LUXEMBOURG
INSTITUTE
OF HEALTH

Combination of Multi-modal Data for Improved Patient Characterization

Petr Nazarov

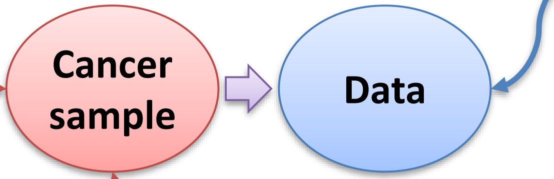
5th course on Computational Systems Biology of Cancer
September 26-30, 2022 – Institut Curie, Paris, France

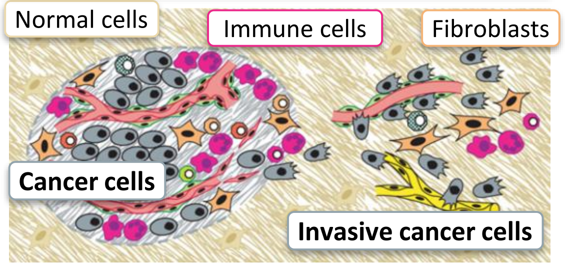
Heterogeneity

Levels of Heterogeneity in Samples of Cancer Patients

Native h. of biological tissues

Technical heterogeneity

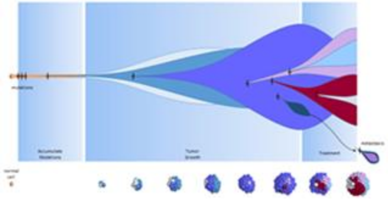




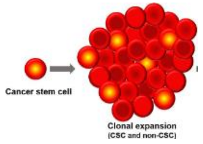
Hanahan, Weinberg. ***Cell* 2011**, 144, 646-74

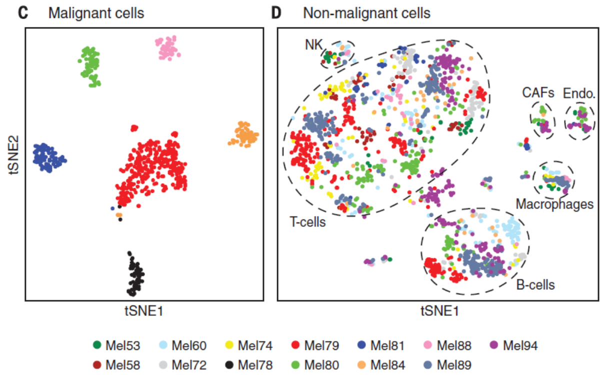
Inter- and intra-tumor heterogeneity

Clonal evolution

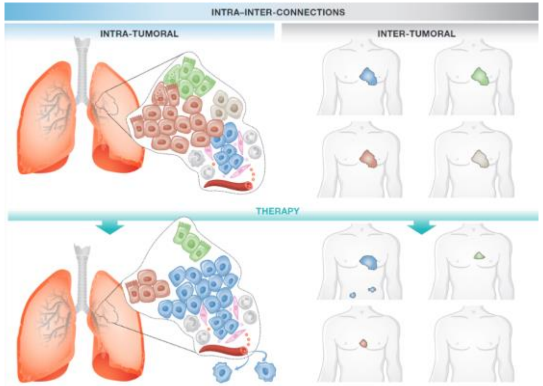


Cancer stem-cells



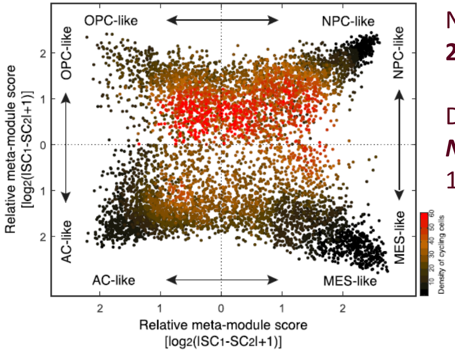


Tirosh, et al. ***Science* 2016**, 352(6282):189



De Sousa E Melo, et al. ***EMBO* 2013**, 14(8):686

Cell plasticity

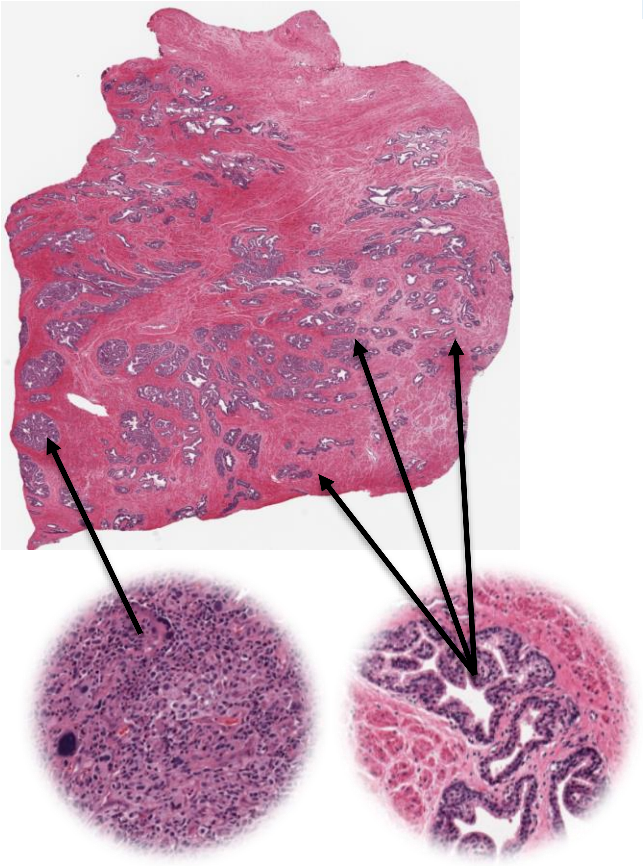


Neftel, et al. ***Cell* 2019**, 178:835

Dirkse, et al.
***Nat Commun* 2019**,
10:1787

Invasive Approach 1: Histopathology

Hematoxylin and Eosin (H&E) stain



Tumor: 1%

Normal: 99%

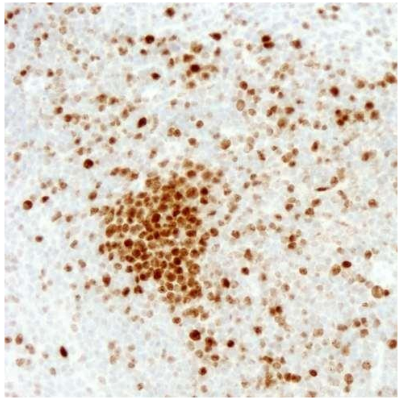
Features of histopathology

- Gold standard!
- Cheap (H&E or 2-3 antibodies in IHC)
- Captures native heterogeneity of tissues
- Shows inter/intra tumor heterogeneity
- Often allows precise diagnostics

Issues in histopathological image analysis:

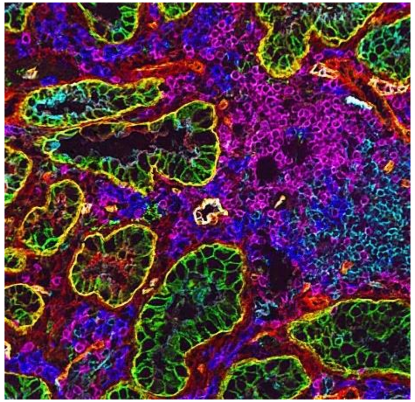
- Tedious analysis
- In some cancers (e.g. prostate) < 1% of the image is cancer-related
- For some cancers, it does not allow precise diagnostics (e.g. some astrocytomas vs oligodendrogliomas)
- Gives non-structured data

Immunohistochemistry (IHC)



Ki-67 - proliferation marker

Multicolor IHC



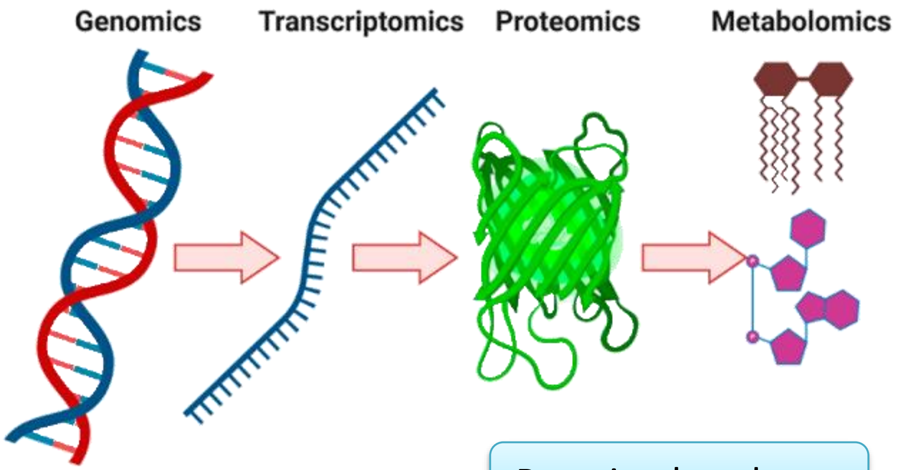
Invasive Approach 2: Molecular Profiling

Mutations

Copy-number variation (CNV)

