



Deconvoluzione computazionale dei dati di trascrittomici per lo studio delle cellule immunitarie infiltranti il tumore

Maddalena Fratelli

maddalena.fratelli@marionegri.it

Unità di Farmacogenomica

Dipartimento di Biochimica e Farmacologia Molecolare

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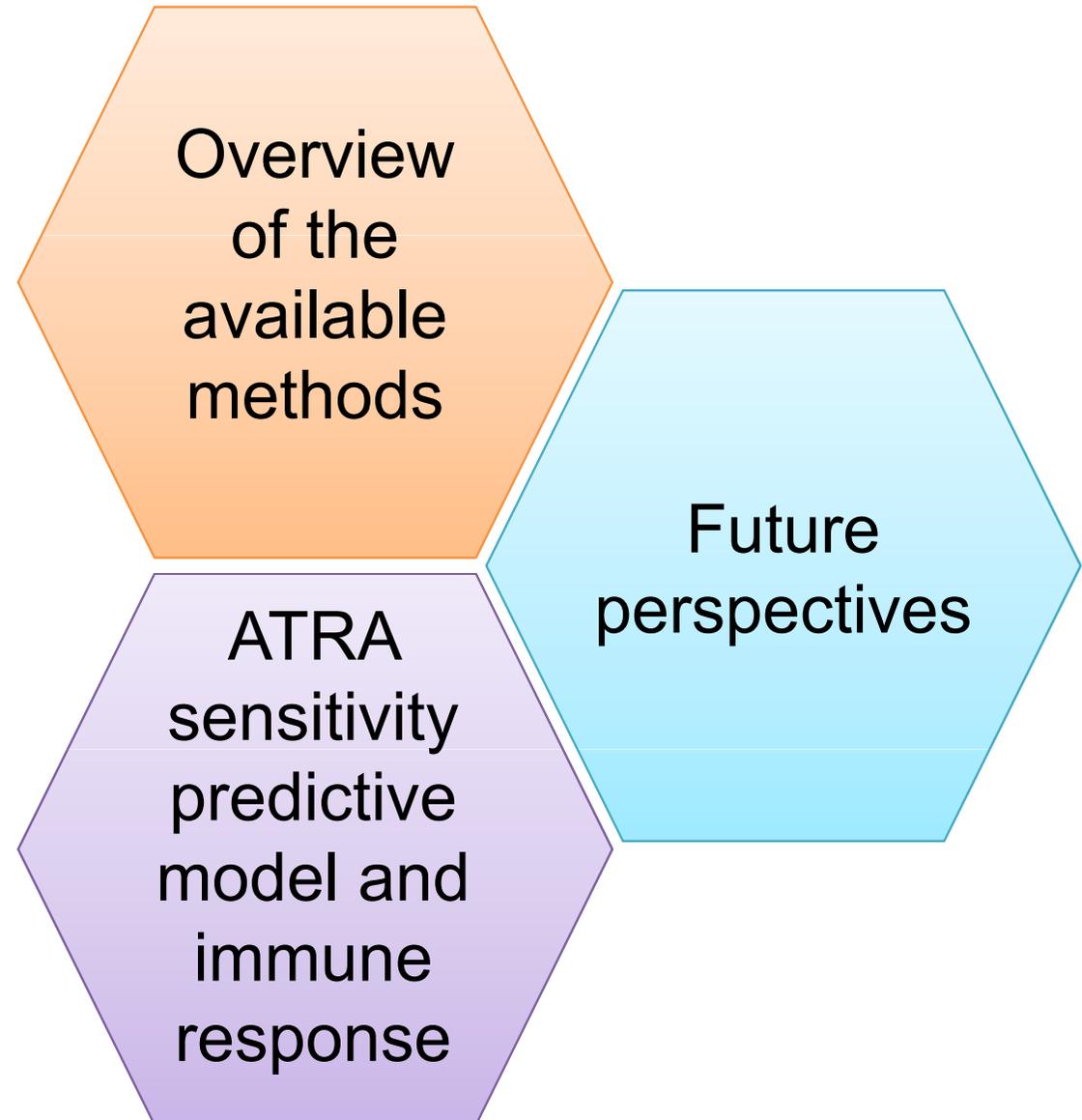
CANOVACCIO

- ❑ bisogni e priorità che sono alla base del tema trattato,
- ❑ evidenze disponibili sulla valutazione del test/tecnica, possibilmente distinguendo fra validità analitica o tecnologica (funziona bene?), validità clinica (è associato alla condizione clinica cercata?) e utilità clinica (produce benefici misurabili?),
- ❑ confronto della metodica proposta con lo standard (di diagnosi o cura) esistente,
- ❑ aspetti relativi alla tipologia e al disegno dello studio da considerare per la valutazione del test/tecnica in oggetto,
- ❑ aspetti pre-analitici (o di preparazione del paziente) che possono condizionare l'accuratezza della misura o della tecnica usata,
- ❑ aspetti post-analitici (criteri decisionali, criticità di interpretazione).

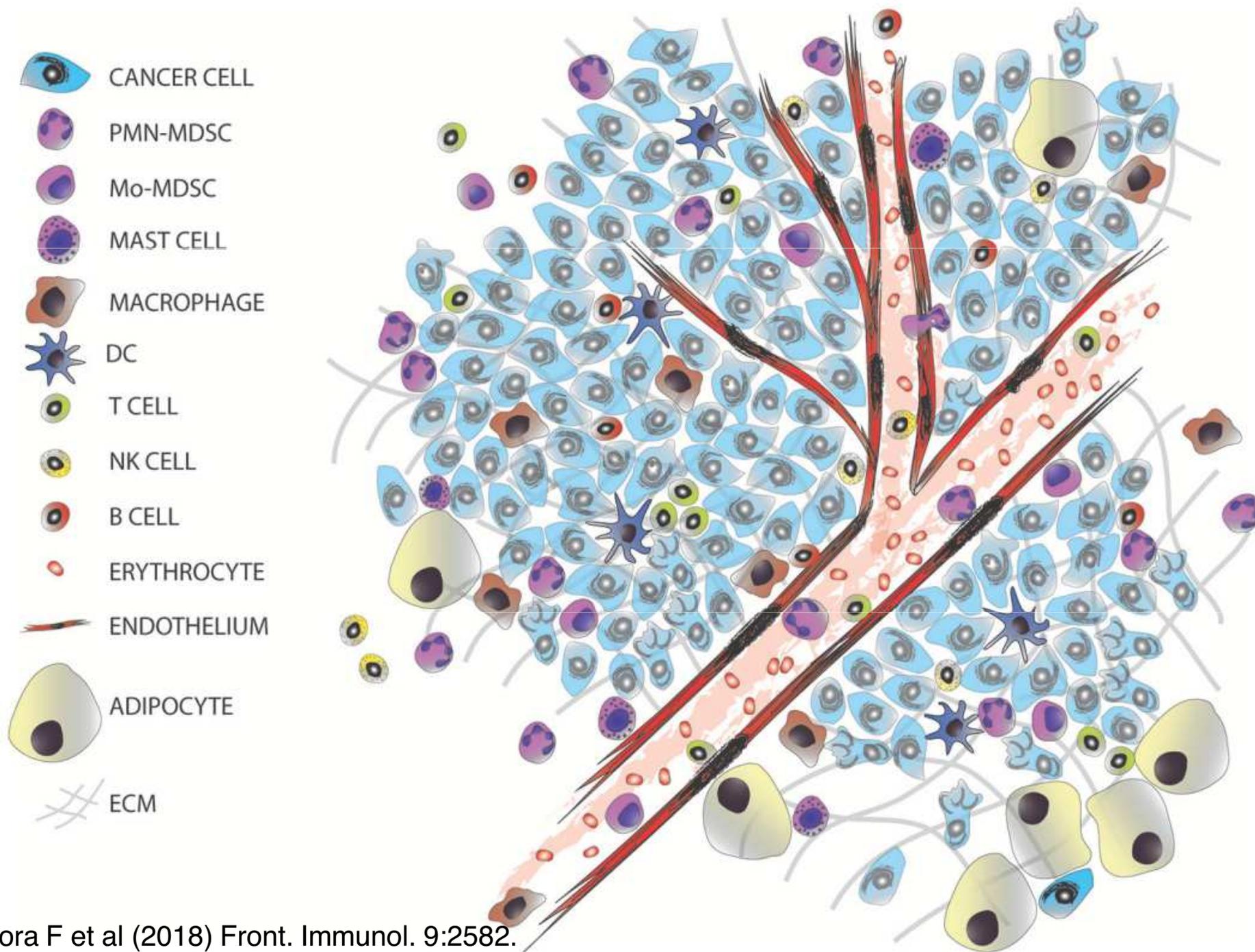
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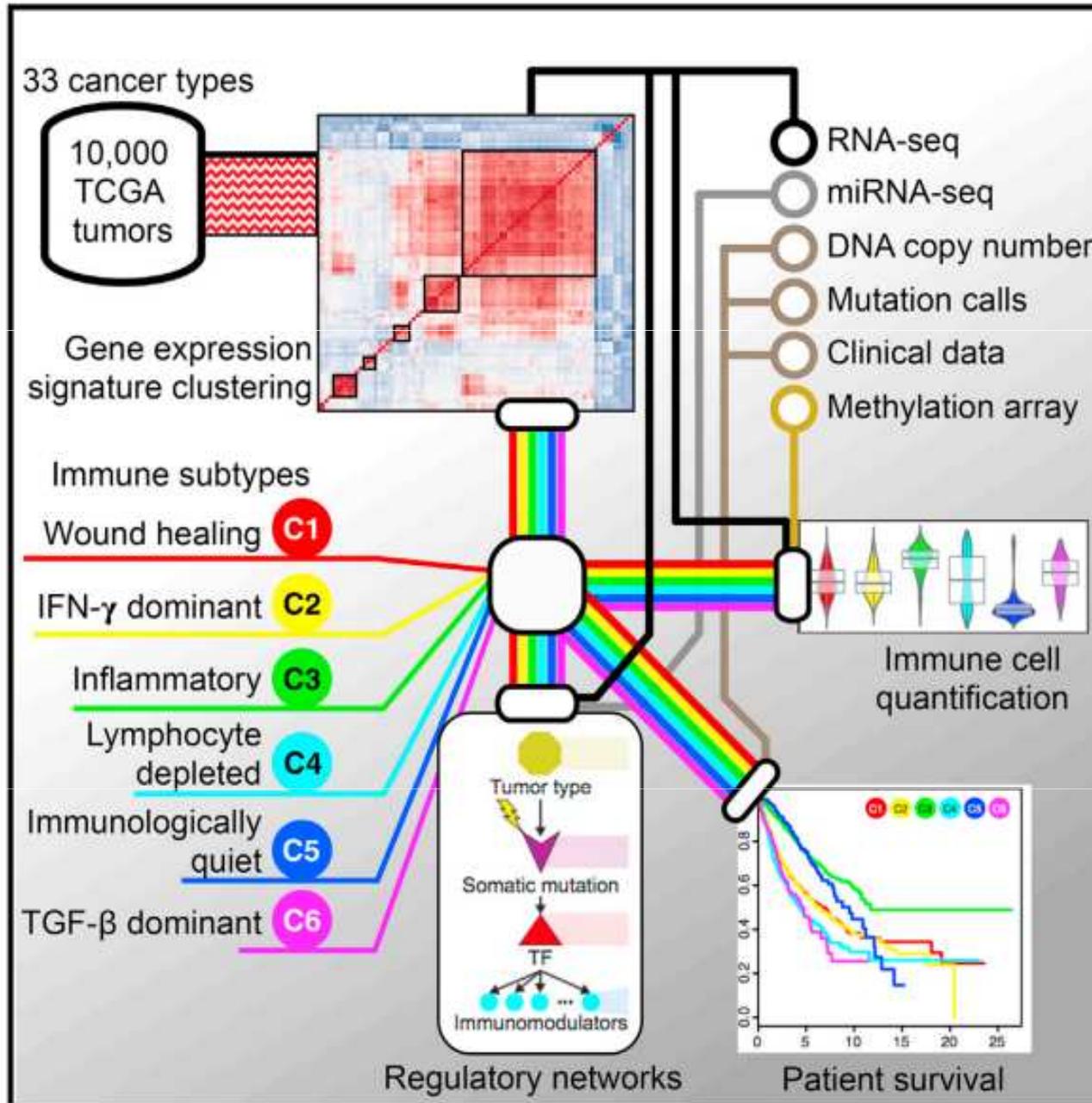
PRESENTATION OUTLINE



