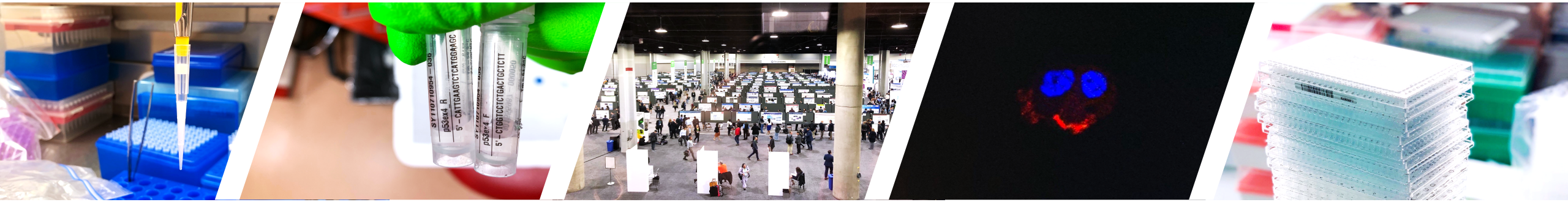

Single-cell RNA-seq of normal cells of origin reveals non-genetic heterogeneity of serous ovarian cancer

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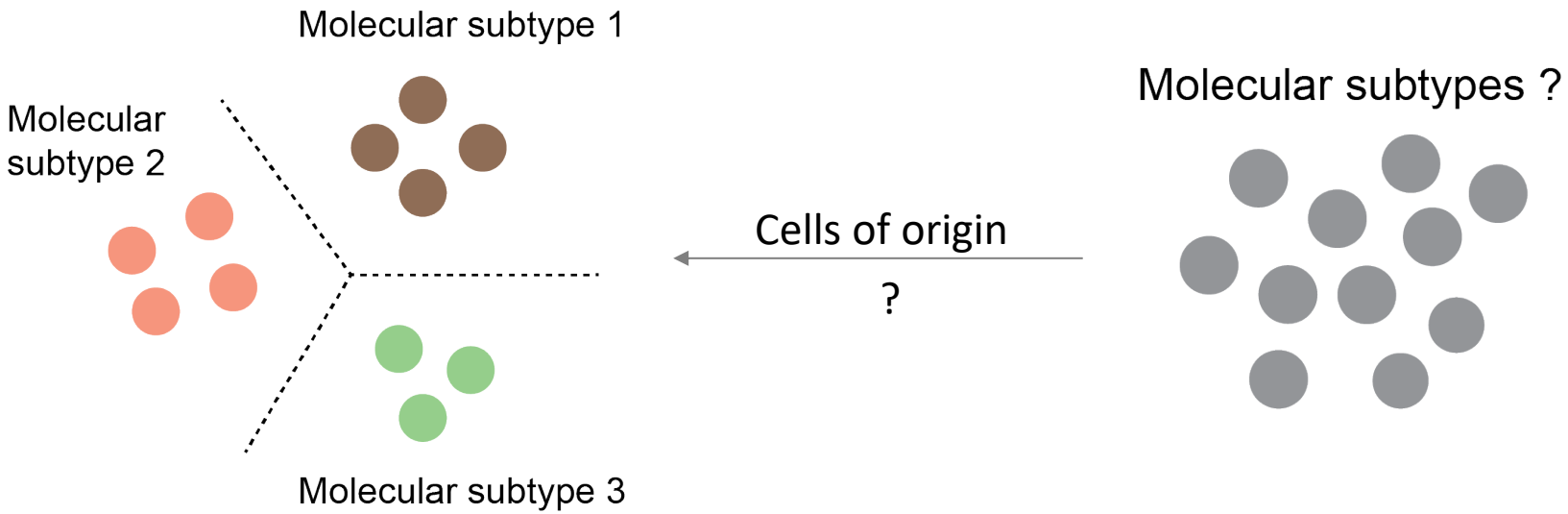
Serous ovarian cancer is the most aggressive subtype without robust molecular classification



