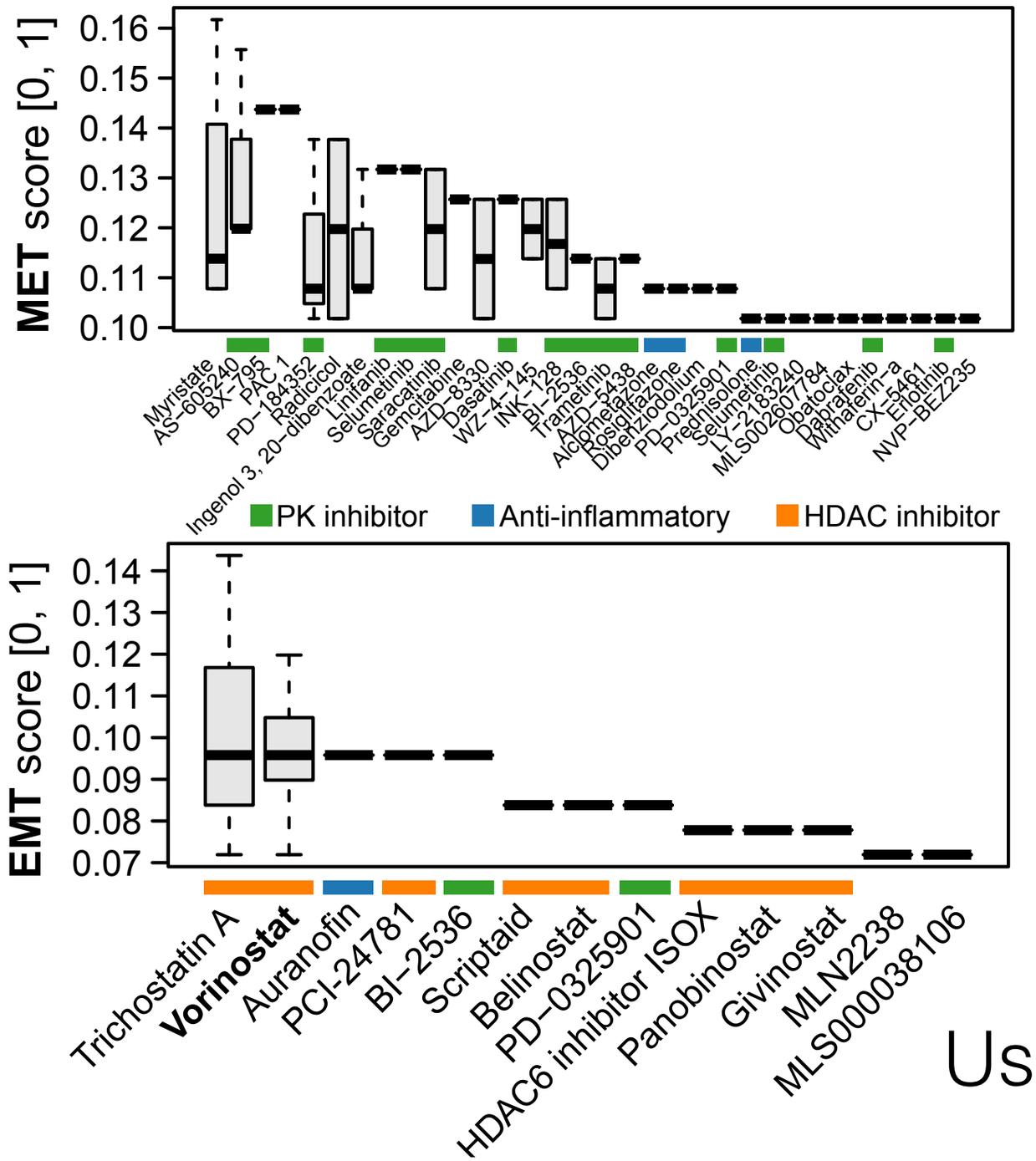


Trans-bimodal coupling of E-cadherin protein with mRNAs





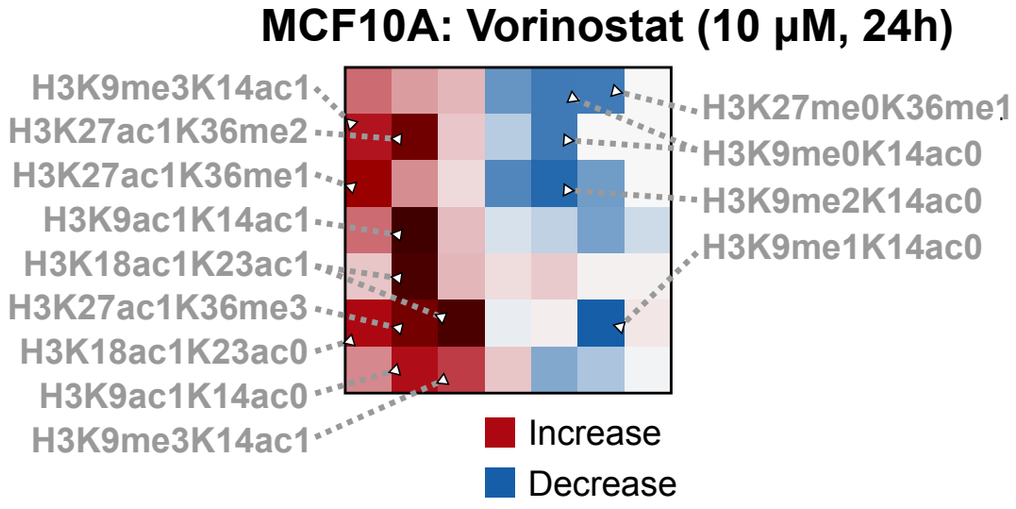
EMT signature overlap with L1000 small-molecule perturbations



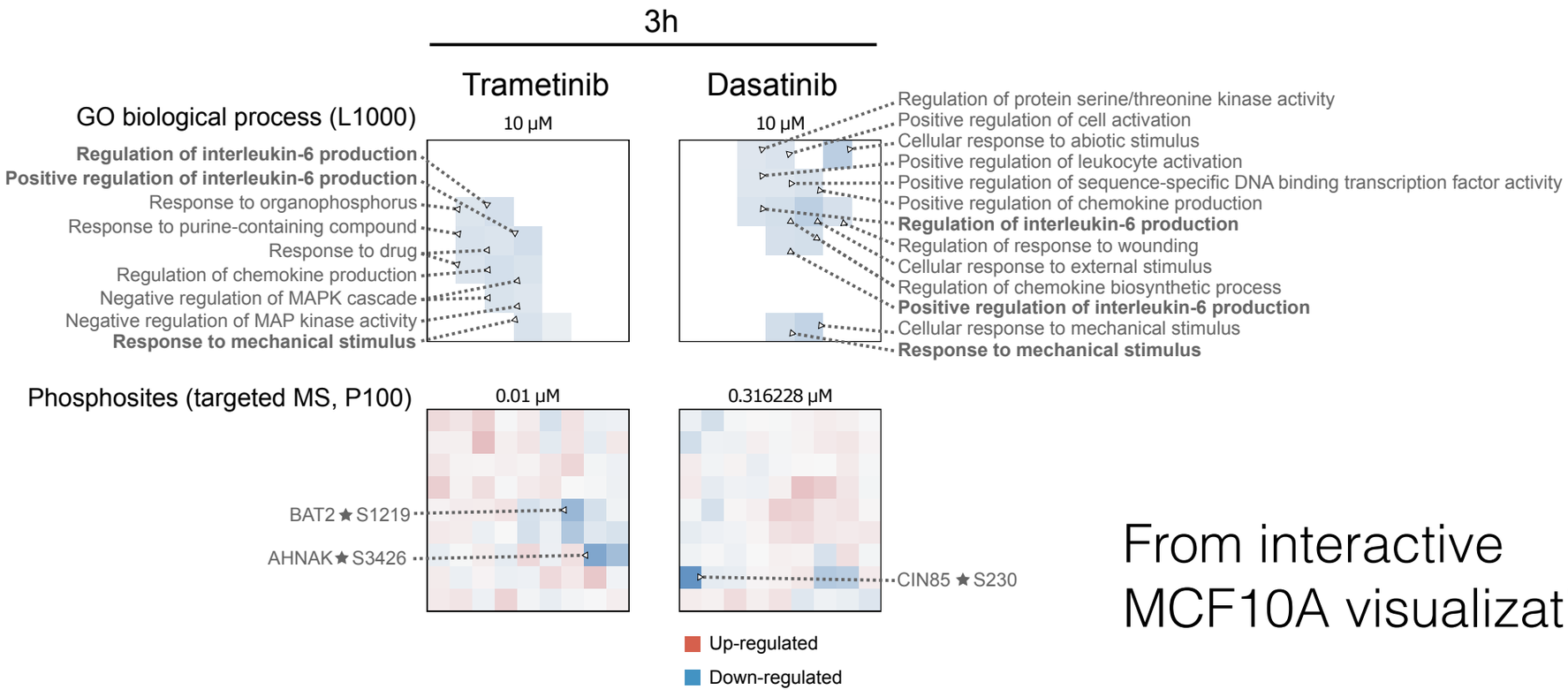
Using L1000CDS2

Comparing effects of small-molecules in MCF10A

HDAC inhibitor



Kinase inhibitors



From interactive MCF10A visualization

Conclusions

- Bimodal models of cell line RPPA data identifies oncogenic transitions.
- Causal models suggest upstream signaling drivers.
- Comparison of protein and mRNA quantifies involved regulatory levels across cell lines.
- Integration with genome-wide mRNA extends molecular characterization of EMT.

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