TUMOR MICROENVIRONMENT

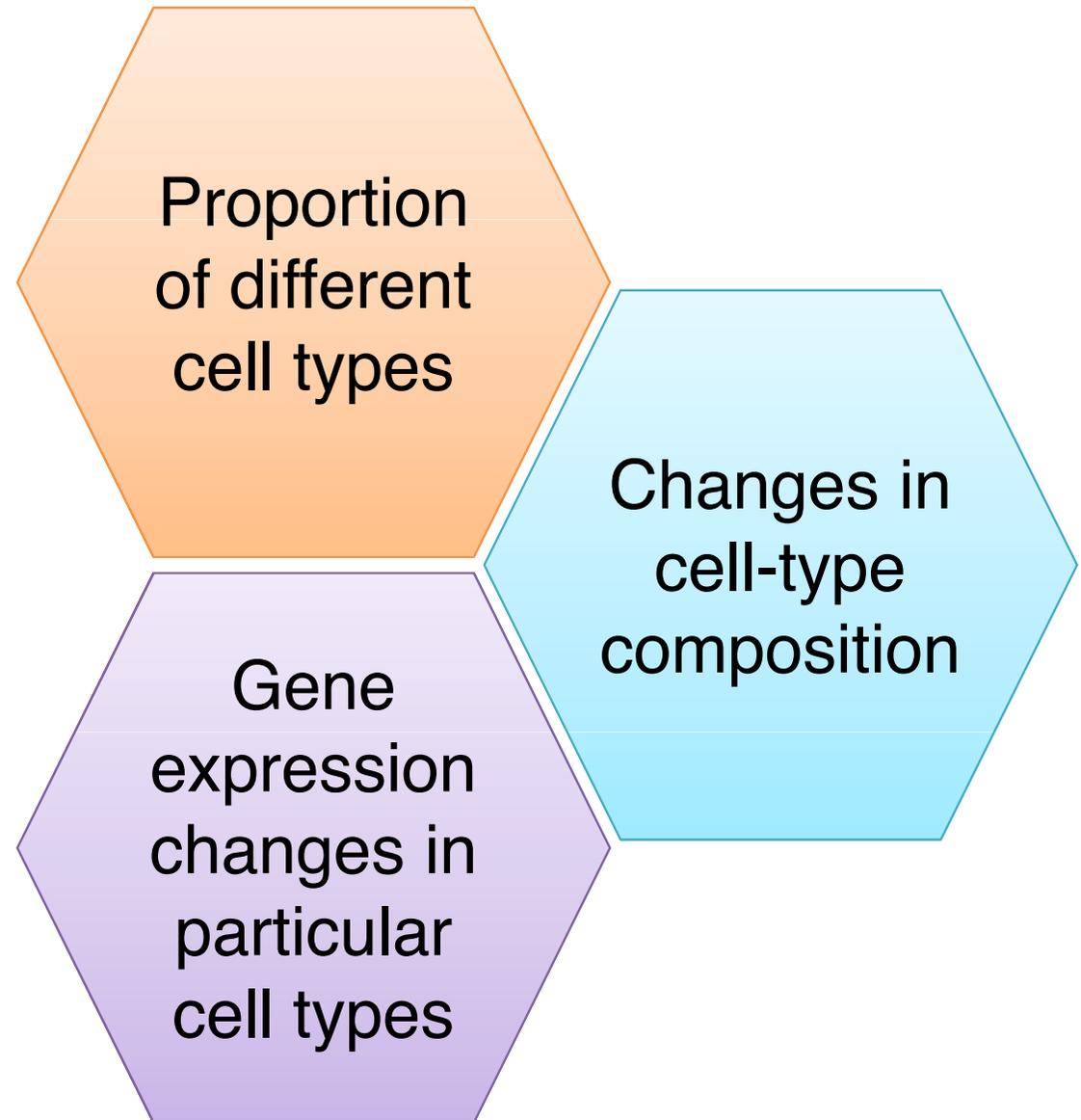


THE IMMUNE LANDSCAPE OF CANCER



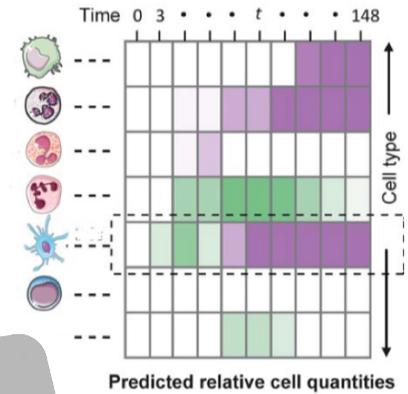
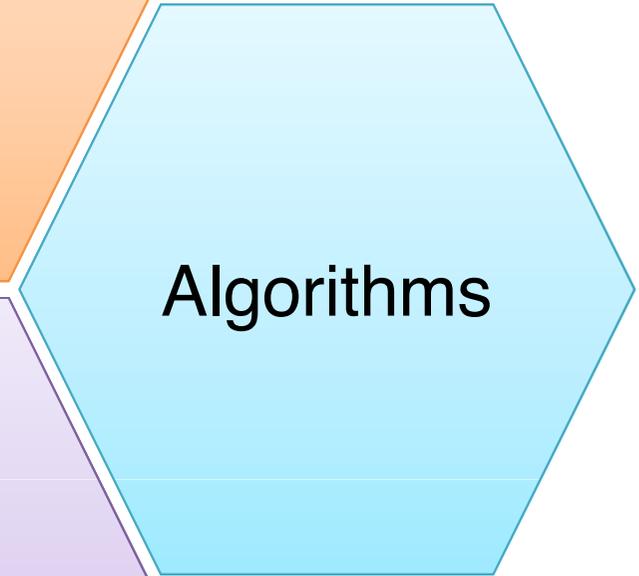
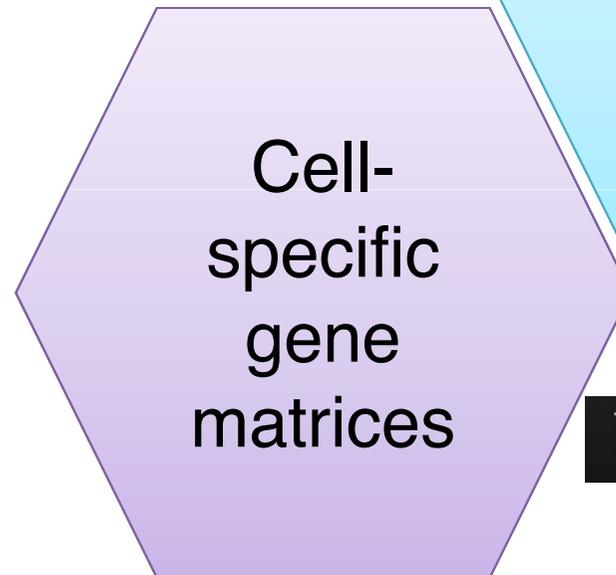
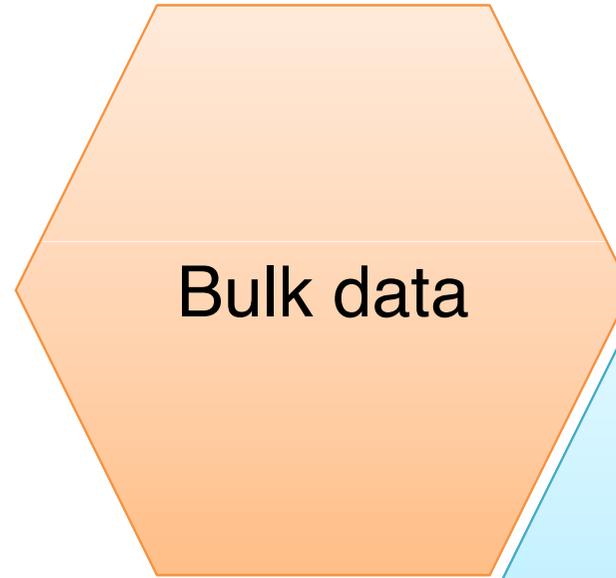
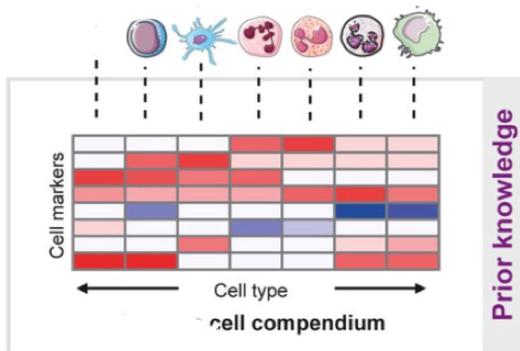
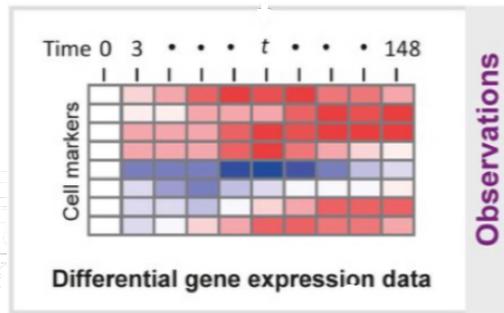
BULK TRANSCRIPTOMICS

SOURCES OF VARIATION:



BULK TRANSCRIPTOMICS DATA DECONVOLUTION

BASED ON:



$$Y_{ig} = \pi_{1,i} N_{1,ig} + \pi_{2,i} N_{2,ig} + \pi_{T,i} T_{ig}$$

WIDE VARIETY OF DECONVOLUTION METHODS...