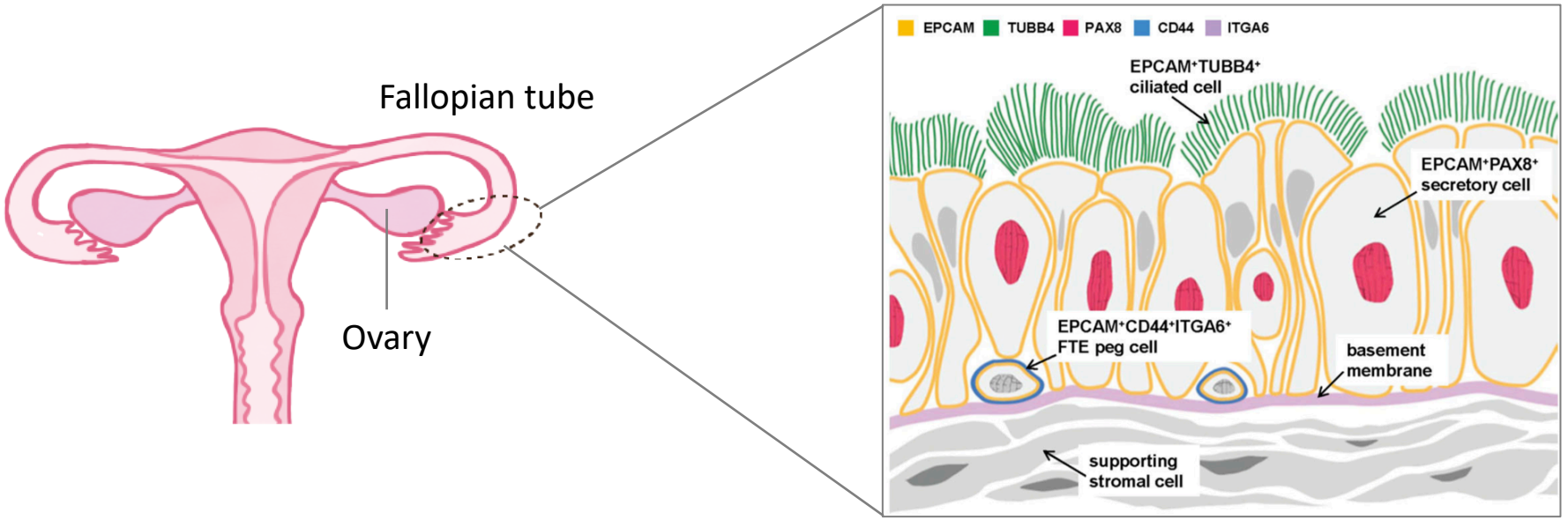
Molecular classifier of tumours

- Prognostic prediction
- Targeted therapy

Serous ovarian cancer

- ~80% ovarian cancer cases
- Five-year survival 30-40%

Knowledge of cells of origin was limited for serous ovarian cancer

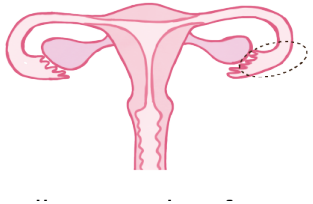


Daniel Paik et al., *Stem Cells,* 2012

Questions:

- Are there additional cellular subtypes in the epithelium?
- What is their connection to ovarian cancer?

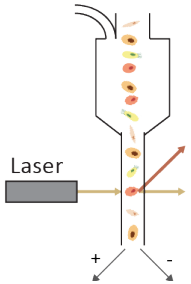
Workflow: identification of novel subtypes in fallopian tube epithelium by single-cell RNA-seq



Fallopian tube samples from ten donors

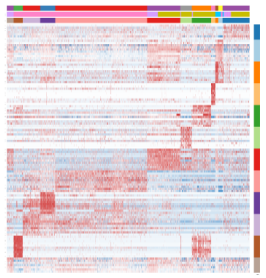
Normal tissues
Not cancer samples

Single-cell suspension

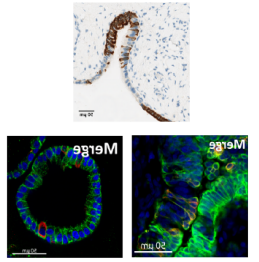


Flow cytometry to isolate single cells

Single-cell RNA-seq (Smart-Seq2)