Chimeric genes

Methylation



Gene expression

Isoform detection

Protein abundance

Chimeric proteins

Abundance of metabolites

Features of molecular approach

- Very specific
- Generate a lot of data
- Generate structured data

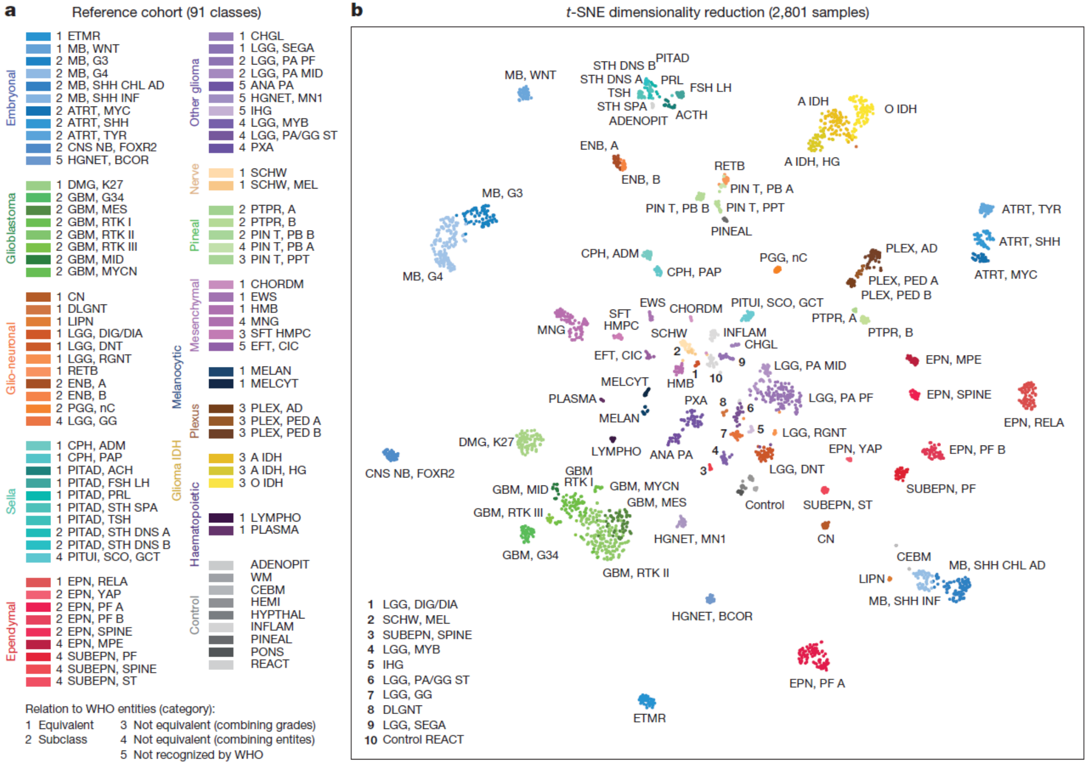
Issues of molecular approach

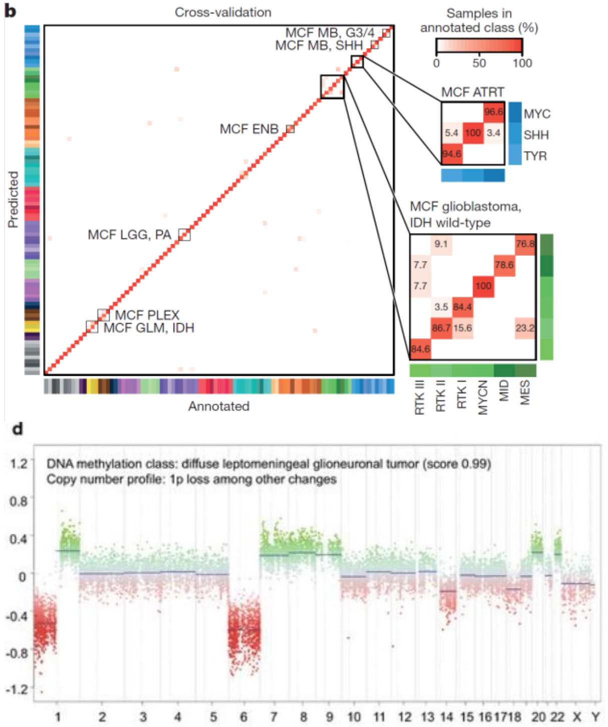
- Quite expensive
- Is sensitive to heterogeneity of samples
- Is sensitive to a technique

Image: Raja et al https://www.mdpi.com/1422-0067/22/3/1160/htm

Molecular Profiling: Example

DNA methylation-based classification of central nervous system tumours





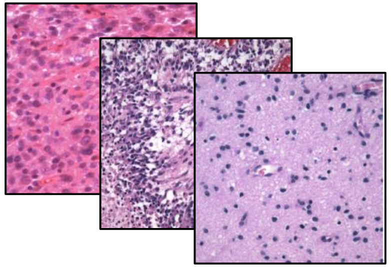
- ➢ Methylation showed more specificity than histopathology identifying types of brain tumors
- ➢ Highly standardized pipeline allowed analysis across many cohorts
- ➢ **Result**: "Heidelberg classifier“ is used by pathologists ☺

Capper et al. ***Nature* 2018**, 555(7697):469

Capper et al. ***Acta Neuropathologica* 2018**, 136:181

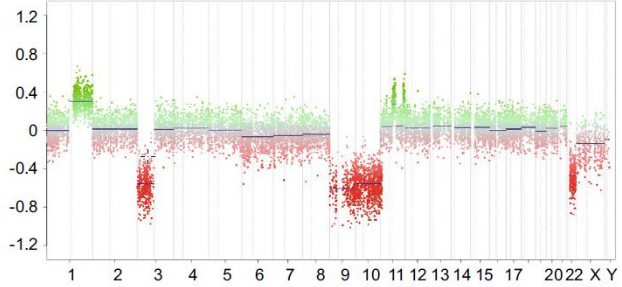
Improvements

1. Histopathology



- Automate analysis
- Transform unstructured data (images) to structured (features)

2. Molecular methods

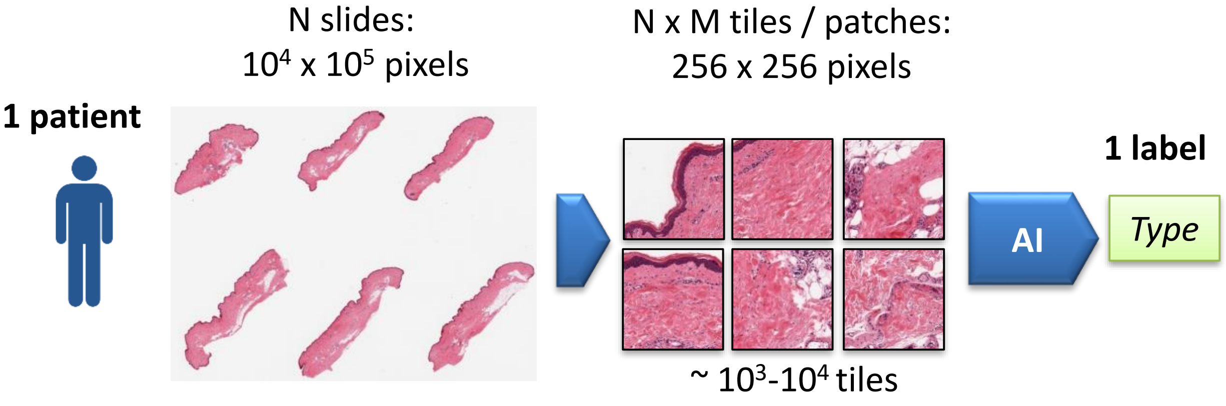


- Deconvolute mixed signals
- Integrate various molecular data

Integrate both approaches for better patient diagnostics and studying molecular processes

1. Digital Histopathology and Feature Extraction

The Task



N slides: 10^4 x 10^5 pixels

N x M tiles / patches: 256 x 256 pixels

1 patient

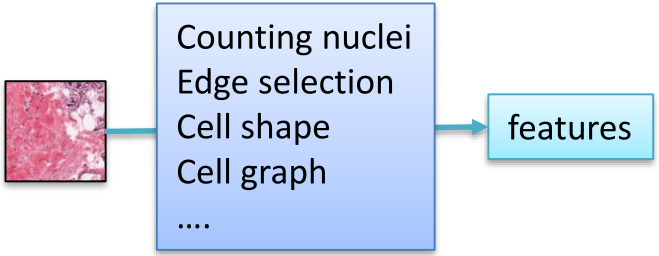
~ 10^3-10^4 tiles

AI

1 label

Type

Classical image analysis approaches

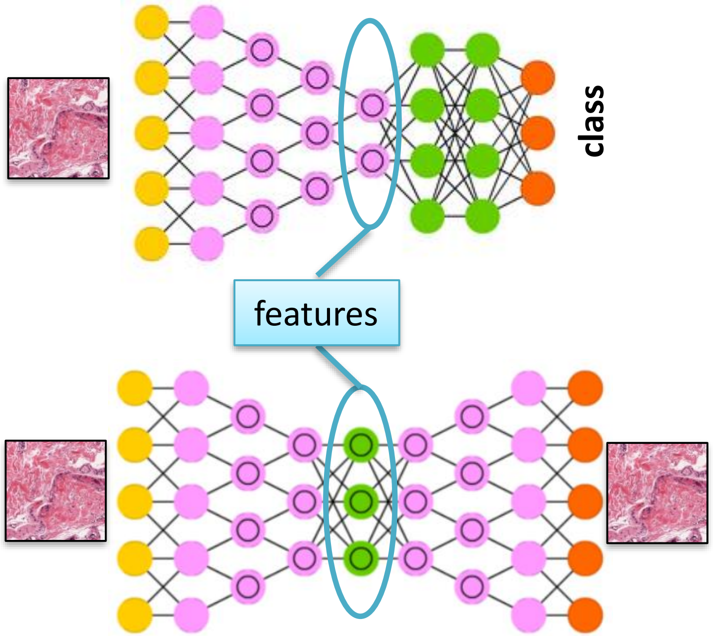


Counting nuclei
Edge selection
Cell shape
Cell graph
….

features

Deep Artificial Neural Networks

Deep convolutional neural network (CNN)

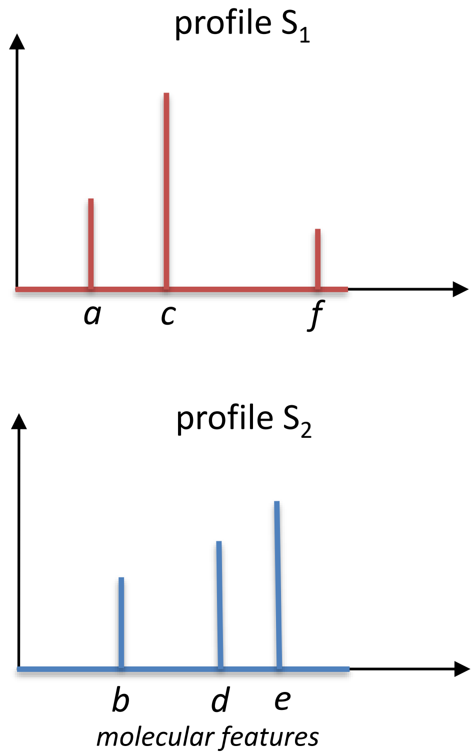


class

features

Convolutional Autoencoder (CAE)