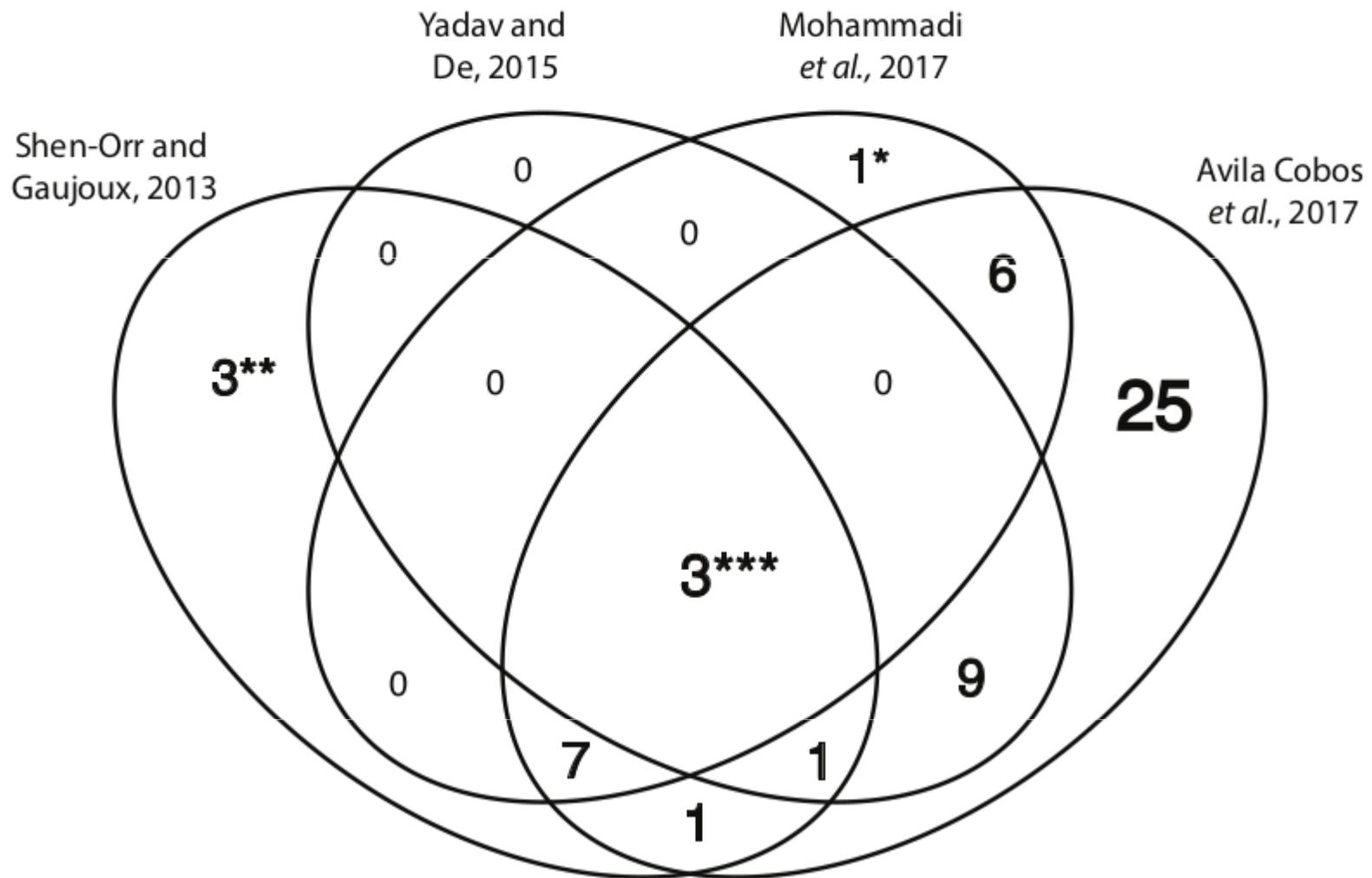
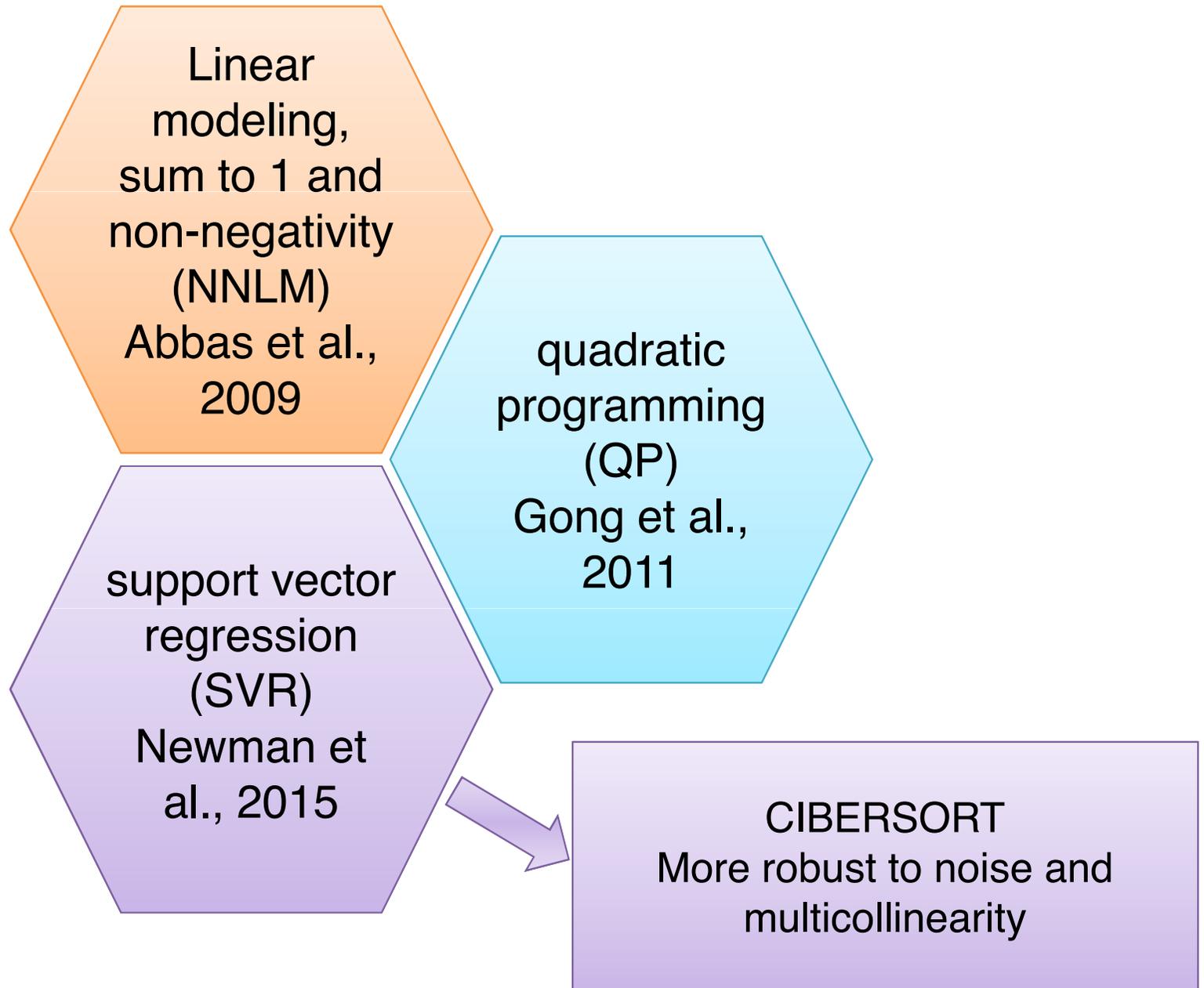
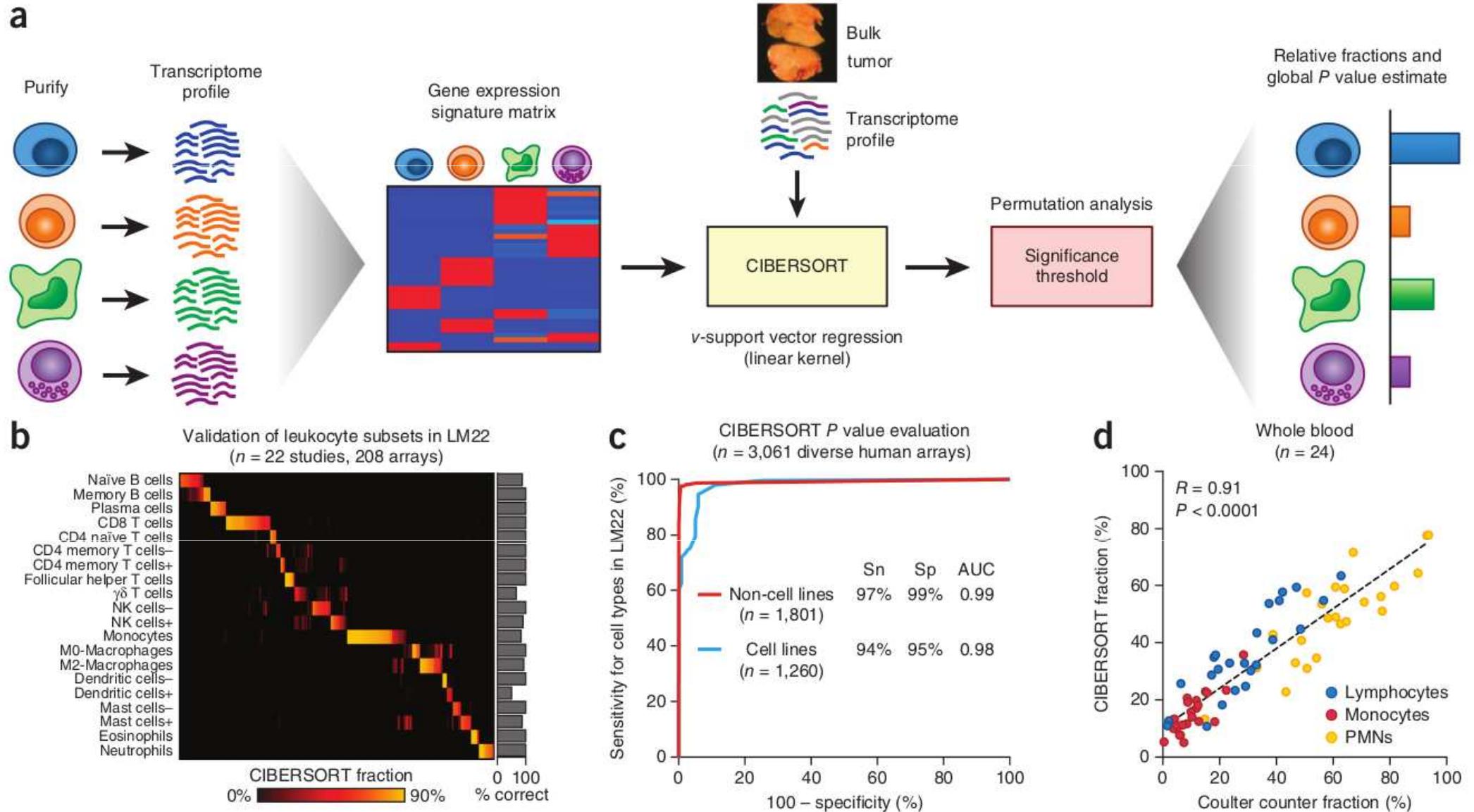


Fig. 1 Venn diagram showing the number of deconvolution methods covered by each review article (using transcriptomics data as input). () We discussed Nano-*