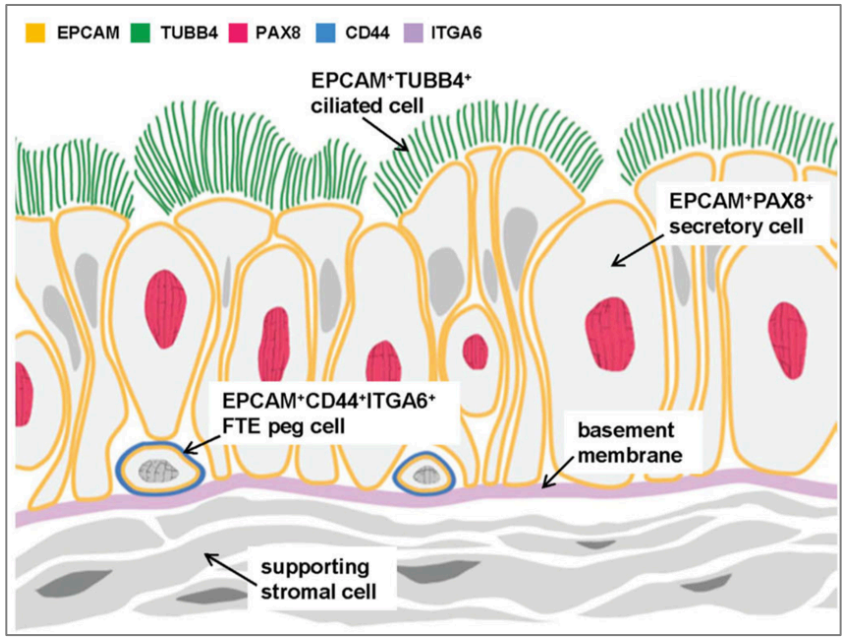


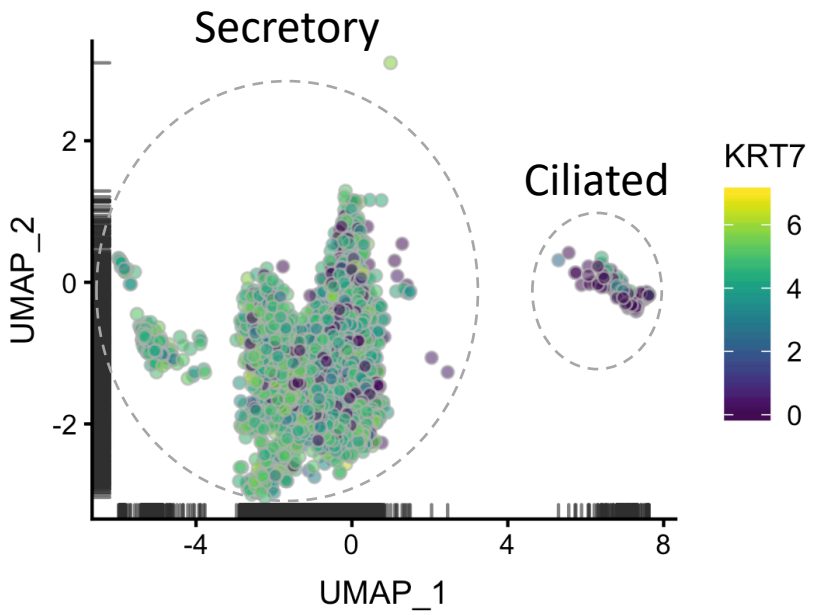
Data analysis