2. Deconvolution: Concept



Mixing →

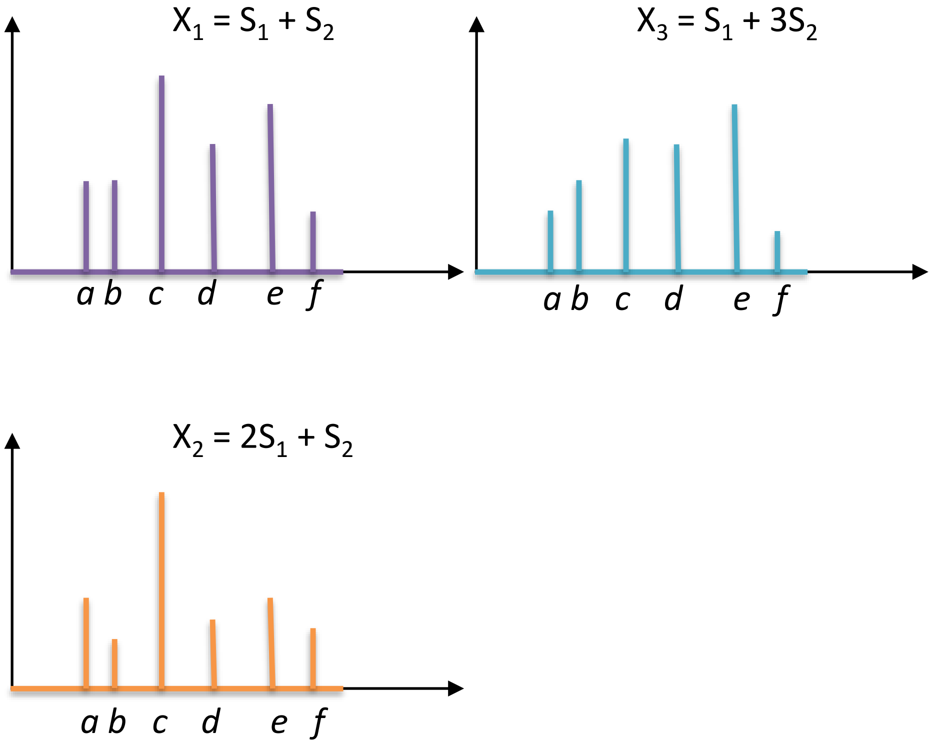
$$\mathbf{X} = \mathbf{S} \times \mathbf{M}$$

$$\mathbf{M} = \begin{array}{|c|c|c|}\hline 1 & 2 & 1 \\ \hline 1 & 1 & 3 \\ \hline\end{array}$$

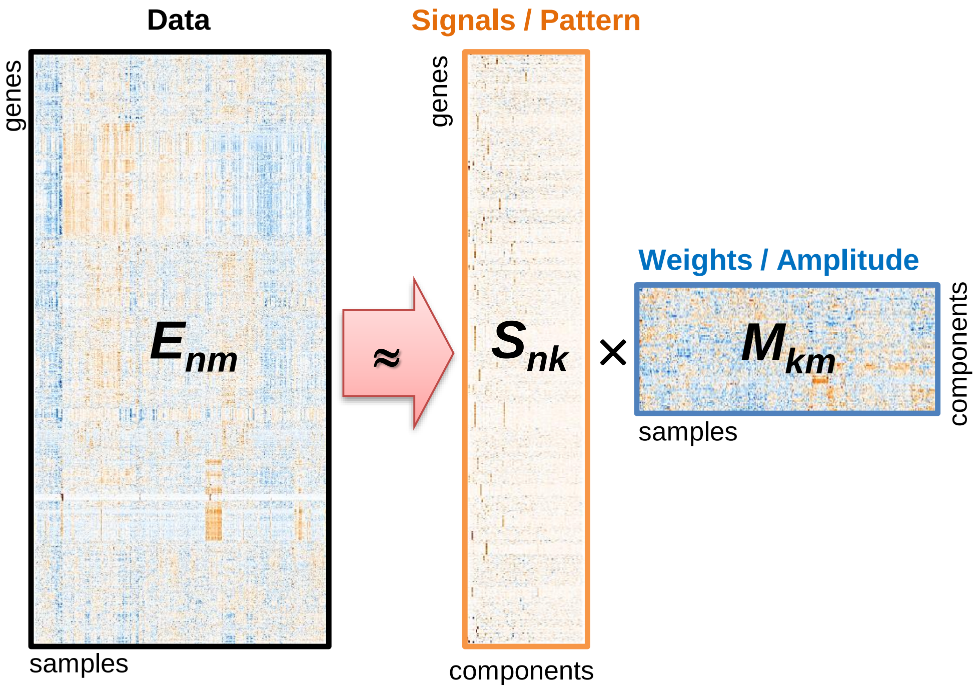
← **De-mixing**

Often called:

- **decomposition**
- **deconvolution**

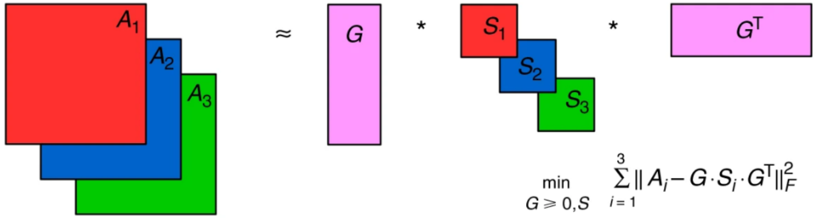


Deconvolution via Matrix Factorization



PCA: principal component analysis
NMF: non-negative matrix factorization
ICA: independent component analysis
etc.

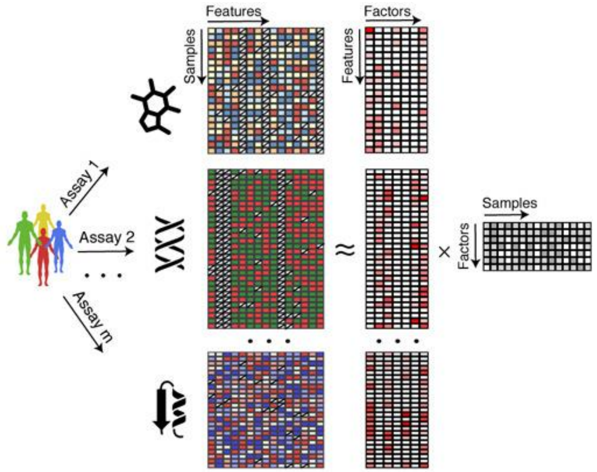
Matrix tri-factorization



$$\min_{G \geq 0, S} \sum_{i=1}^{3} \| A_i - G \cdot S_i \cdot G^T \|_F^2$$

Malod-Dognin et al. ***Nat Commun* 2019**, 10:805

Multi-omics Factor Analysis

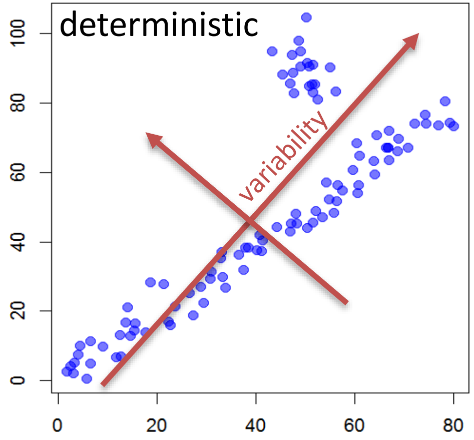


Argelaguet et al. ***Mol Syst Biol* 2018**, 14:e8124

Stein-O'Brien et al. ***Trends in Genetics* 2018**, 34(10):790

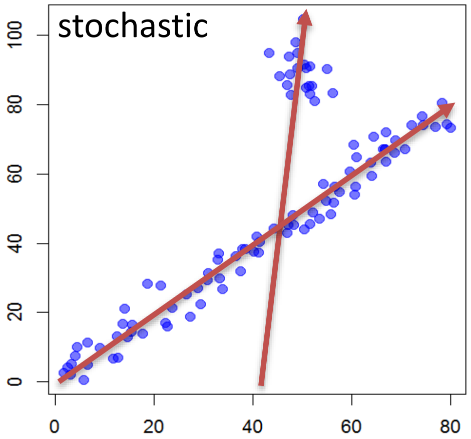
Deconvolution Methods

PCA



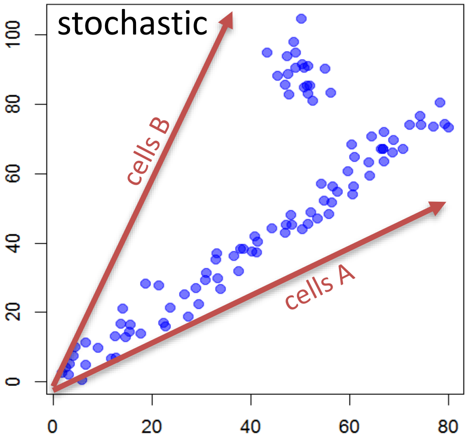
- + deterministic & fast
- + any number of samples
- + unsupervised
- – often biological factors are presented by a sum of several components
- – positive and negative values

ICA



- + **correlates with biology**
- + **unsupervised (agnostic)**
- + **quite stable**
- – stochastic
- – needs a lot of samples
- – positive and negative values

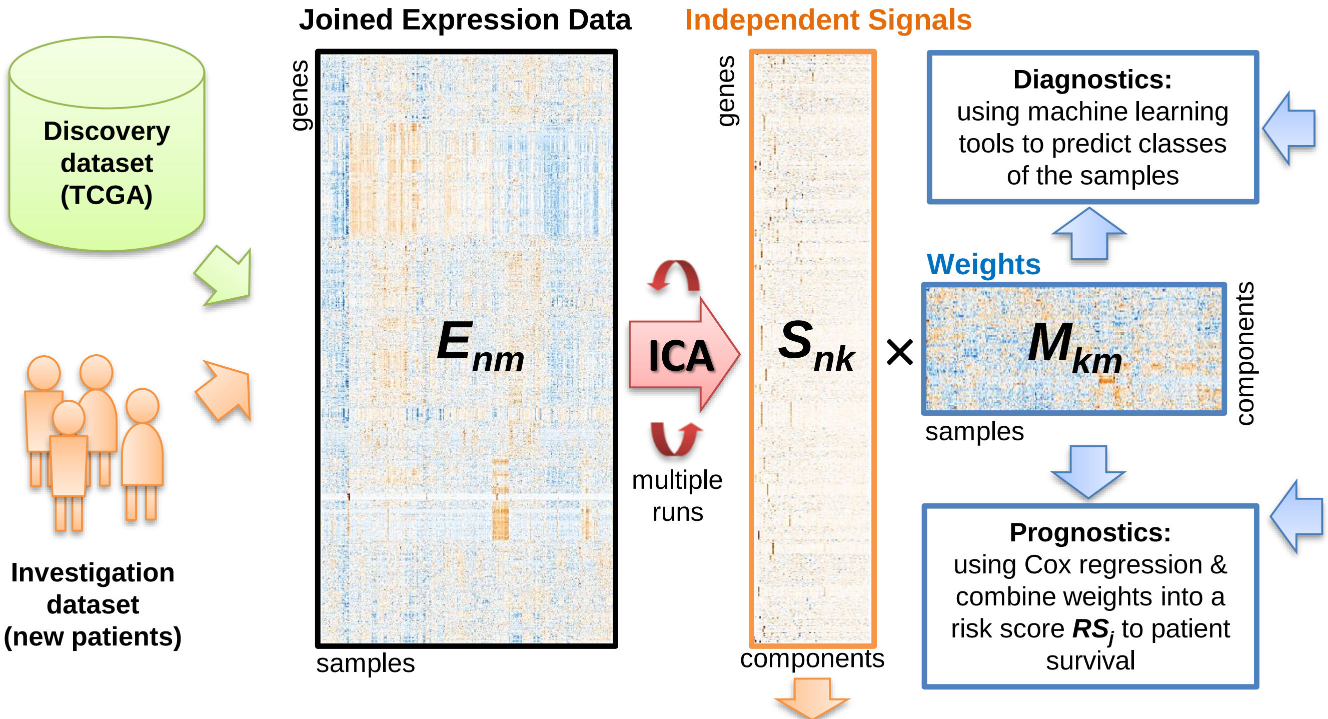
NMF



- + semi-unsupervised
- + easy to interpret
- – stochastic
- – unstable

Sompairac et al, Int J Mol Sci, 2019 (link)
Cantini el al, Bioinformatics, 2019 (link)