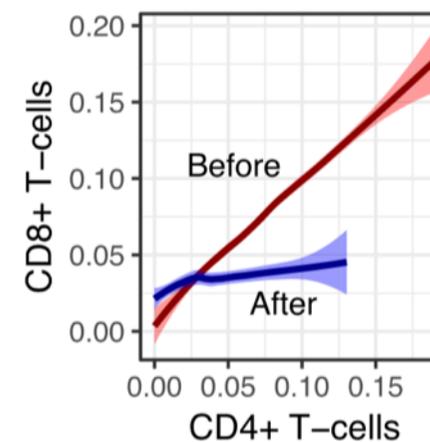
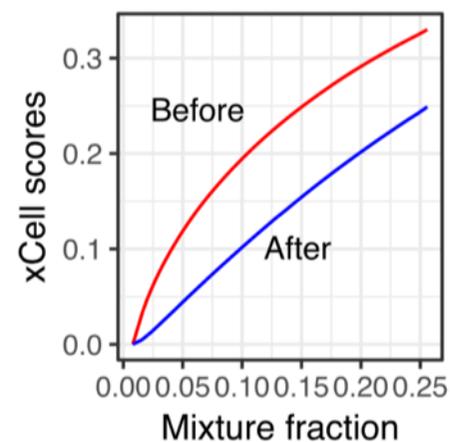
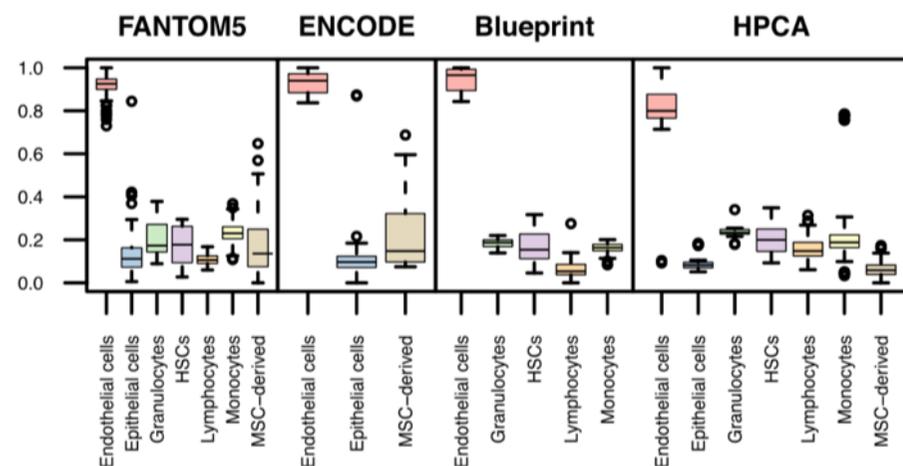
...BASED ON A VARIETY OF APPROACHES