Validation by IF or IHC

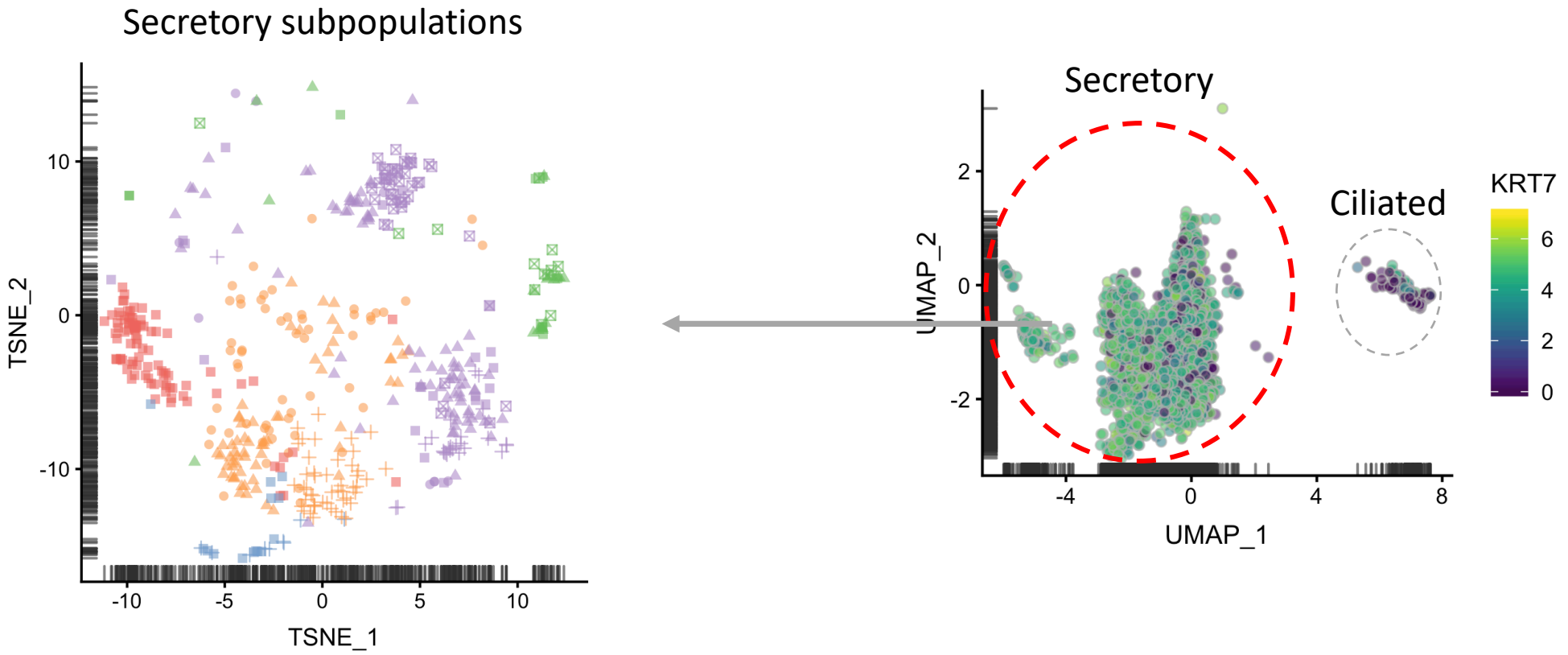
Clustering shows the ciliated and secretory populations