Research Focus: Deconvolution of Omics Data

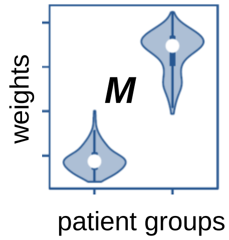


Diagnostics: using machine learning tools to predict classes of the samples

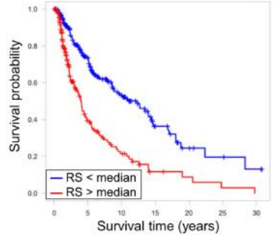
Prognostics: using Cox regression & combine weights into a risk score RS_j to patient survival

Functional annotation: linking components to biological processes and cell types

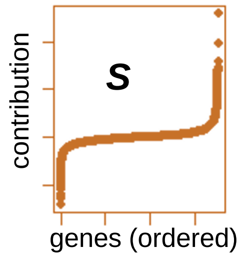
Weights *M* in patient groups



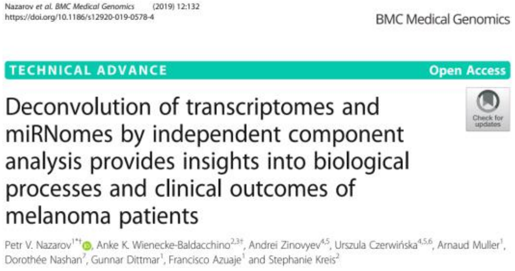
$$RS_j = \sum_{i=1}^{i=k} R_i^2 H_i M^*_{i,j}$$



Genes, contributing to one component



Data driven!


Nazarov *et al. BMC Medical Genomics* (2019) 12:132
https://doi.org/10.1186/s12920-019-0578-4

BMC Medical Genomics

TECHNICAL ADVANCE Open Access

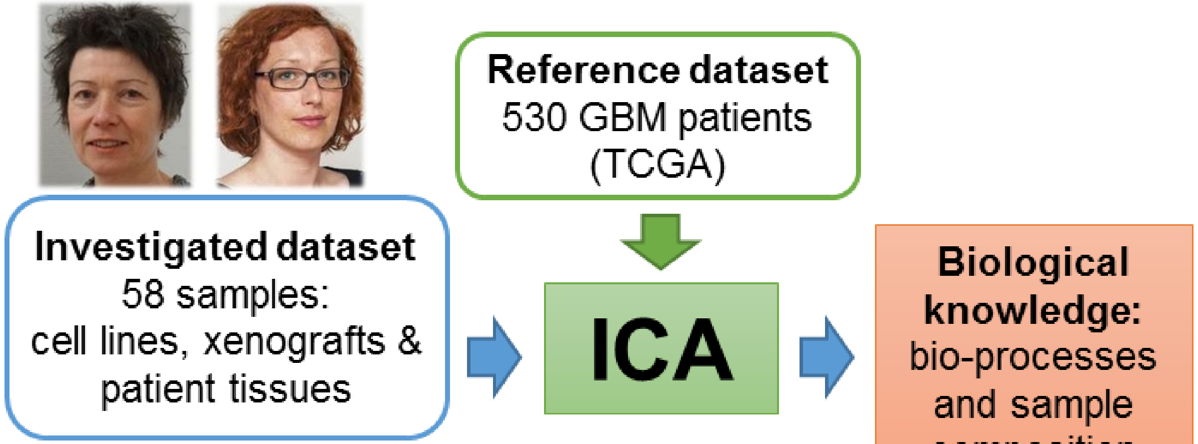
Deconvolution of transcriptomes and miRNomes by independent component analysis provides insights into biological processes and clinical outcomes of melanoma patients

Check for updates

Petr V. Nazarov[1*†], Anke K. Wienecke-Baldacchino[2,3†], Andrei Zinovyev[4,5], Urszula Czerwińska[4,5,6], Arnaud Muller[1], Dorothée Nashan[7], Gunnar Dittmar[1], Francisco Azuaje[1] and Stephanie Kreis[2]

consICA: Nazarov et al **BMC Medical Genomics**, 2019 (link)
ICA review: Sompairac, et al **Int J Mol Sci**, 2019 (link)
Application: Golebiewska et al**, Acta Neuropathol**, 2020
Scherer, Nazarov et al, **Nat Protoc**, 2020

GBM Cell Lines



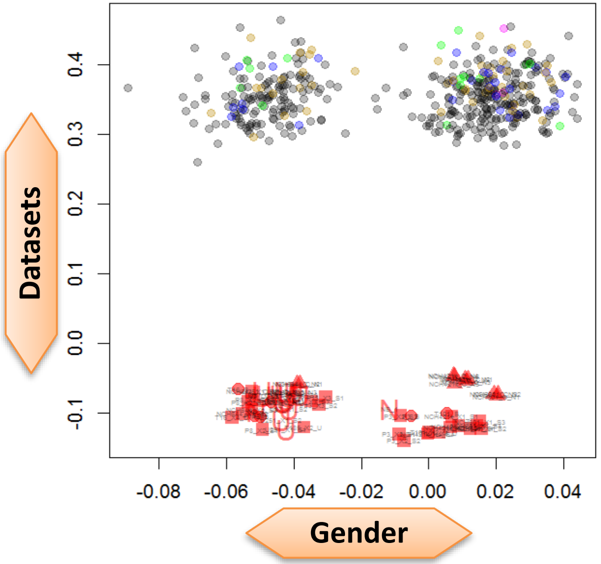
Reference dataset
530 GBM patients
(TCGA)

Investigated dataset
58 samples:
cell lines, xenografts &
patient tissues

ICA

Biological knowledge:
bio-processes
and sample
composition

Technical/trivial components: gender and platforms



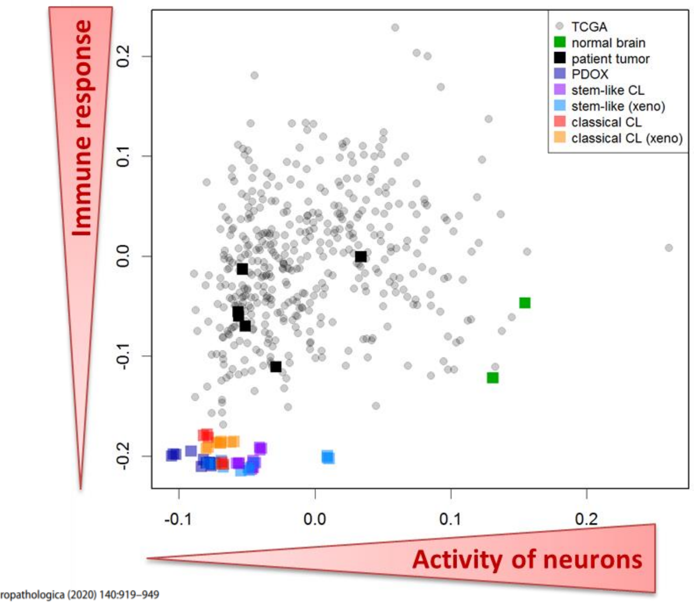
- We were able to map in-house cell line data onto TCGA dataset (GBM)

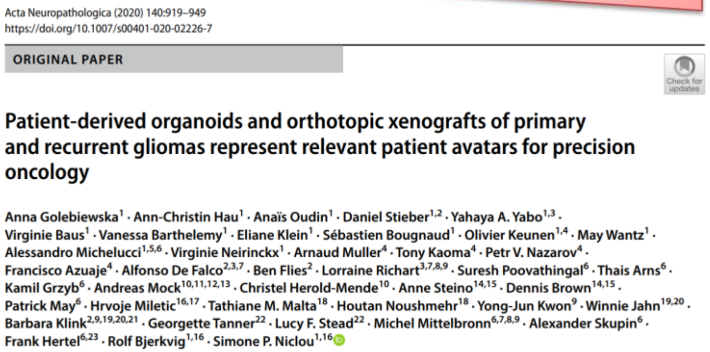
- Some components captured *technical factors* → (and thus clean other components from them)

- Other – relevant *biological information*: cell cycle, cell migration, presence of stromal and immune cells. We were able to predict phenotype of cell lines using their transcriptomes.

GBM Cell Lines

ICA correctly predicts sample composition & phenotype



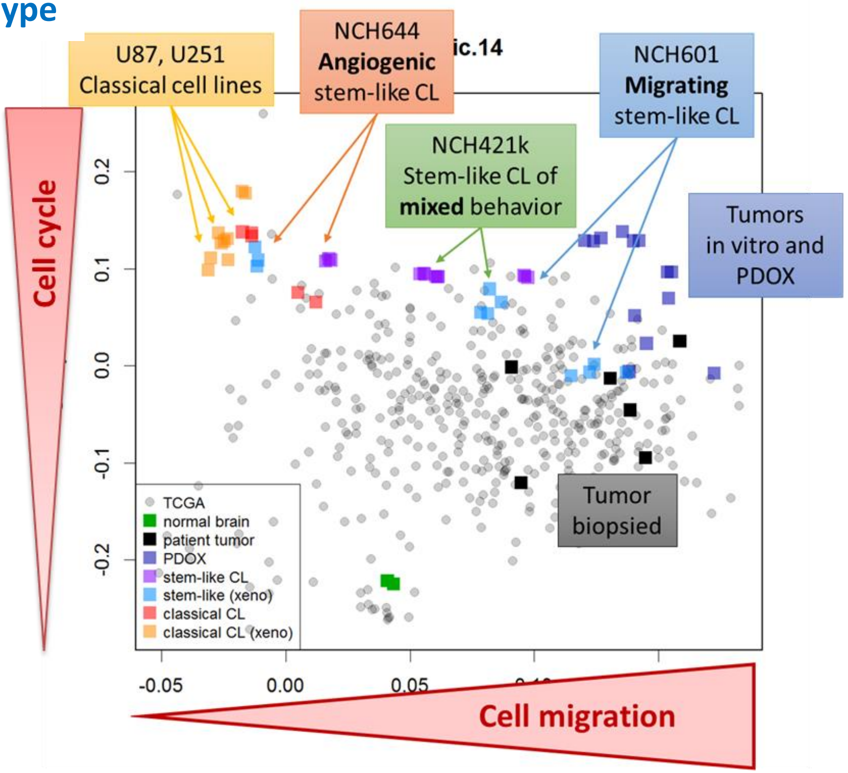


Acta Neuropathologica (2020) 140:919–949
https://doi.org/10.1007/s00401-020-02226-7