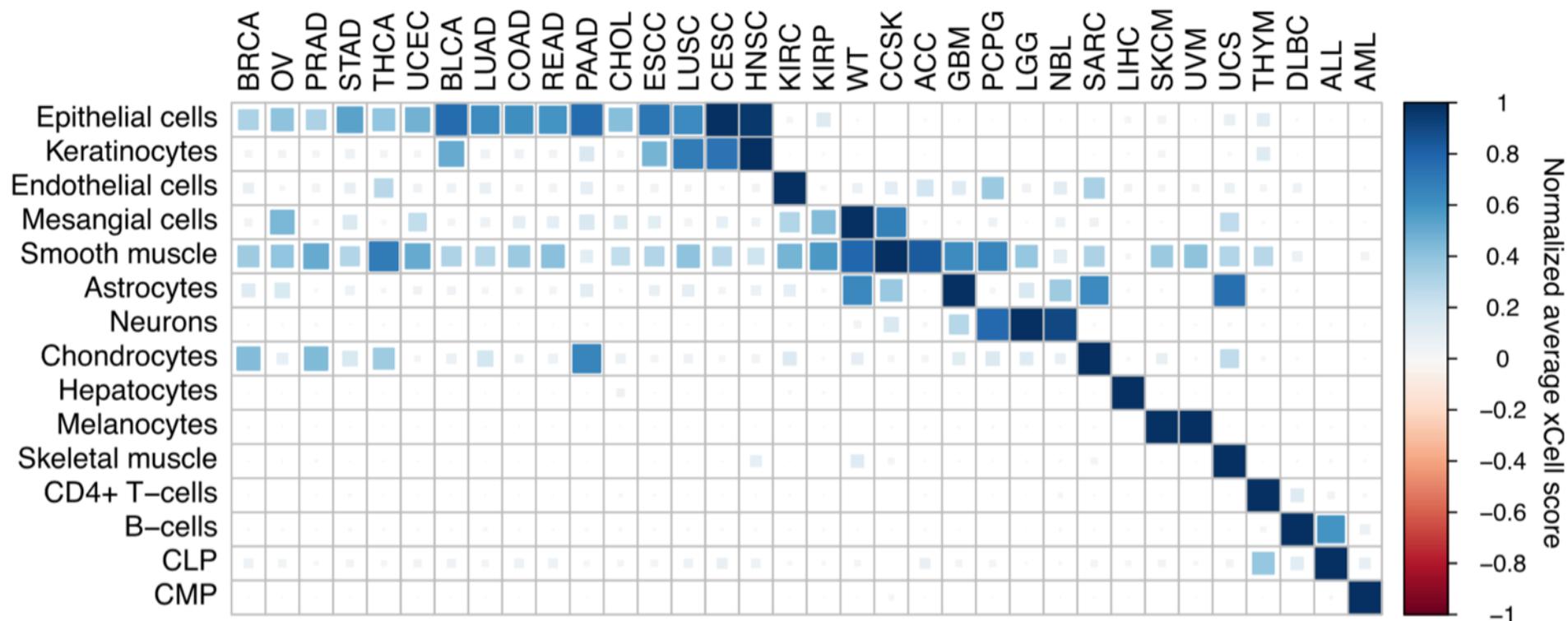
CIBERSORT



ALTERNATIVE METHOD USING RANK BASED ENRICHMENT ANALYSIS: XCELL

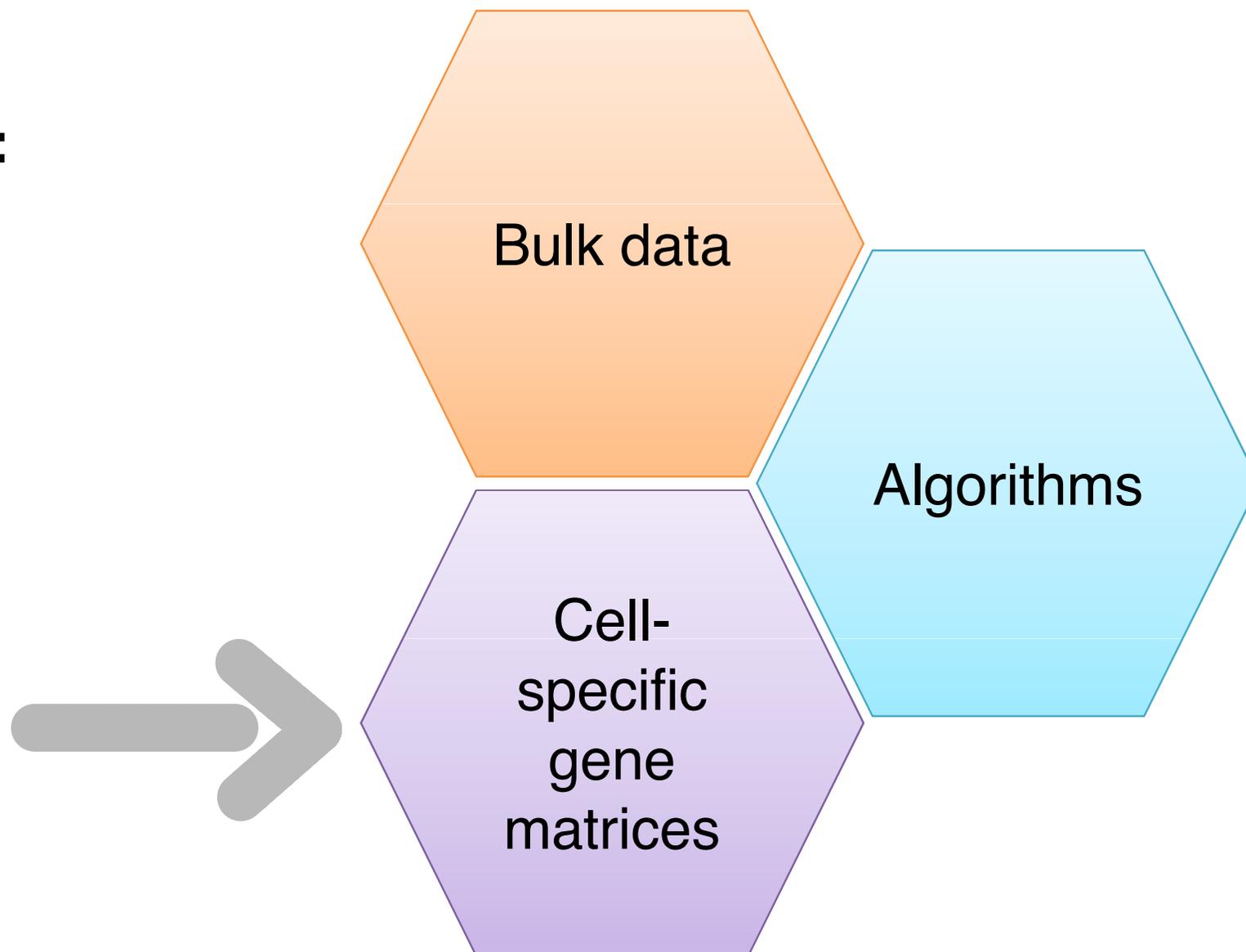


ENRICHMENT OF TUMOR-SPECIFIC CELL TYPES IN TCGA

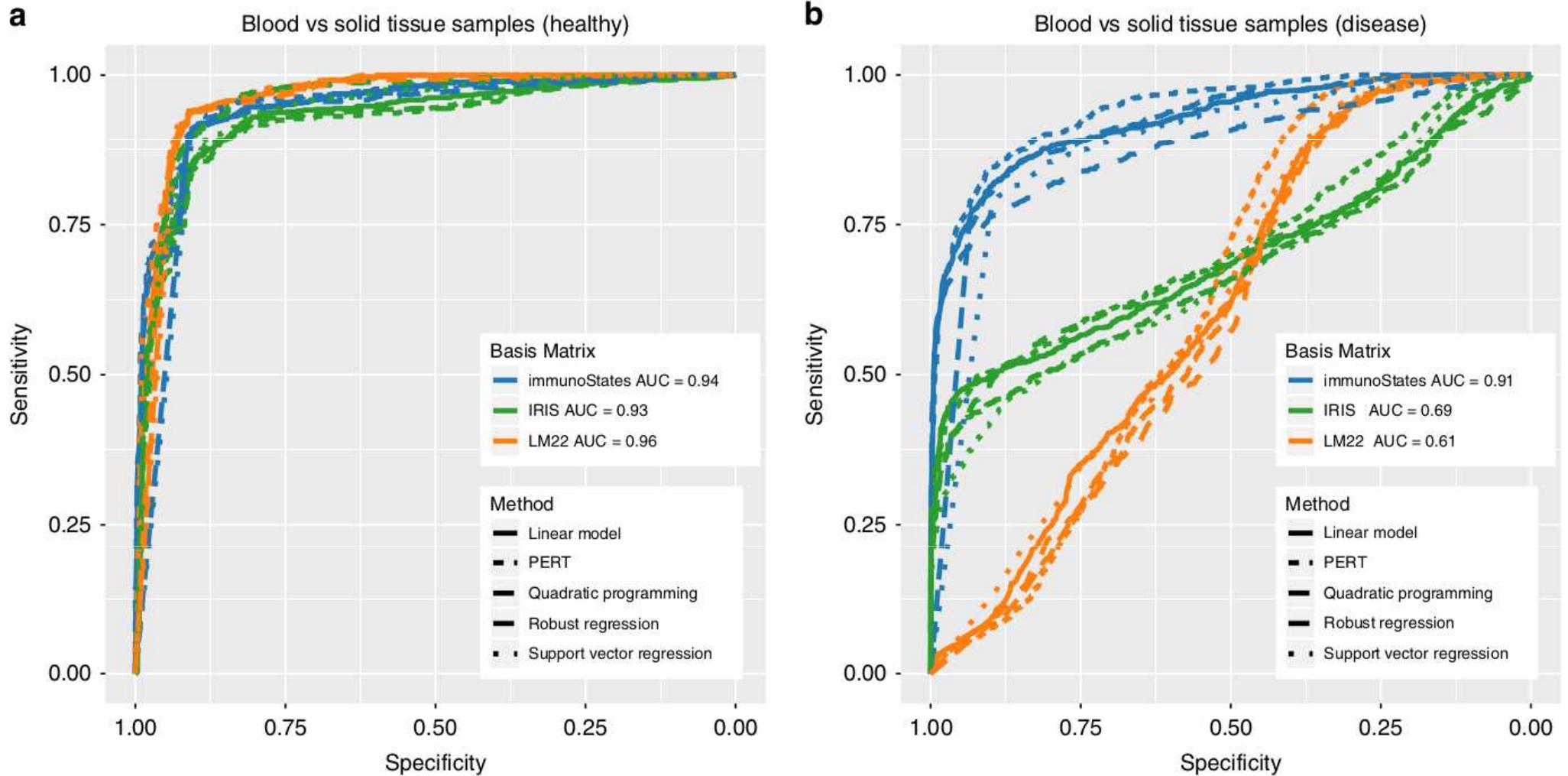


BULK TRANSCRIPTOMICS DATA DECONVOLUTION

BASED ON:

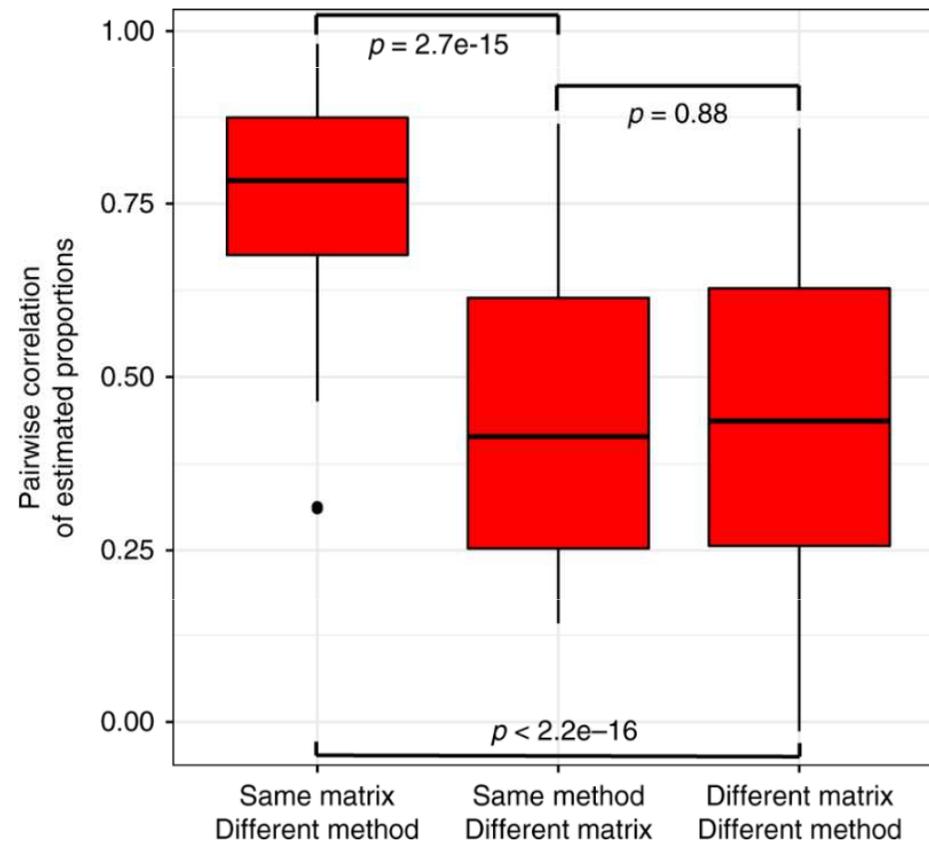


IMMUNOSTATES: A GENE MATRIX LEVERAGING HETEROGENEITY AND DISEASE CONDITIONS

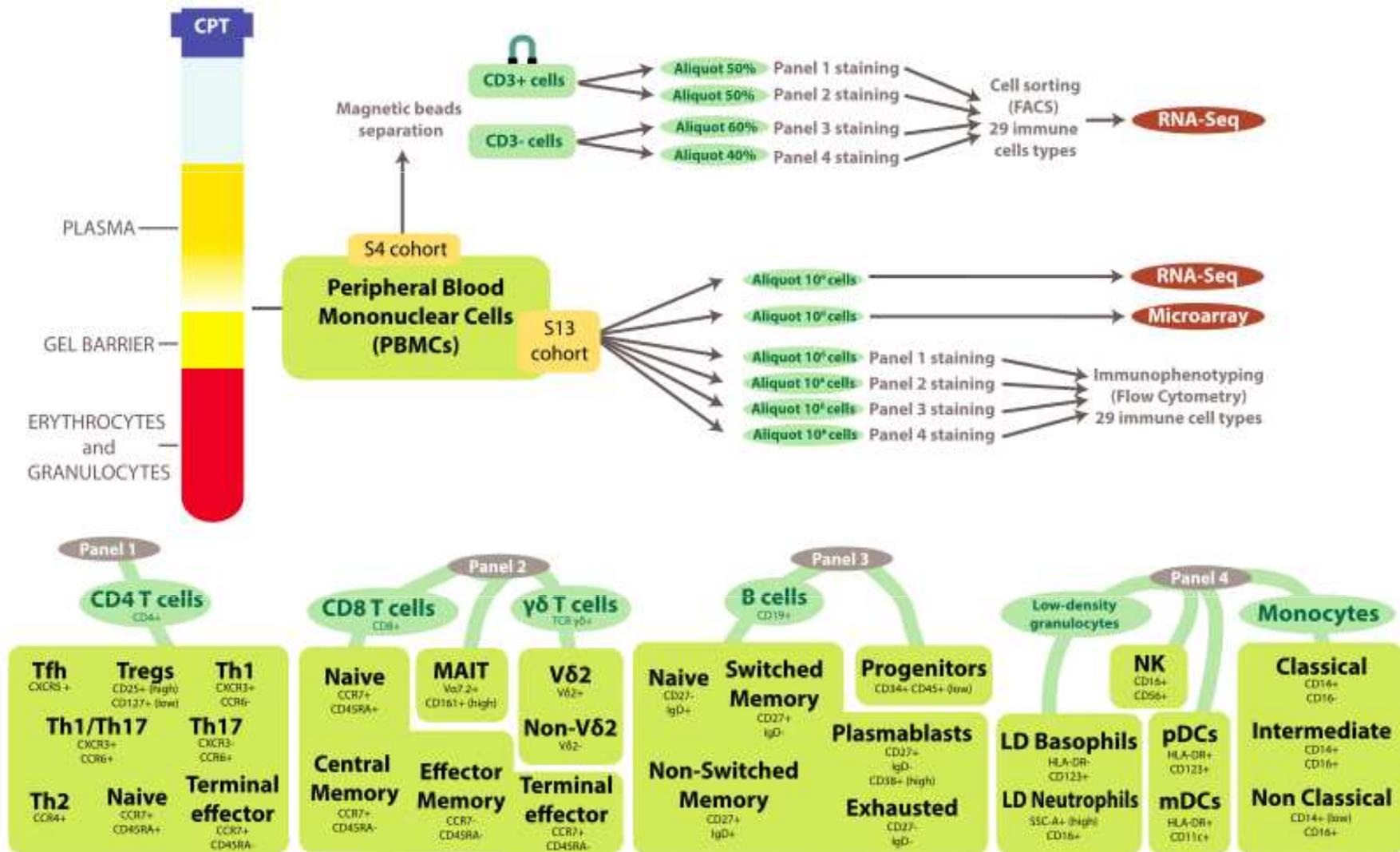


THE QUALITY OF THE RESULTS DEPENDS MORE ON THE GENE MATRICES THAN ON THE ALGORITHMS

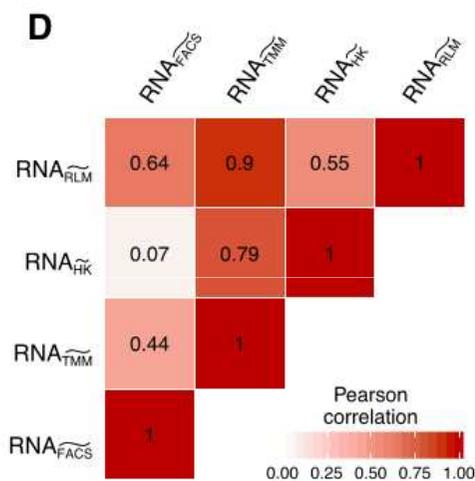
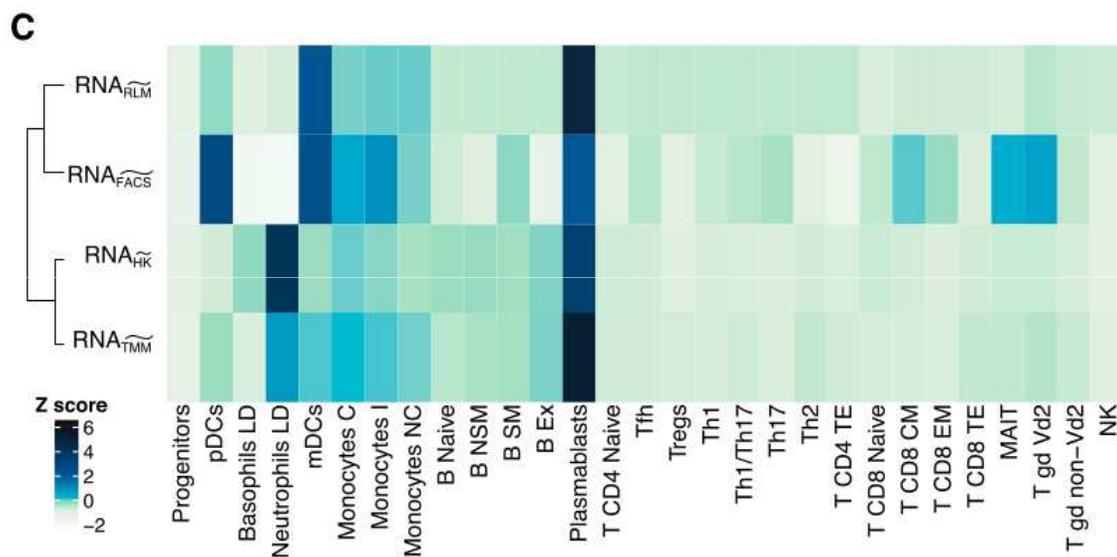
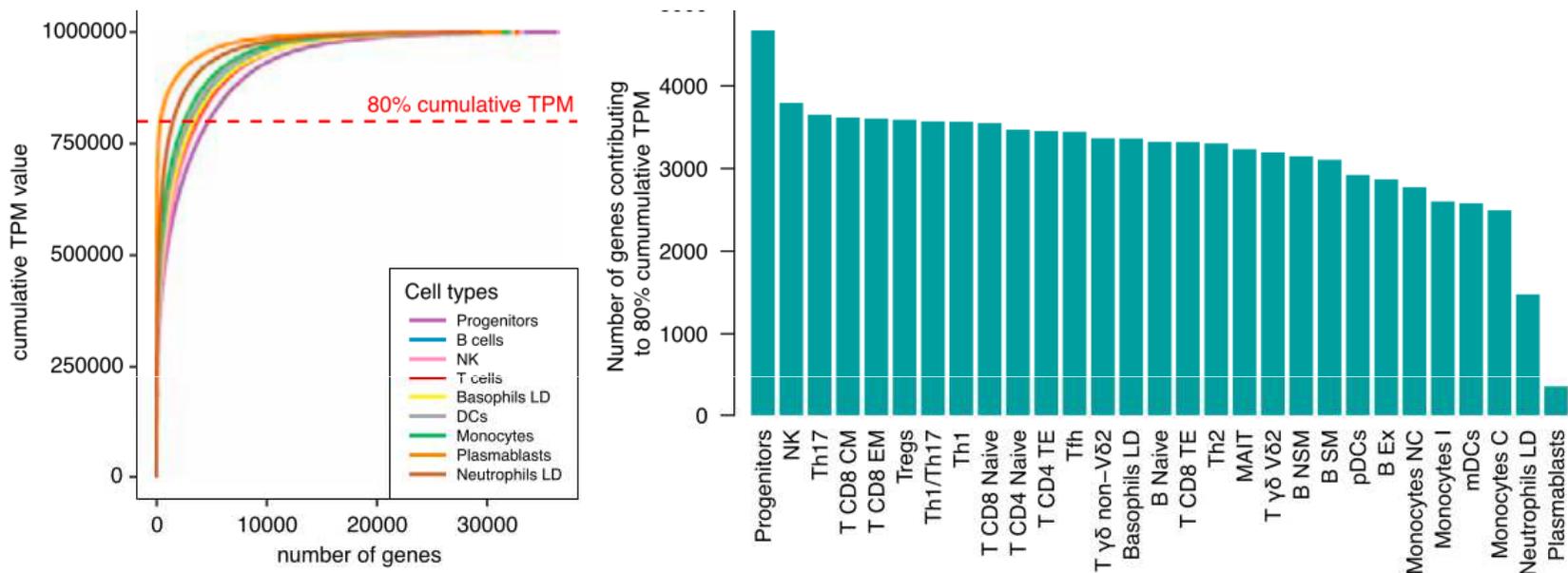
DECONVOLUTION CONCORDANCE BY MATRIX AND METHOD:



CHARACTERIZATION OF 29 HUMAN IMMUNE CELL TYPES BY RNA-SEQ AND FLOW CYTOMETRY

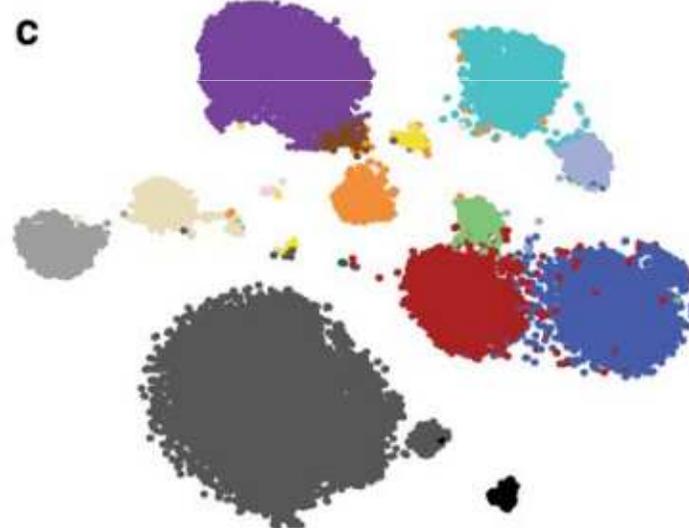
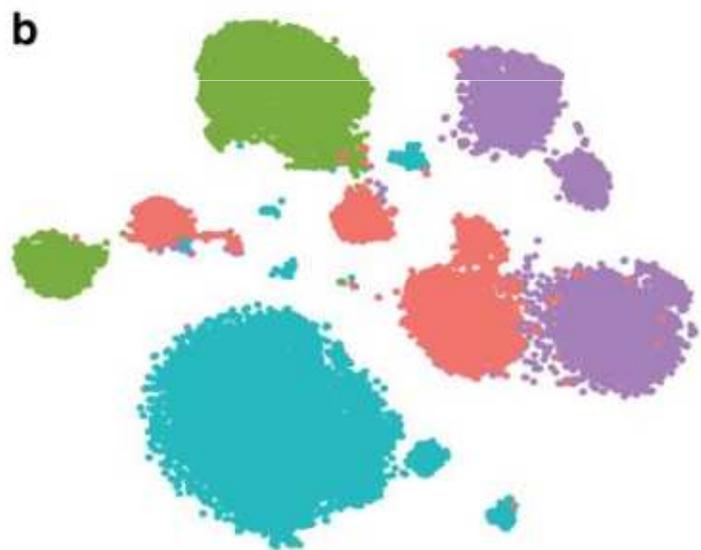
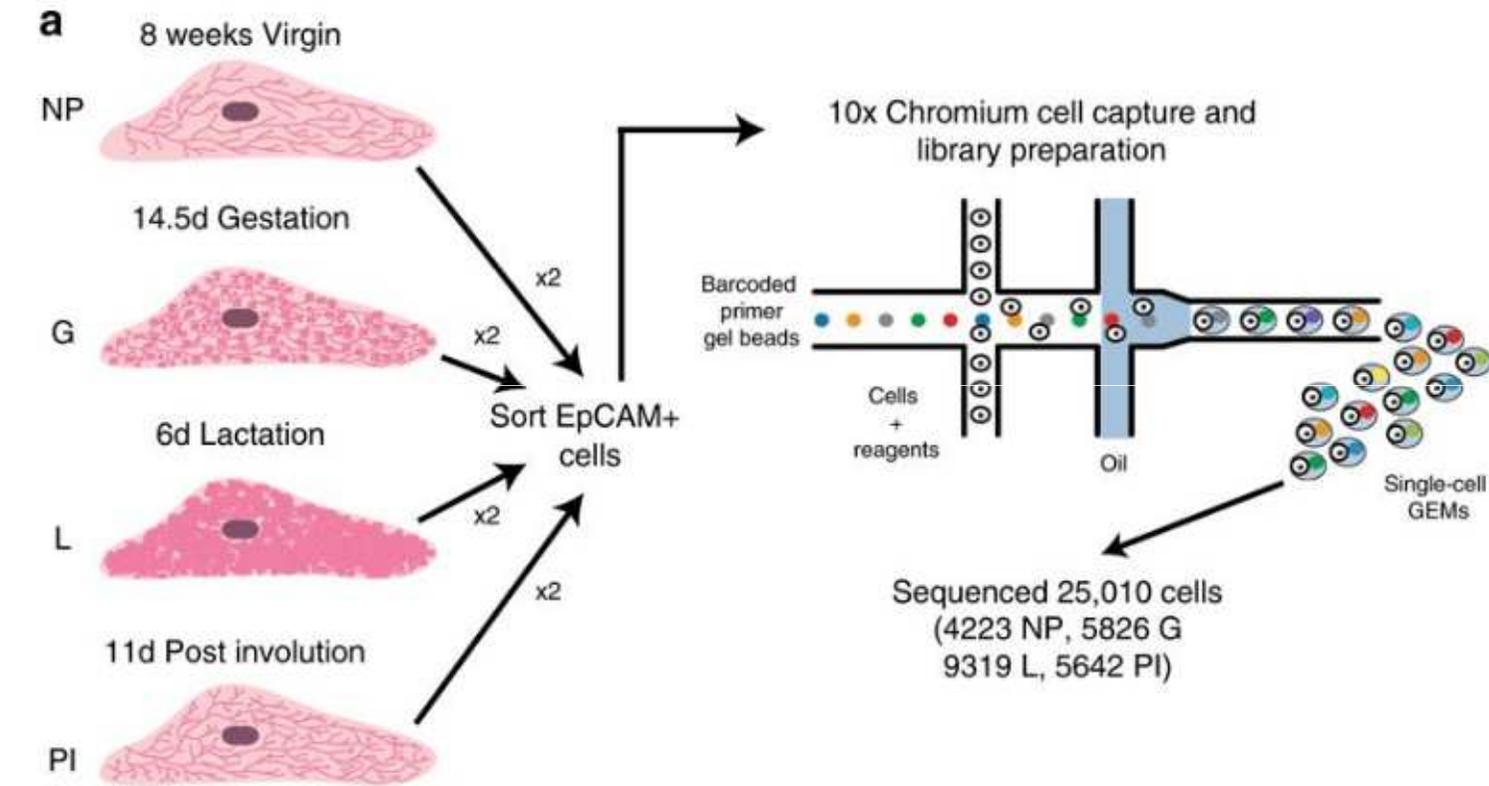


THE ENDLESS PROBLEM OF NORMALIZATION



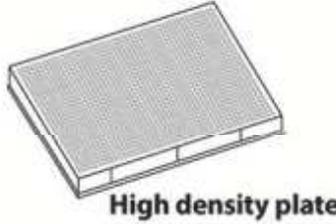
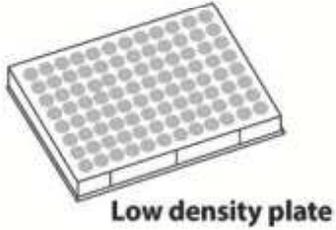
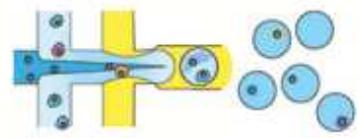
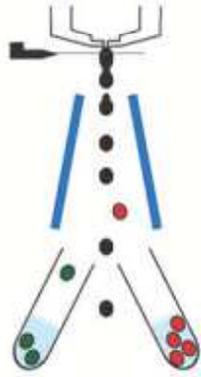
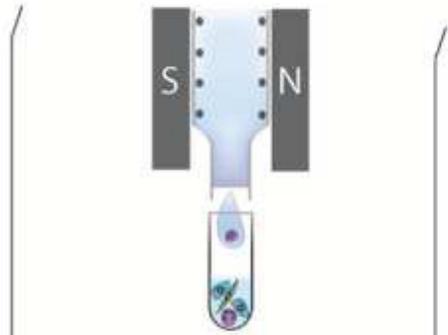
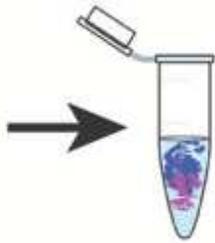
BEST APPROACH: scale the TPM values by a factor that minimizes the error between flow cytometry and deconvolution proportions

SINGLE CELL SEQUENCING



UPCOMING METHODS

-  PCR amplification
-  IVT amplification
-  3'-RNAseq
-  Full-length RNAseq
-  UMIs
-  Cost
-  Labor intensity