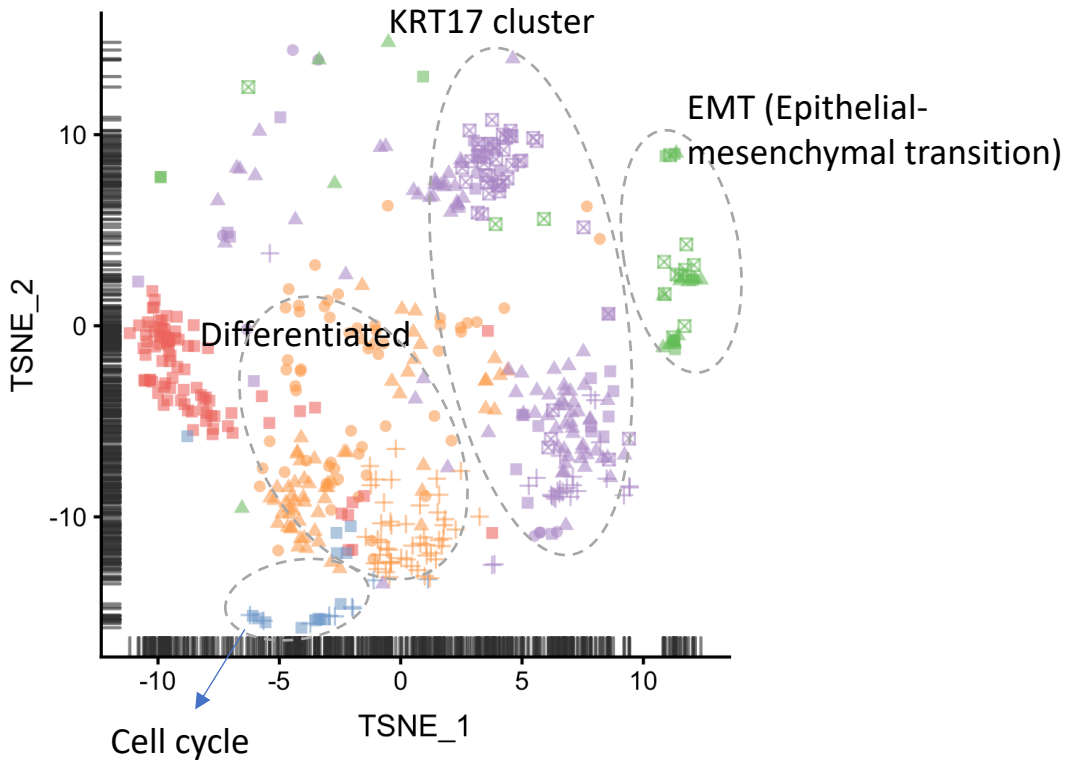


Z Hu et al. bioRxiv (2019)

The clustering algorithm, ClinCluster, identifies 4 novel secretory subpopulations



Single-cell RNA-seq refines the cellular landscape of fallopian tube epithelium



Secretory subpopulations

Differentiated cluster
RNA synthesis ↑

KRT17 cluster
KRT17+ Keratins+ MHCII+

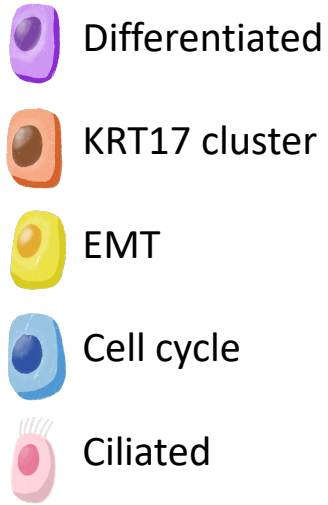
EMT cluster
RGS16+ Extracellular matrix ↑

Cell cycle cluster
STMN1+ Cell cycle ↑ DNA repair ↑

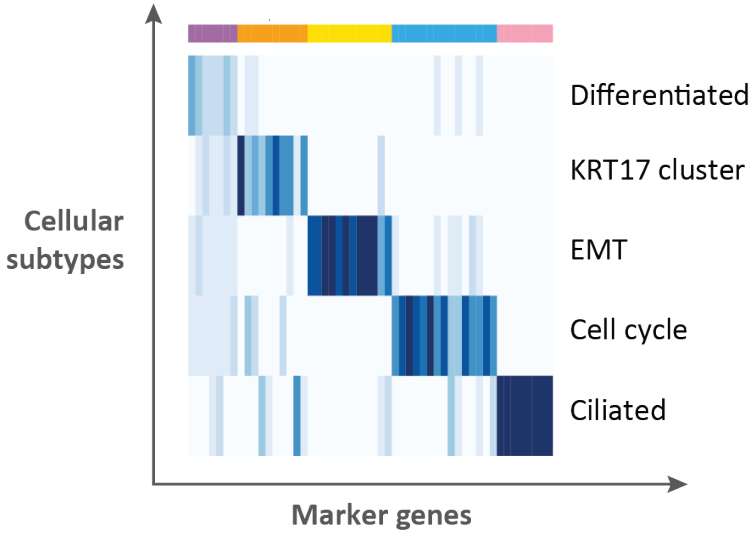
Ciliated cells

Bulk tumours are decomposed by transcriptomic signatures derived from single-cell RNA-seq data