ORIGINAL PAPER

Patient-derived organoids and orthotopic xenografts of primary and recurrent gliomas represent relevant patient avatars for precision oncology

Anna Golebiewska[1] · Ann-Christin Hau[1] · Anaïs Oudin[1] · Daniel Stieber[1,2] · Yahaya A. Yabo[1,3] · Virginie Baus[1] · Vanessa Barthelemy[1] · Eliane Klein[1] · Sébastien Bougnaud[1] · Olivier Keunen[1,4] · May Wantz[1] · Alessandro Michelucci[1,5,6] · Virginie Neirinckx[1] · Arnaud Muller[4] · Tony Kaoma[4] · Petr V. Nazarov[4] · Francisco Azuaje[4] · Alfonso De Falco[2,3,7] · Ben Flies[2] · Lorraine Richart[3,7,8,9] · Suresh Poovathingal[6] · Thais Arns[6] · Kamil Grzyb[6] · Andreas Mock[10,11,12,13] · Christel Herold-Mende[10] · Anne Steino[14,15] · Dennis Brown[14,15] · Patrick May[6] · Hrvoje Miletic[16,17] · Tathiane M. Malta[18] · Houtan Noushmehr[18] · Yong-Jun Kwon[9] · Winnie Jahn[19,20] · Barbara Klink[2,9,19,20,21] · Georgette Tanner[22] · Lucy F. Stead[22] · Michel Mittelbronn[6,7,8,9] · Alexander Skupin[6] · Frank Hertel[6,23] · Rolf Bjerkvig[1,16] · Simone P. Niclou[1,16]



U87, U251 Classical cell lines

NCH644 **Angiogenic** stem-like CL

NCH601 **Migrating** stem-like CL

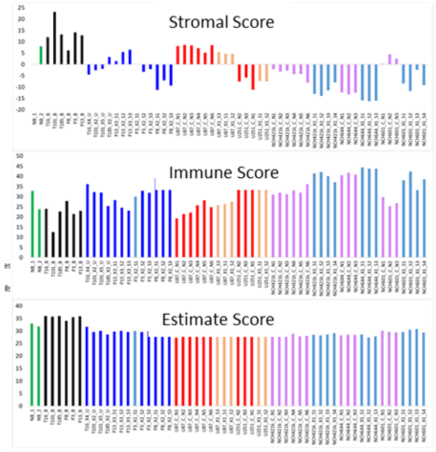
NCH421k Stem-like CL of **mixed** behavior

Tumors in vitro and PDOX

Tumor biopsied

- ICA deconvolution is reasonable and predicts phenotypic behavior of cell lines
- Tumor cells show higher mobility in xenografts

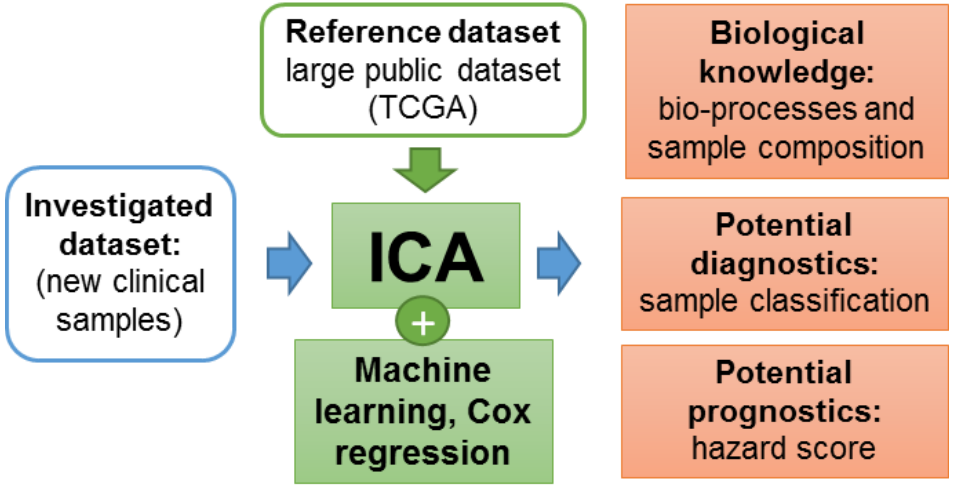
ESTIMATE was confused



Golebiewska A. et al, **Acta Neuropathologica, 2020** (link)

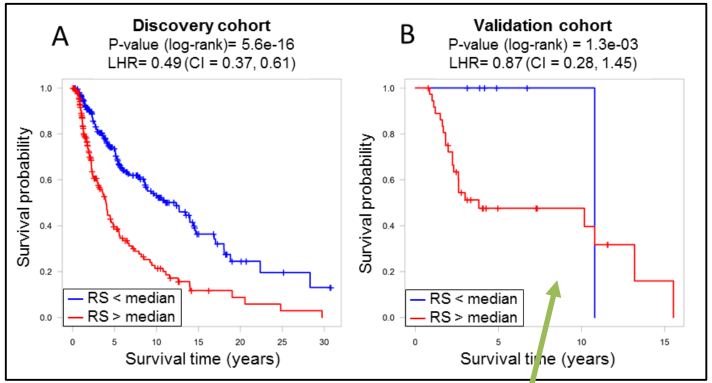
Phenotype of cell lines were predicted using unsupervised deconvolution of their transcriptomes!

Melanoma


Reference dataset
large public dataset (TCGA)
Investigated dataset: (new clinical samples)
ICA
+
Machine learning, Cox regression
Biological knowledge: bio-processes and sample composition
Potential diagnostics: sample classification
Potential prognostics: hazard score

Cross-validation on the same cohort

Cluster			
Accuracy	Actual cluster		
90.0%	immune	keratine	MITF-low
immune	160	9	6
keratine	9	91	6
MITF-low	1	2	47



Independent cohort, different platform

$$RS_j = \sum_{i=1}^{i=k} R_i^2 H_i M^*_{i,j}$$

j – patient index

i – component index

$R^2{}_i$ – stability of i-th component (from 0 to 1)

H_i – Cox' log hazard ratio calculated on **training set**

$M^*{}_{i,j}$ – element of centered & scaled M-matrix

- In addition to diagnostics and prognostics, ICA allowed ranking patients based on the activity of biological processes: cell cycle, signals of leukocytes, etc.

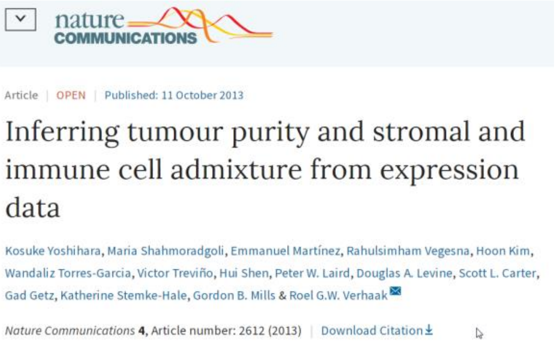
Nazarov et al, BMC Medical Genomics, 2019

Melanoma

Deciphering biological processes and cell types

Cluster	Component	Risk (p-value)	Meaning	P2PM	P4PM	P6PM	P4NS	NHEM
Immune	RIC2	decreased (1.8e-4)	B cells	0.11	0.07	0.02	0.19	0.01
	RIC25	decreased (2.8e-7)	T cells	0.26	0.06	0.24	0.18	0.00
	RIC27	no effect	B cells	0.80	0.37	0.31	0.80	0.00
	RIC28	no effect	response to wounding	0.34	0.57	0.78	0.43	0.84
	RIC37	no effect	IFN signalling pathway	0.97	0.66	0.99	0.90	1.00
	RIC57	no effect	monocytes	0.00	0.25	0.24	0.02	0.00
	MIC20	decreased (1.2e-4)	T cells, chr1q32.2	0.14	0.08	0.37	0.02	0.19
Stromal and angiogenic	RIC13	no effect	cells of stroma	0.81	0.40	0.50	0.86	0.03
	RIC49	no effect	endothelial cells	0.73	0.12	0.29	0.84	0.00
	MIC22	no effect	miR-379/miR-410 cluster, chr14q32.2,14q32.31	0.29	0.20	0.27	0.38	0.16
	MIC25	no effect	stromal cells; clusters: chr1q24.3, 5q32, 17p13.1, 21q21.1	0.97	0.85	0.76	0.80	0.26
Skin-related	RIC5	increased (5.8e-3)	epidermis development and keratinisation	0.92	0.93	0.96	0.92	0.87
	RIC7	increased (8.9e-6)	epidermis development and keratinisation	0.94	0.93	0.93	0.95	0.57
	RIC19	increased (4.0e-2)	epidermis development and keratinisation	1.00	0.62	0.22	1.00	0.93
	RIC31	increased (2.2e-2)	epidermis development and keratinisation	0.98	0.85	0.89	0.99	0.28
	MIC9	increased (2.9e-2)	skin-specific miRNAs	0.95	0.88	0.87	0.91	0.83
Melanocytes	RIC4	increased (5.4e-3)	melanin biosynthesis	0.62	0.77	1.00	0.21	0.96
	RIC16	decreased (5.1e-4)	melanosomes (negative gene list)	0.68	0.77	0.54	0.75	0.39
	MIC11	no effect	potential regulators of malignant cells, chrXq27.3	0.21	0.96	0.62	0.13	0.48
	MIC14	decreased (1.5e-2)	potential regulators of melanocytes, chrXq26.3	0.01	0.29	0.67	0.29	0.38
Other	RIC55	increased (3.0e-2)	cell cycle	0.48	0.46	0.88	0.00	0.53
	RIC6	decreased (5.5e-3)	potentially linked to neuron differentiation	0.43	0.73	0.59	0.46	0.01
	MIC1	increased (9.4e-4)	regulators of EMT	0.11	0.07	0.02	0.19	0.01