- Drop-Seq/DroNc-seq**
- inDrop**
- Chromium 10X**
- MARS-seq**
- CEL-seq2**
- SMART-seq2**
- Nano SN-RNAseq**
- Seq-well**
- Microwell-seq**
- SciRNA-seq**
- Split-seq**

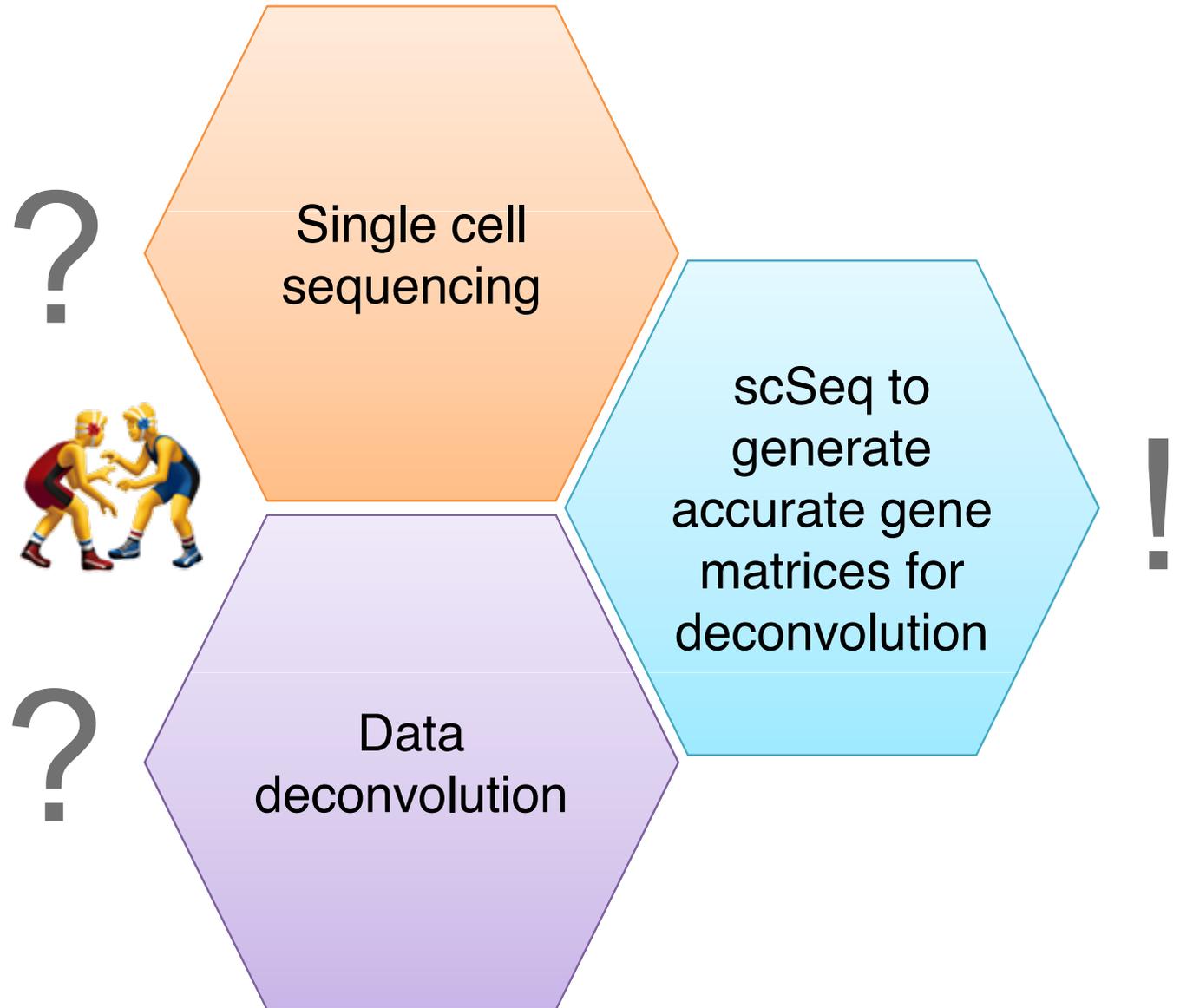
Single cell/ nucleus preparation of complex tissue

Cell labeling and/or separation/enrichment

Cell capture and barcoding

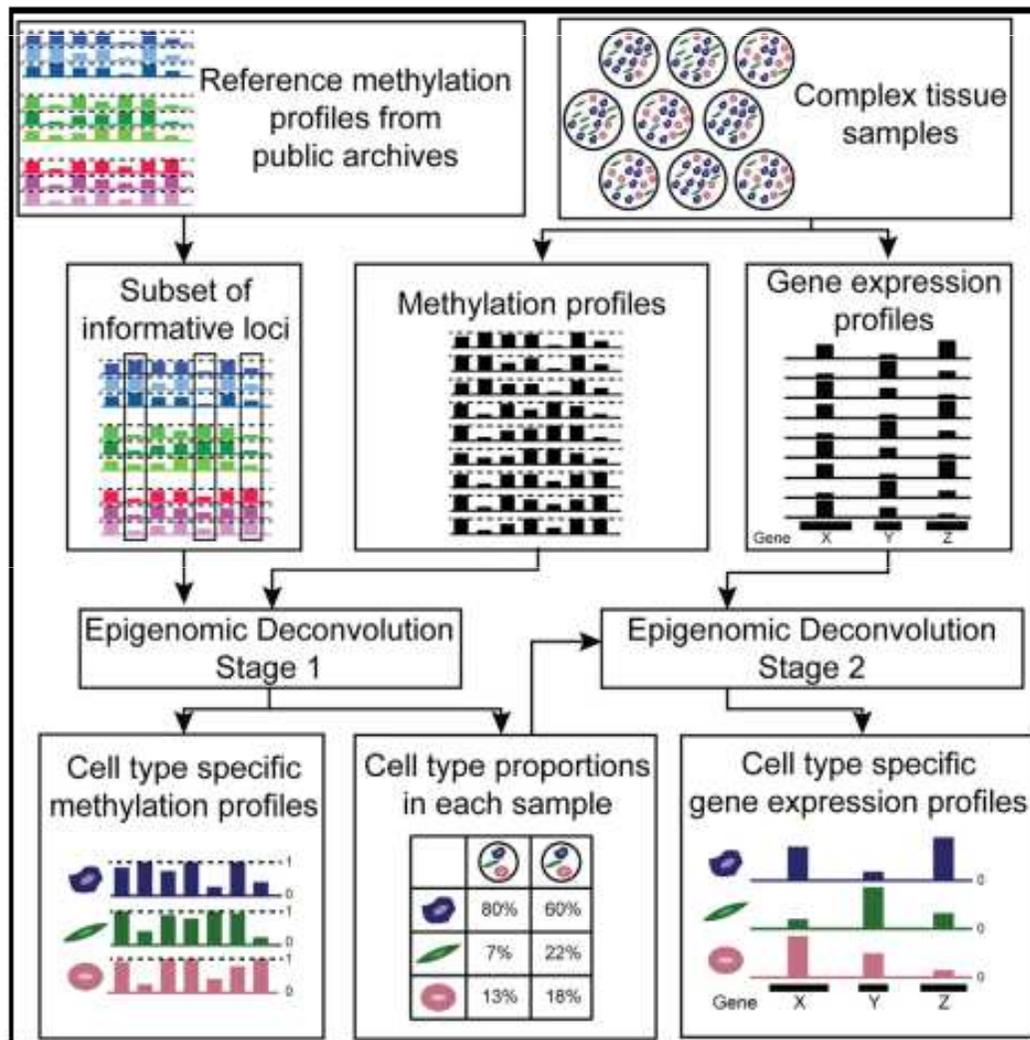
Valdes-Mora F et al (2018) Front. Immunol. 9:2582.

THE FUTURE



Epigenomic Deconvolution of Breast Tumors Reveals Metabolic Coupling between Constituent Cell Types

Graphical Abstract



Authors

Vitor Onuchic, Ryan J. Hartmaier, David N. Boone, ..., Matt E. Roth, Adrian V. Lee, Aleksandar Milosavljevic

Correspondence

onuchic@bcm.edu (V.O.), amilosav@bcm.edu (A.M.)

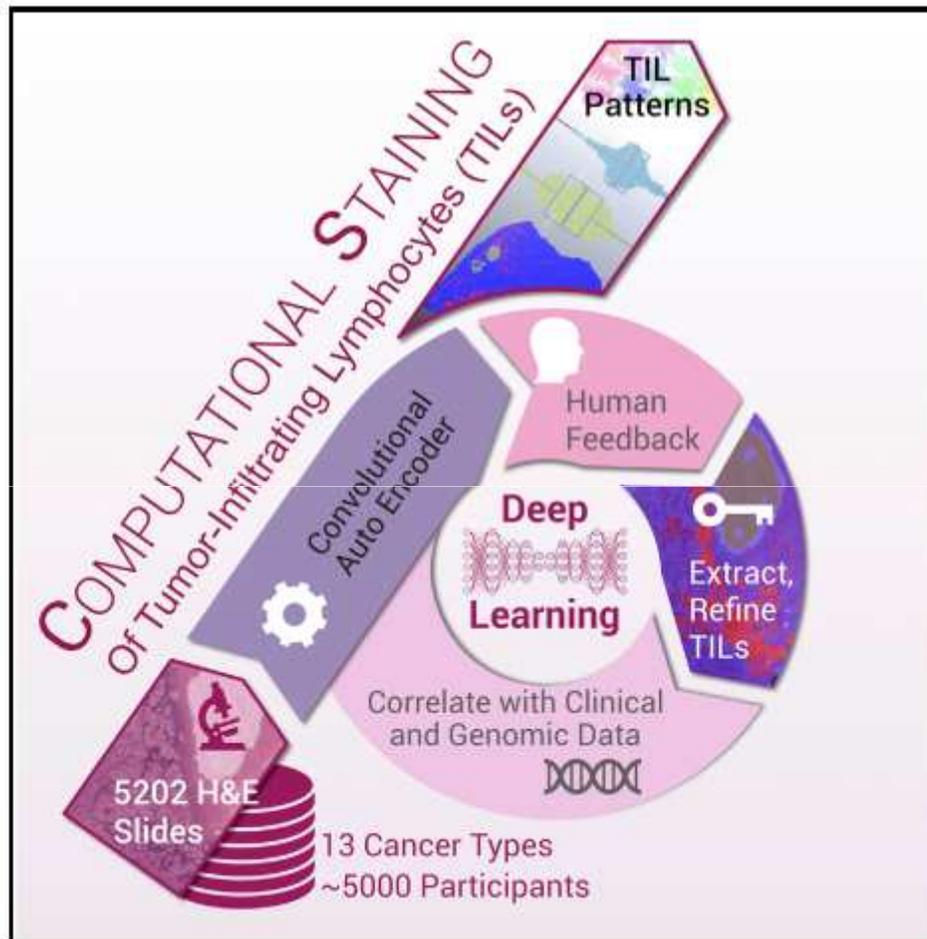
In Brief

Onuchic et al. develop an in silico deconvolution technique (EDec) that can accurately estimate cell type composition and molecular profiles of constituent cell types in the context of breast tumors. Application to breast cancers from TCGA data reveals association between stromal composition and the metabolic phenotype of breast tumors. Explore consortium data at the Cell Press IHEC webportal at www.cell.com/consortium/IHEC.