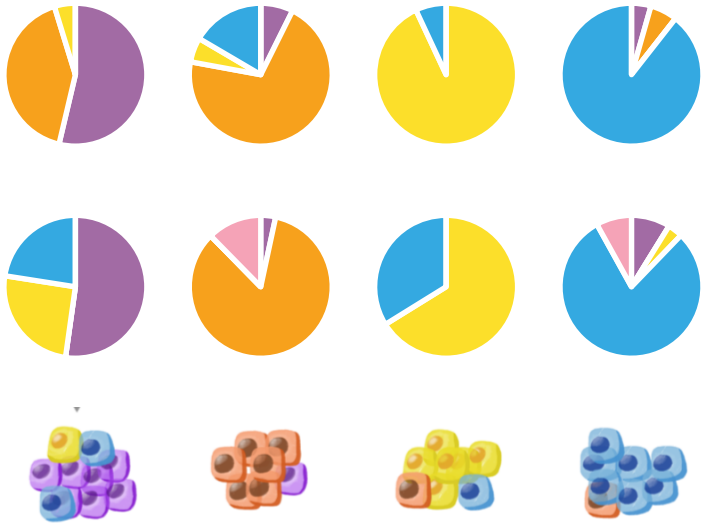
Single-cell profiling of fallopian tube epithelium



Reference matrix of cell-type derived signatures



Decomposition of bulk serous ovarian tumours

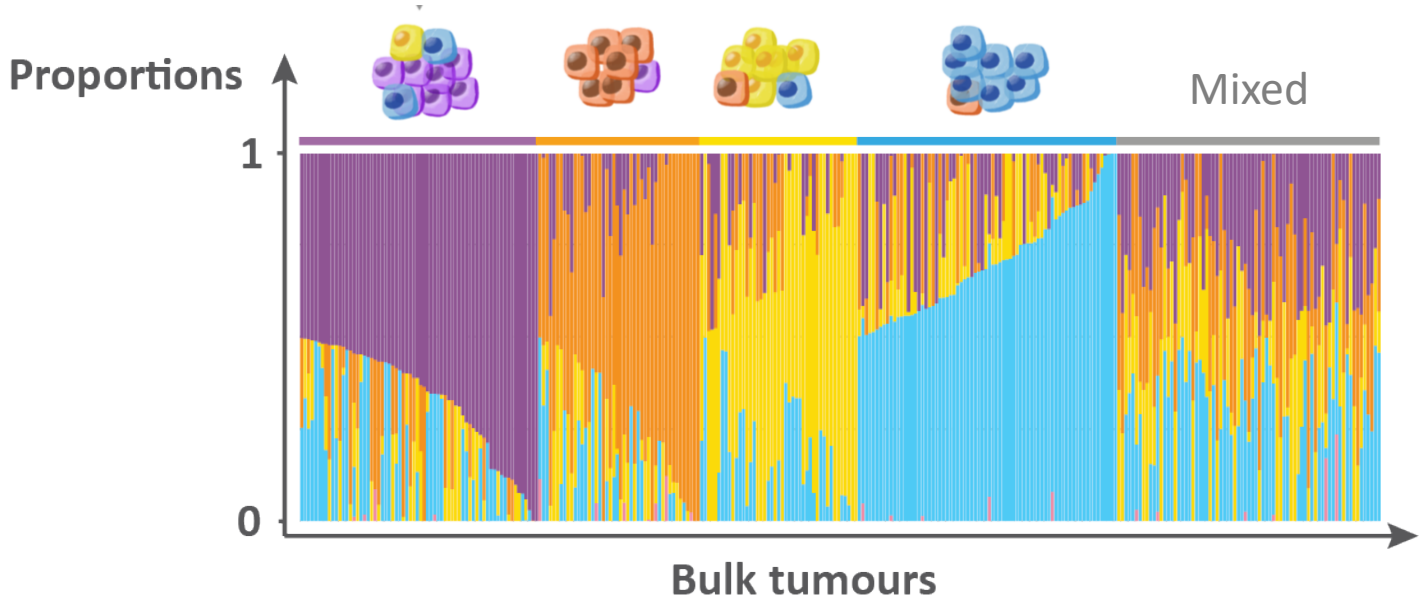


Deconvolution reveals the linkage between cell subtypes in tissue-of-origin and tumour subtypes