ESTIMATE

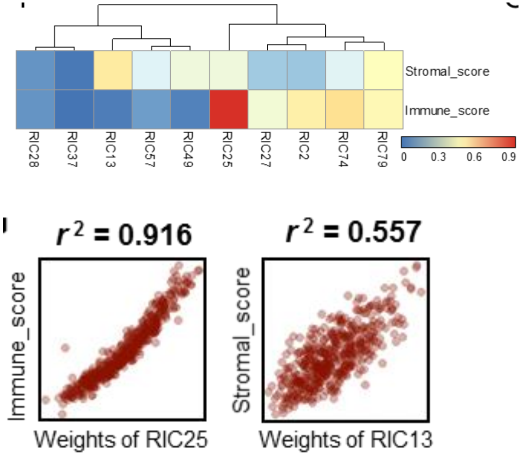


Article | OPEN | Published: 11 October 2013

Inferring tumour purity and stromal and immune cell admixture from expression data

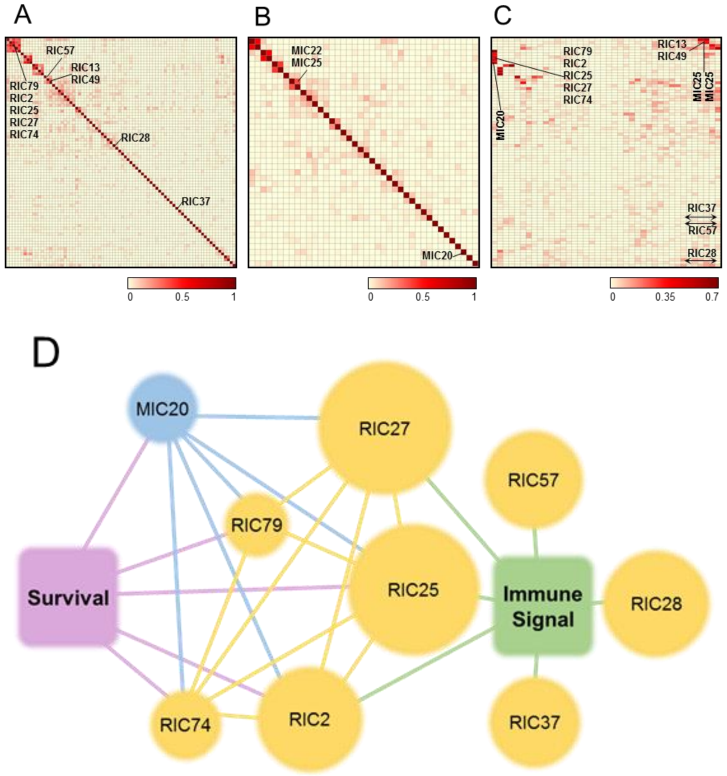
Kosuke Yoshihara, Maria Shahmoradgoli, Emmanuel Martínez, Rahulsimham Vegesna, Hoon Kim, Wandaliz Torres-Garcia, Victor Treviño, Hui Shen, Peter W. Laird, Douglas A. Levine, Scott L. Carter, Gad Getz, Katherine Stemke-Hale, Gordon B. Mills & Roel G.W. Verhaak

Nature Communications **4**, Article number: 2612 (2013) | Download Citation



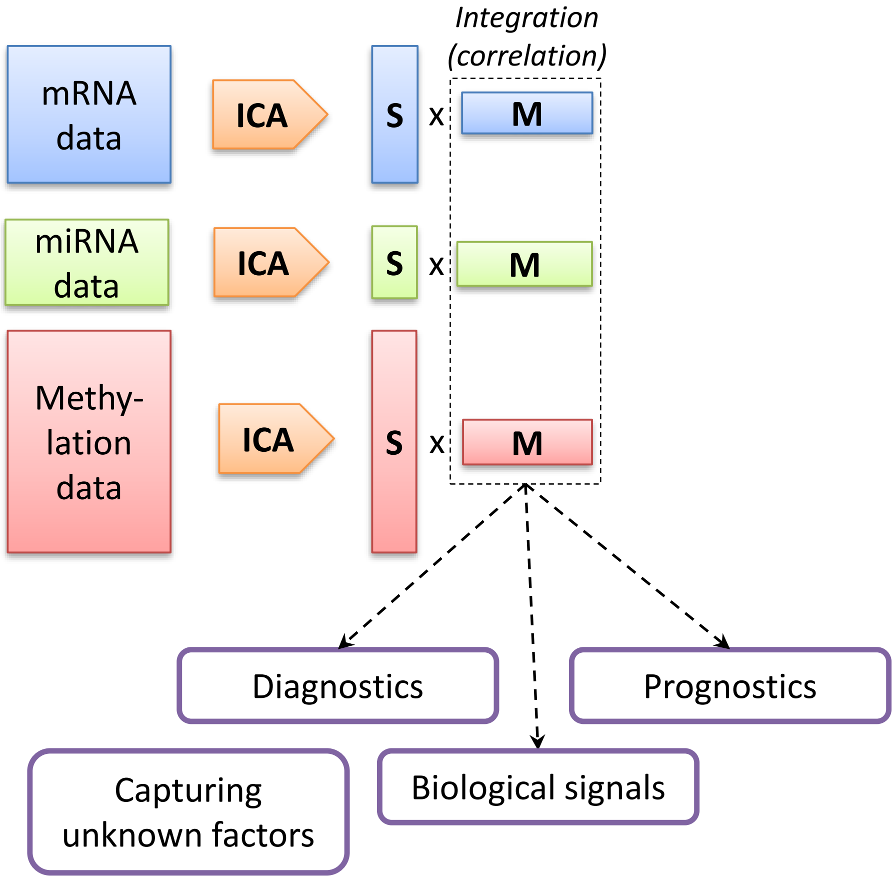
← New samples are mapped to the space defined by reference data.

Data integration: mRNA + miRNA + …



Multi-omics Data Integration via Deconvolution

ICA: independent runs



Integration (correlation)

mRNA data

miRNA data

Methylation data

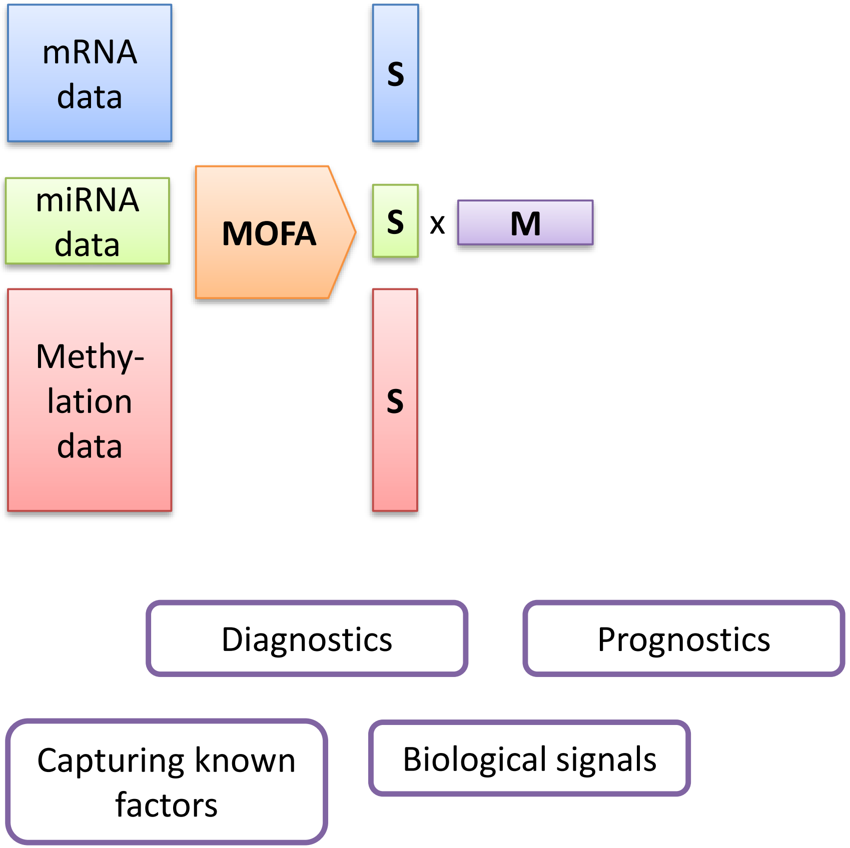
Diagnostics

Prognostics

Capturing unknown factors

Biological signals

MOFA: simultaneous analysis



mRNA data

miRNA data

Methylation data

Diagnostics

Prognostics

Capturing known factors

Biological signals

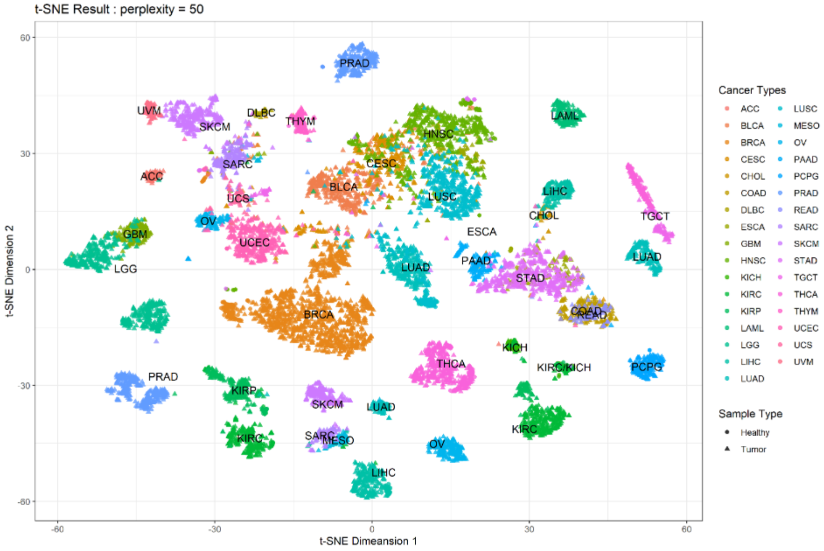
Pan-Cancer Data Integration

TCGA

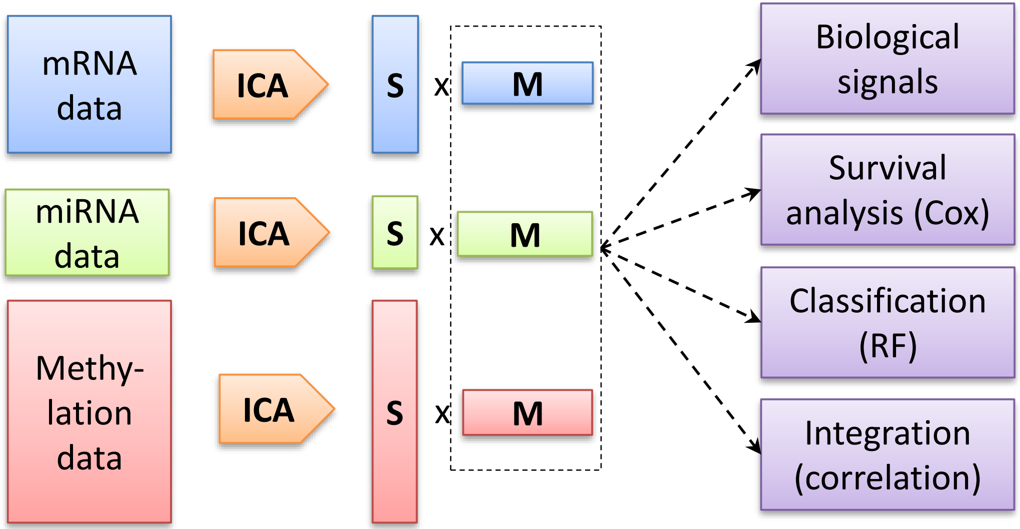
The Cancer Genome Atlas

>11k patients, 33 types of tumors

- **clinical data** (age, gender, survival...)
- **mRNA** (10k samples, 20k features)
- **miRNA** (> 9k samples, ~1k features)
- **methylation** (>9k samples, 450k features)