Cell Reports

Spatial Organization and Molecular Correlation of Tumor-Infiltrating Lymphocytes Using Deep Learning on Pathology Images

Graphical Abstract



Authors

Joel Saltz, Rajarsi Gupta, Le Hou, ...,
Alexander J. Lazar, Ashish Sharma,
Vésteinn Thorsson

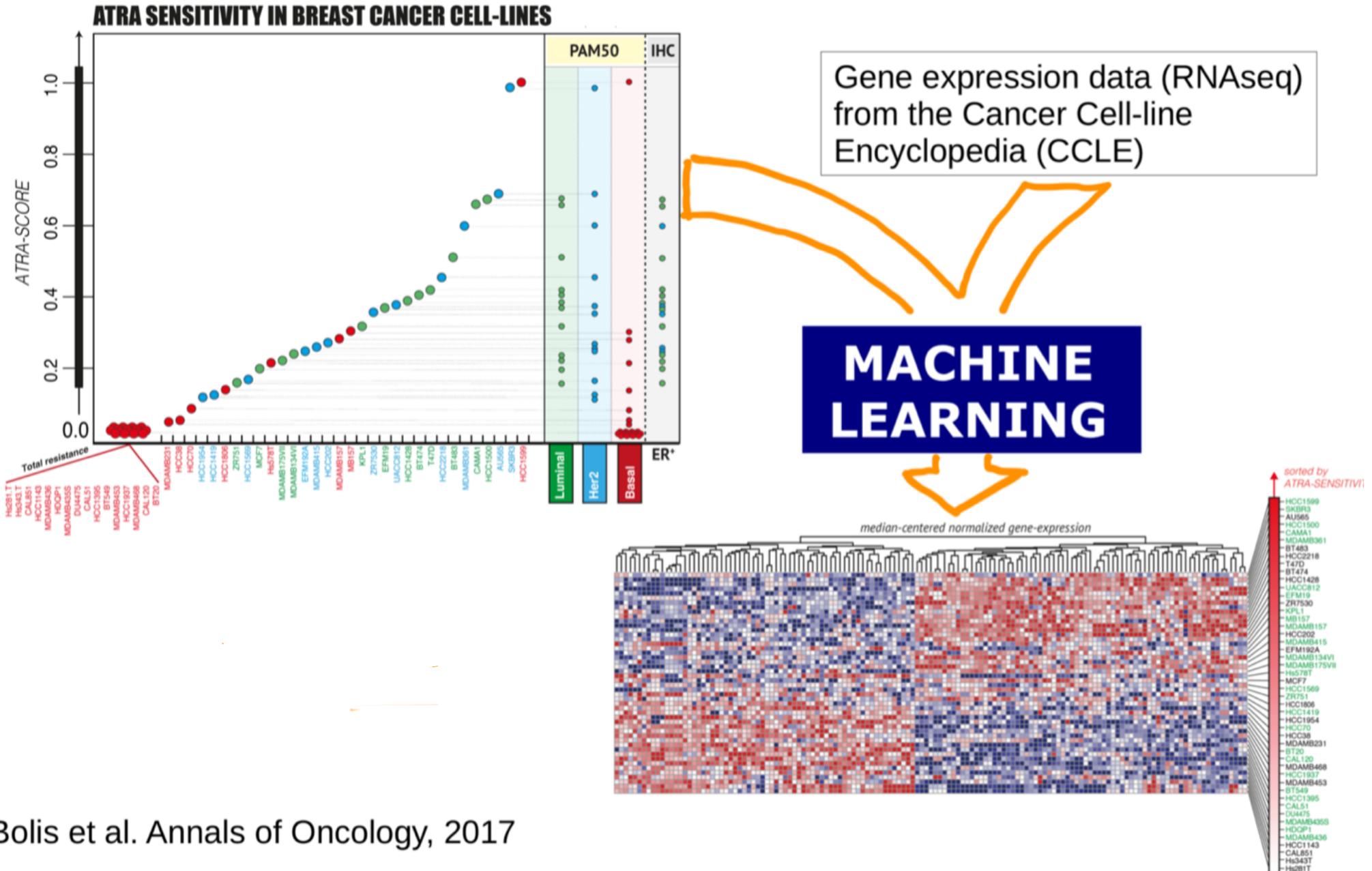
Correspondence

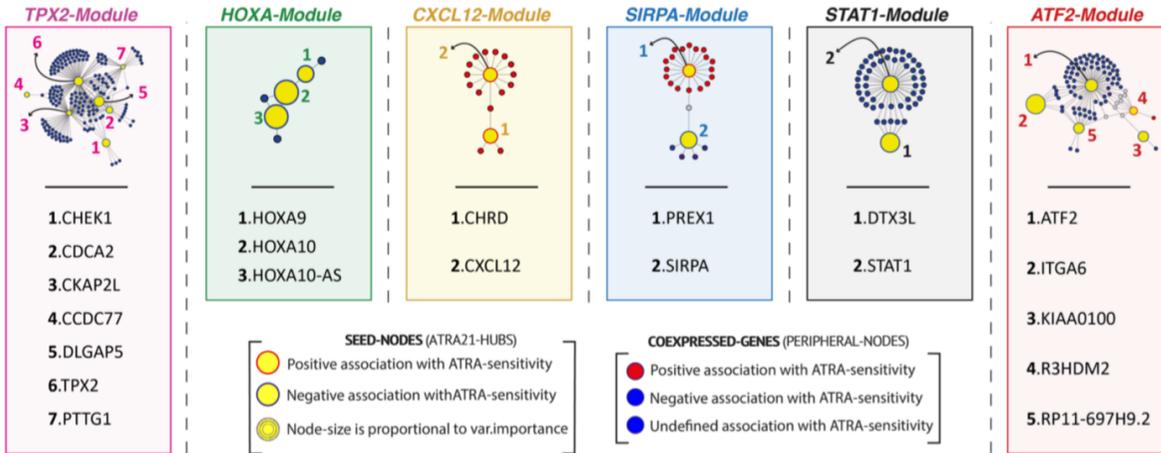
joel.saltz@stonybrookmedicine.edu
(J.S.),
vesteinn.thorsson@systemsbiology.org
(V.T.)

In Brief

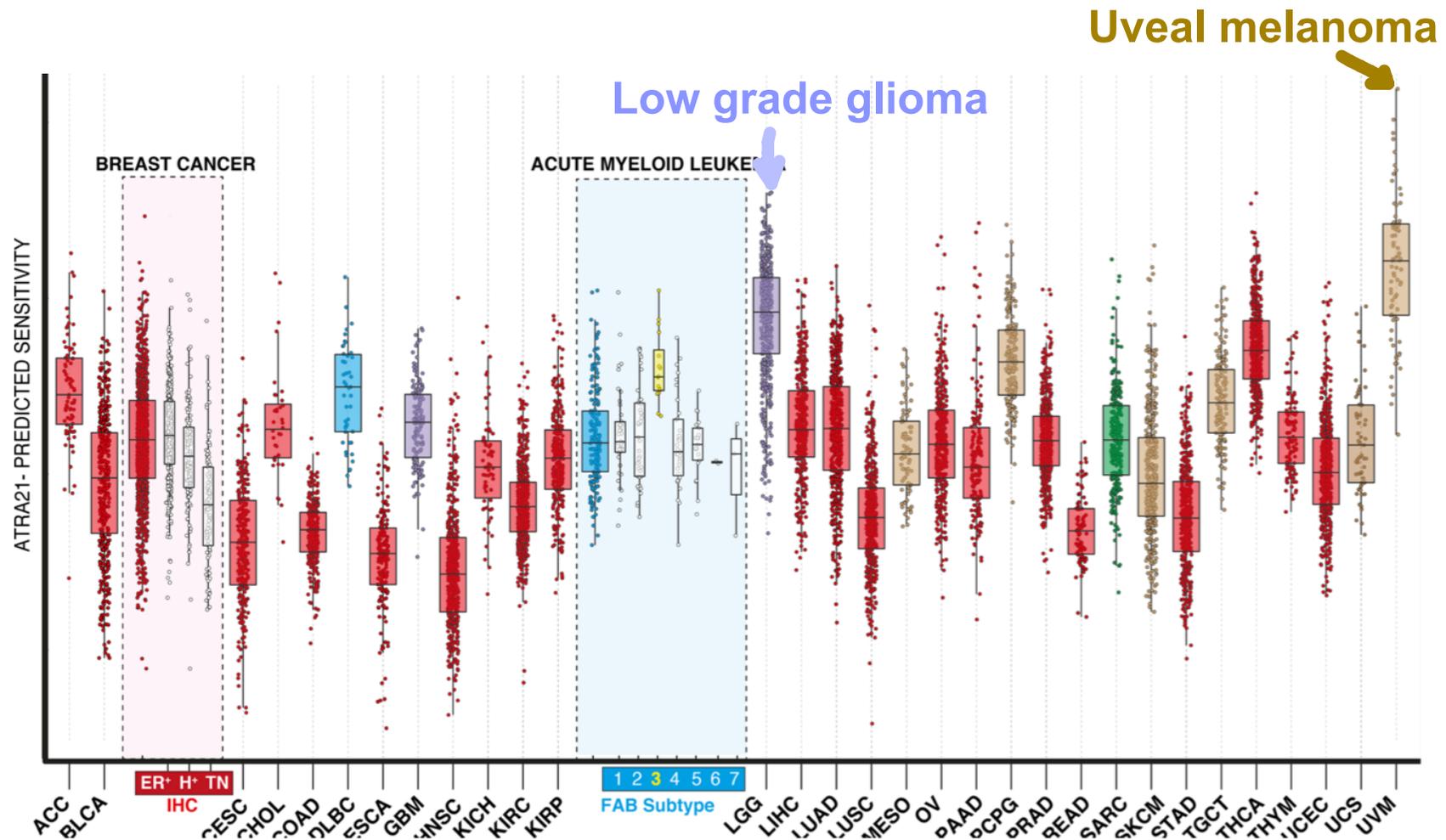
Tumor-infiltrating lymphocytes (TILs) were identified from standard pathology cancer images by a deep-learning-derived “computational stain” developed by Saltz et al. They processed 5,202 digital images from 13 cancer types. Resulting TIL maps were correlated with TCGA molecular data, relating TIL content to survival, tumor subtypes, and immune profiles.

DEVELOPMENT OF A GENE EXPRESSION-BASED MODEL OF RETINOIC ACID SENSITIVITY





ATRA-21 GENES AND PREDICTIONS IN TCGA TUMORS



LAB MEMBERS

Molecular Biology Lab:

Gabriela Paroni
Adriana Zanetti
Federica Biancardi
Mineko Terao
Maurizio Gianni
Mami Kurosaki
Enrico Garattini

Pharmacogenomics Unit:

Alessandra Castagna
Arianna Vallerga
Giada Cassanmagnago
Martina Troiani
Enrico Cabri
Marco Bolis
Maddalena Fratelli

COLLABORATORS

Tiziana Castrignanò
CINECA-Consortio Interuniversitario per il
Calcolo Automatico, Roma



Linda Pattini
Marco Masseroli
Department of Electronics, Information and
Bioengineering, Politecnico di Milano



data access: project #9522
'Retinoid-based anti-tumor strategies'

FUNDING



FONDAZIONE
ANTONIO CARLO MONZINO

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