Fallopian tube epithelium

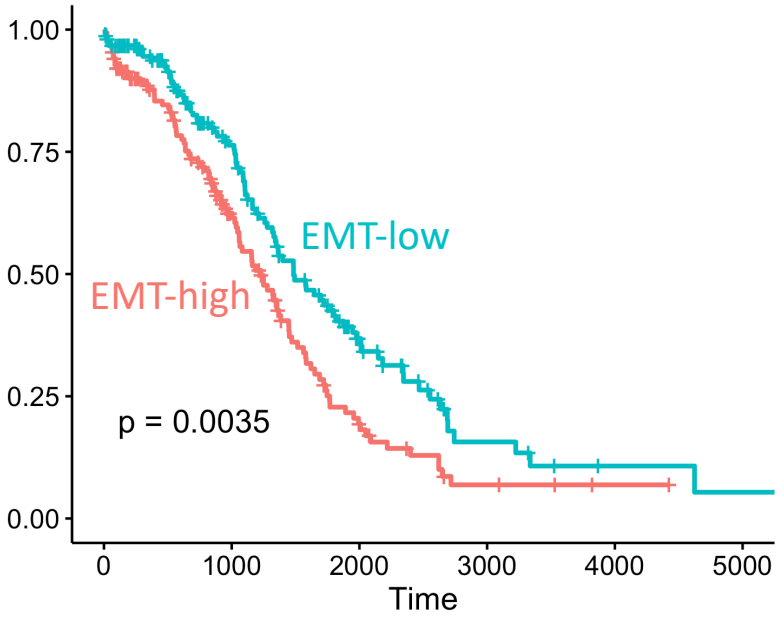
- Differentiated
- KRT17 cluster
- EMT
- Cell cycle
- Ciliated