Approach



mRNA data → ICA → S x M

miRNA data → ICA → S x M

Methy-lation data → ICA → S x M

Biological signals

Survival analysis (Cox)

Classification (RF)

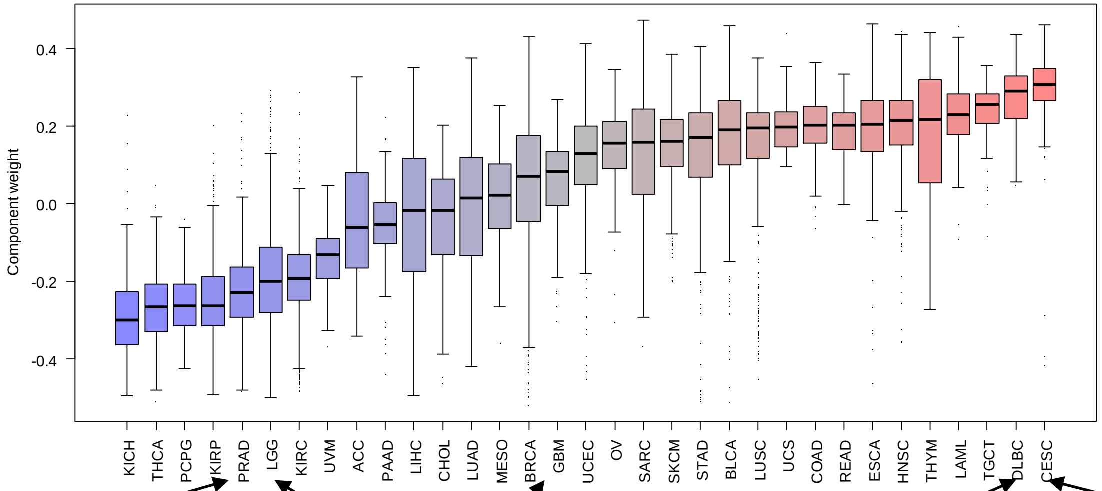
Integration (correlation)

Here we used *consICA* with 100 components & 40 runs

Pan-cancer: ICA Components

ICA Results: Cell Cycle

RIC27: Mitotic Cell Cycle



prostate adenocarcinoma

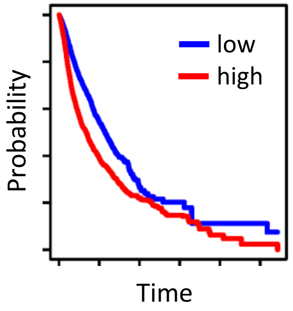
low grade glioma

glioblastoma (IDHwt)

diffuse lymphoma

cervical s.c.c & endoservical a.c.

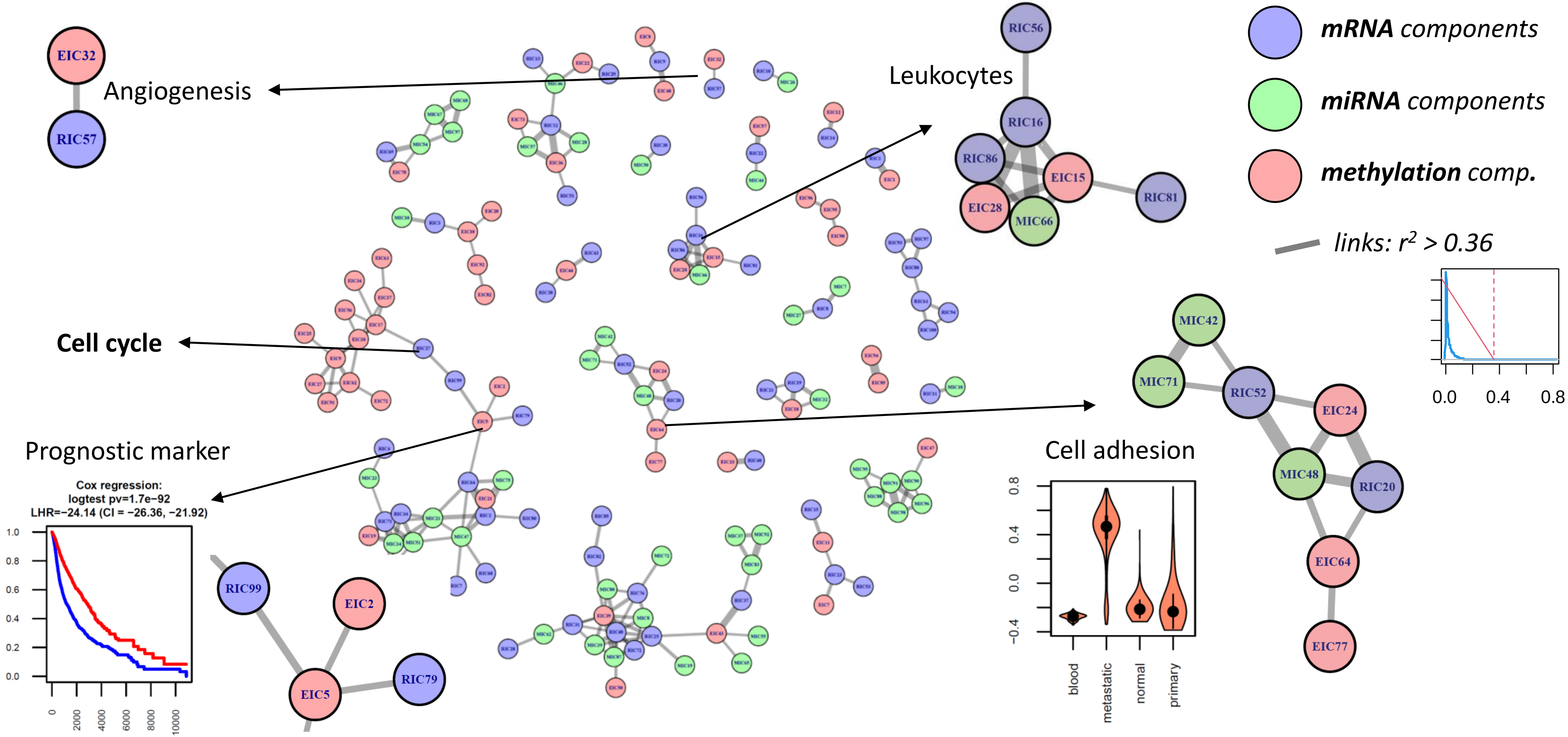
Cox regression:
logtest pv=8.7e−57
LHR=1.35 (CI = 1.18, 1.52)



Code	Study Name
ACC	Adrenocortical carcinoma
BLCA	Bladder urothelial carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical sq. cell carcinoma and endocervical adenocarcinoma
CHOL	Cholangiocarcinoma
COAD	Colon adenocarcinoma
DLBC	Lymphoid neoplasm diffuse large b-cell lymphoma
ESCA	Esophageal carcinoma
GBM	Glioblastoma multiforme
HNSC	Head and neck squamous cell carcinoma
KICH	Kidney chromophobe
KIRC	Kidney renal clear cell carcinoma
KIRP	Kidney renal papillary cell carcinoma
LAML	Acute myeloid leukemia
LCML	Chronic myelogenous leukemia
LGG	Brain lower grade glioma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MESO	Mesothelioma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PCPG	Pheochromocytoma and paraganglioma
PRAD	Prostate adenocarcinoma
READ	Rectum adenocarcinoma
SARC	Sarcoma
SKCM	Skin cutaneous melanoma
STAD	Stomach adenocarcinoma
TGCT	Testicular germ cell tumors
THCA	Thyroid carcinoma
THYM	Thymoma
UCEC	Uterine corpus endometrial carcinoma
UCS	Uterine carcinosarcoma
UVM	Uveal melanoma

Pan-cancer: ICA-based Data Integration

LUXEMBOURG INSTITUTE OF HEALTH



Angiogenesis

Leukocytes

Cell cycle

Prognostic marker

Cell adhesion

mRNA components

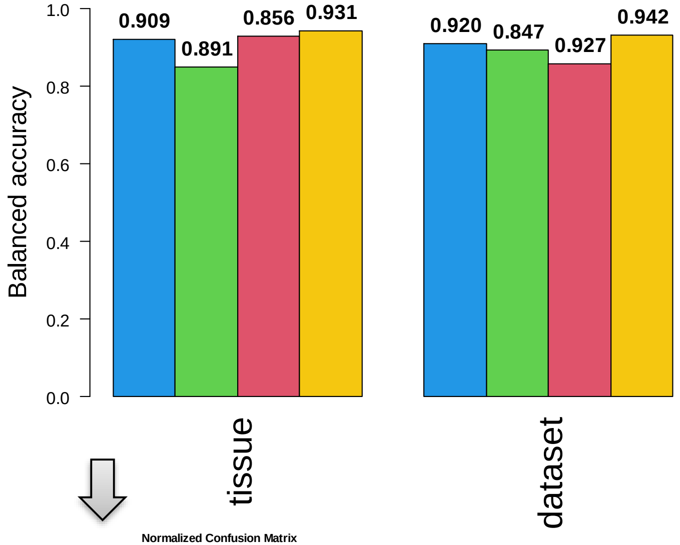
miRNA components

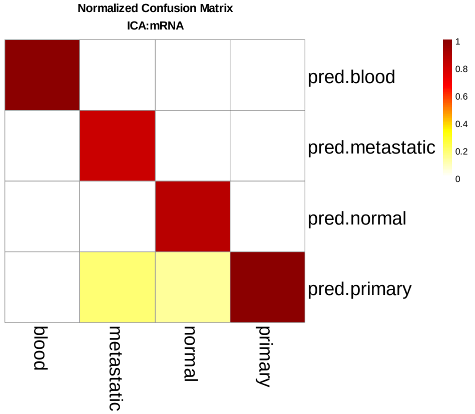
methylation comp.