Deconvolution results of TCGA bulk tumours



TCGA: The Cancer Genome Atlas

EMT-high tumours are associated with poor prognosis

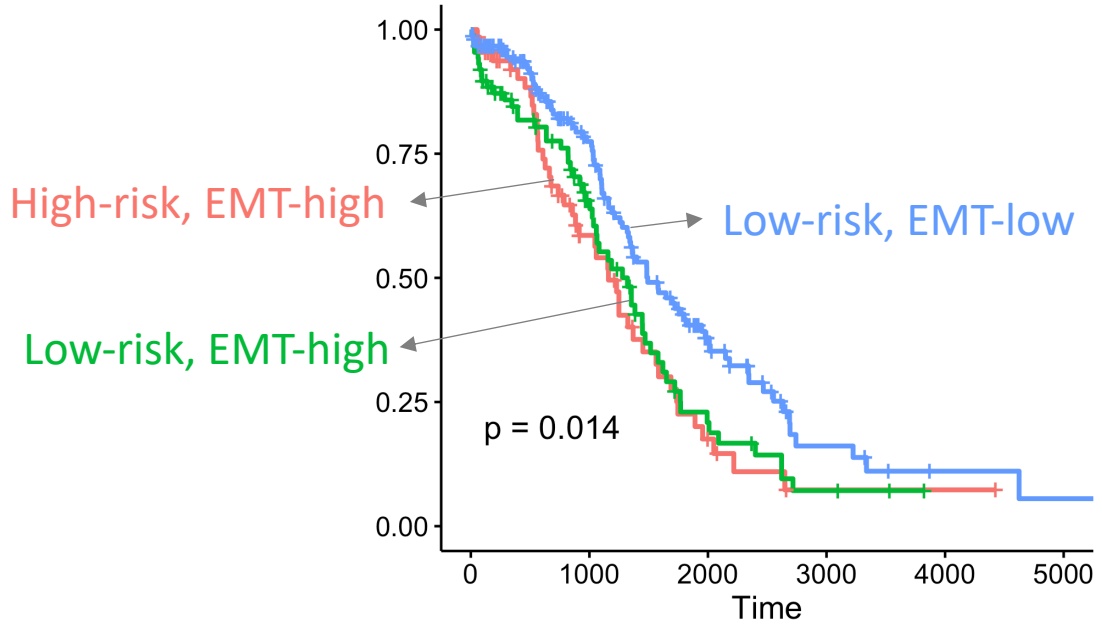


Hazard ratio = 2.29 between
EMT enrichment and overall survival

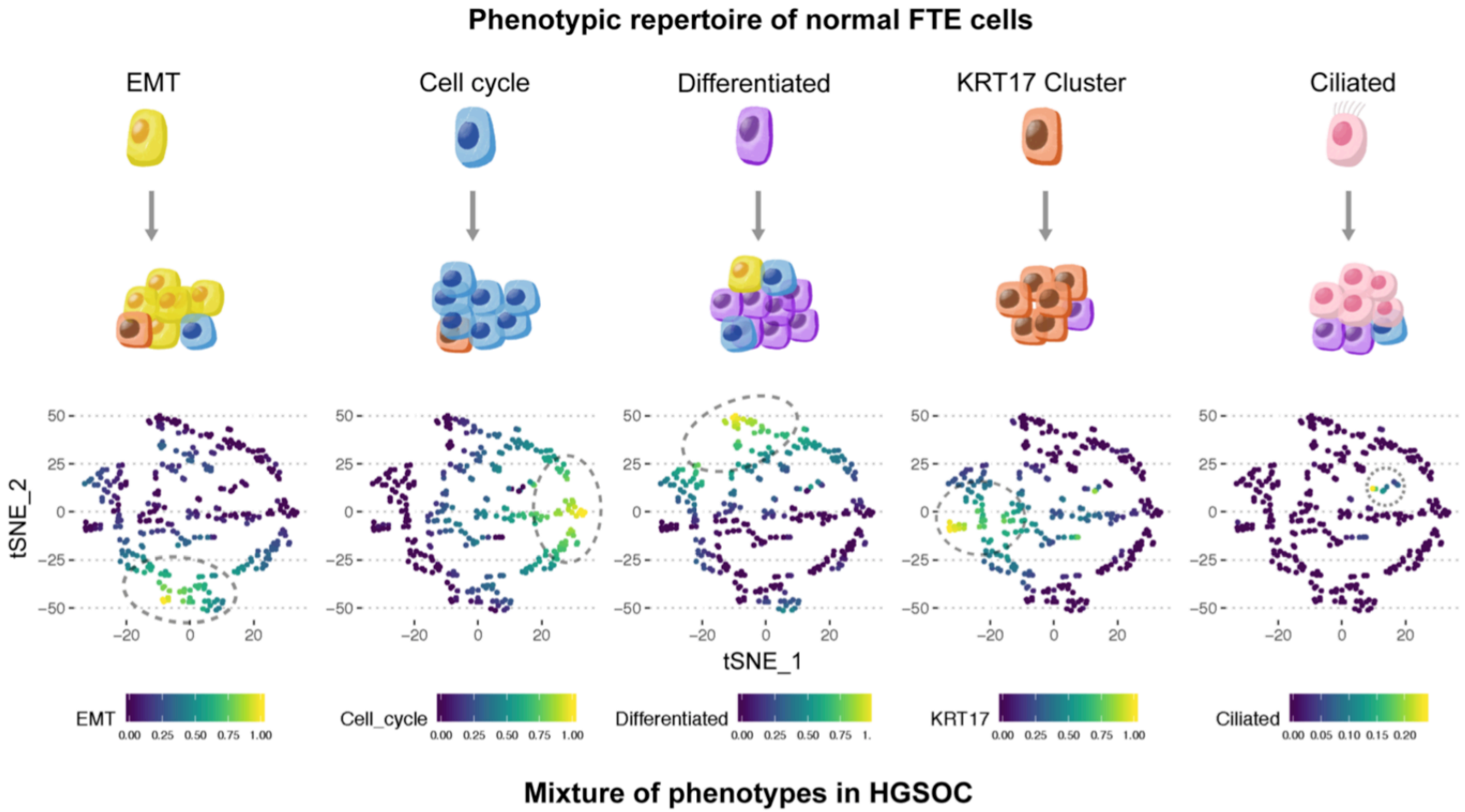
Our prognostic predictor refines the previous clustering-based classifier

Previous studies:

Using clustering on over 1K genes to identify high-risk (mesenchymal-like) and low-risk (other subtypes) tumours



Take-home message



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WIMM Flow Cytometry Facility

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Nuffield Department of Women's & Reproductive Health

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Ovarian Cancer Action
CSC-NDM Studentship

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