links: $r^2 > 0.36$

Pan-cancer: Classification

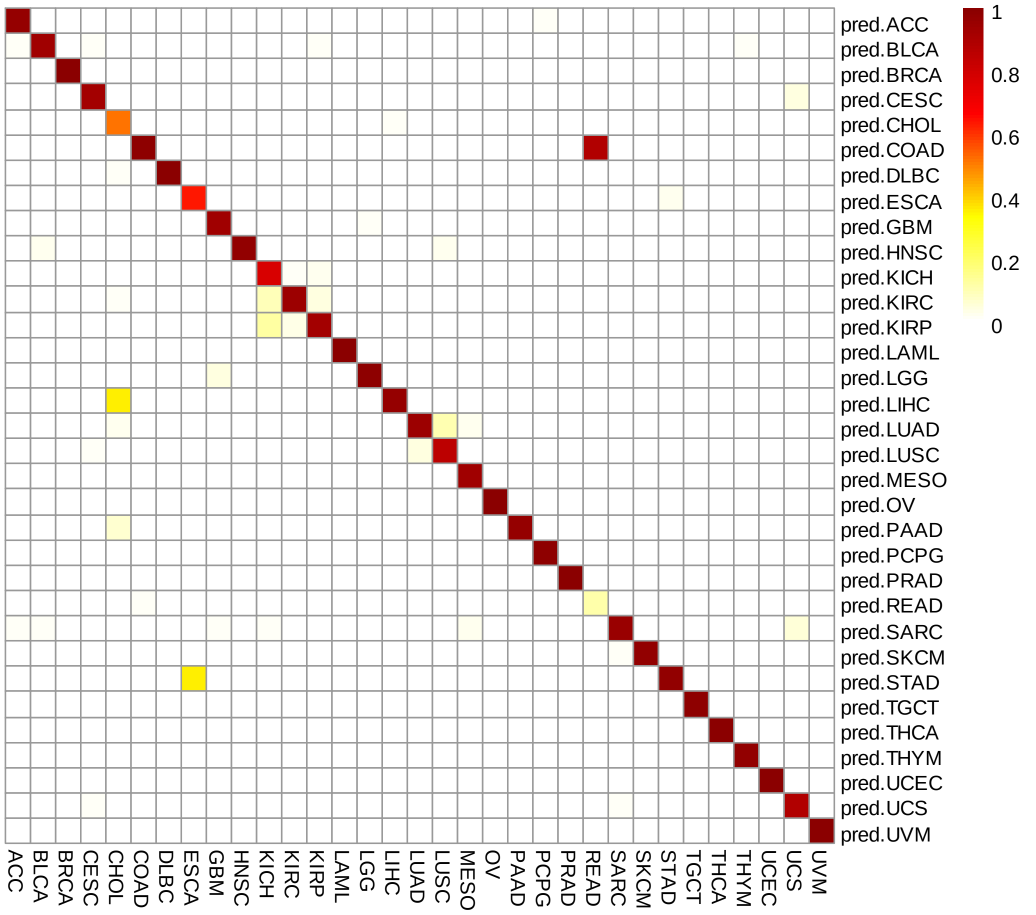
Classification by RF





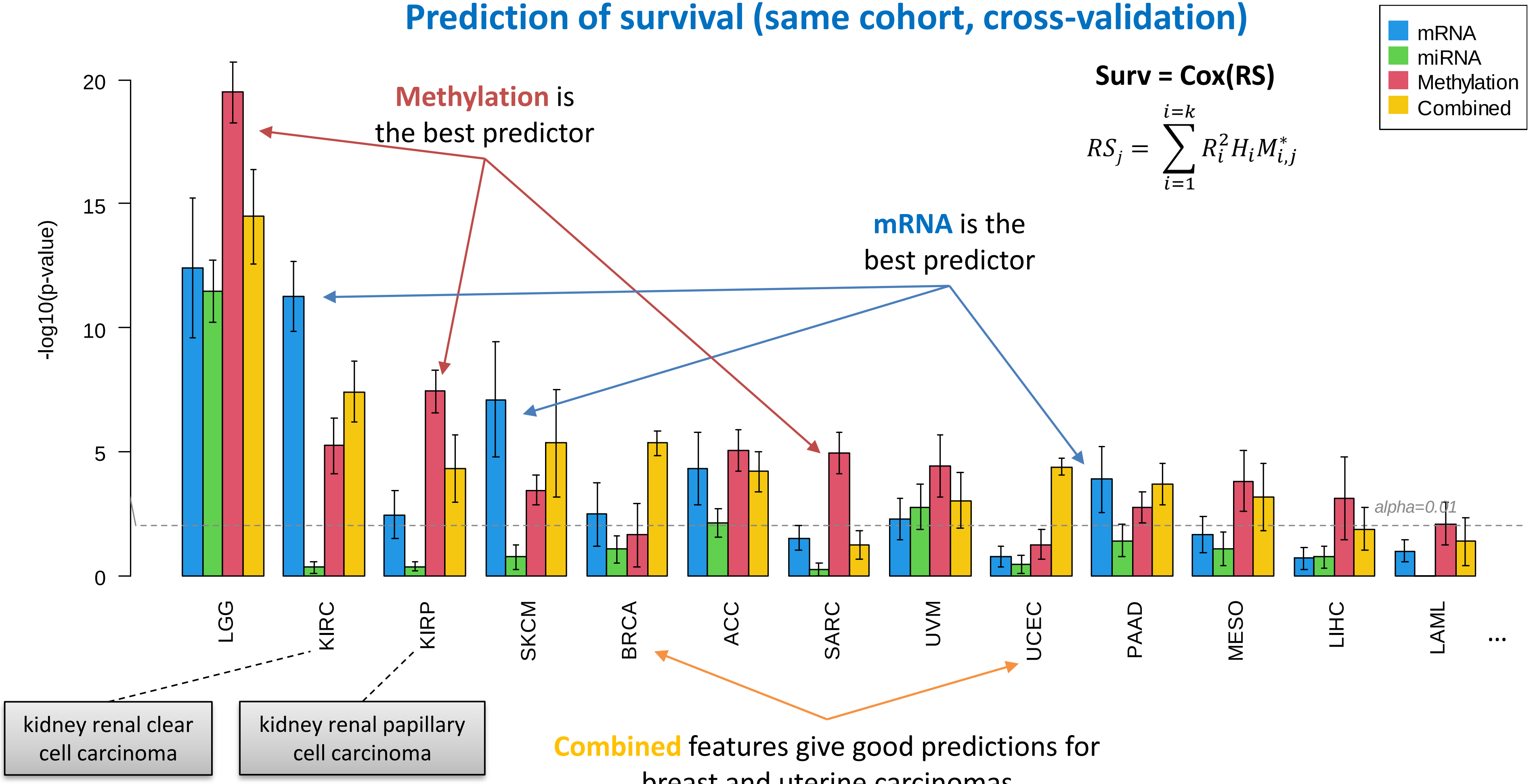
Normalized Confusion Matrix

ICA:mRNA



Pan-cancer: Prognosis

Prediction of survival (same cohort, cross-validation)



Methylation is the best predictor

mRNA is the best predictor

Surv = Cox(RS)

$$RS_j = \sum_{i=1}^{i=k} R_i^2 H_i M_{i,j}^*$$

kidney renal clear cell carcinoma

kidney renal papillary cell carcinoma

Combined features give good predictions for breast and uterine carcinomas

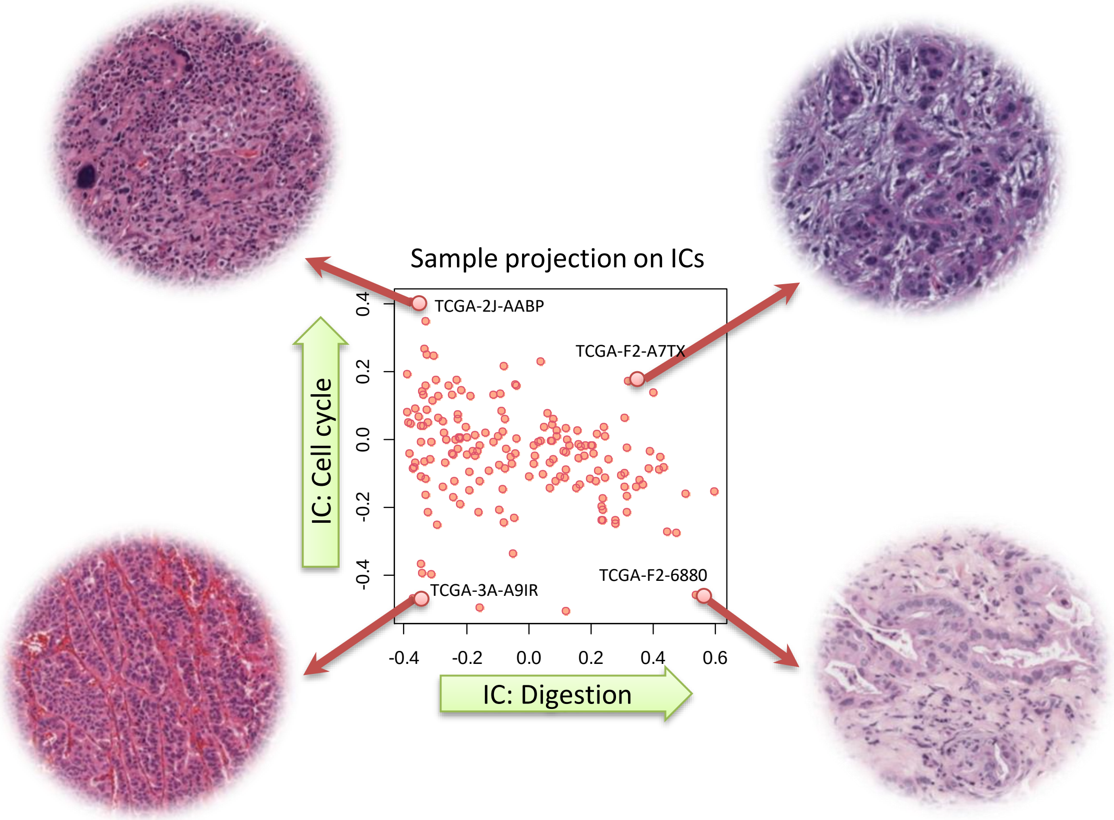
Take Home Message 1

- ICA-based deconvolution:
  - Corrects technical biases
  - Extracts "cleaned" biological signals from bulk-sample data
  - Maps new samples into the space of biologically meaningful components
  - Extracts prognostic features and features with classification power
  - Can be used to integrate multi-omics data
  - Diagnostic & prognostic properties could be expected for many cancers
  - Reduce dimensionality

- Was validated:
  - Using acceptable computational methods (cross-validation)
  - On cell lines
  - Independent cohorts of patients

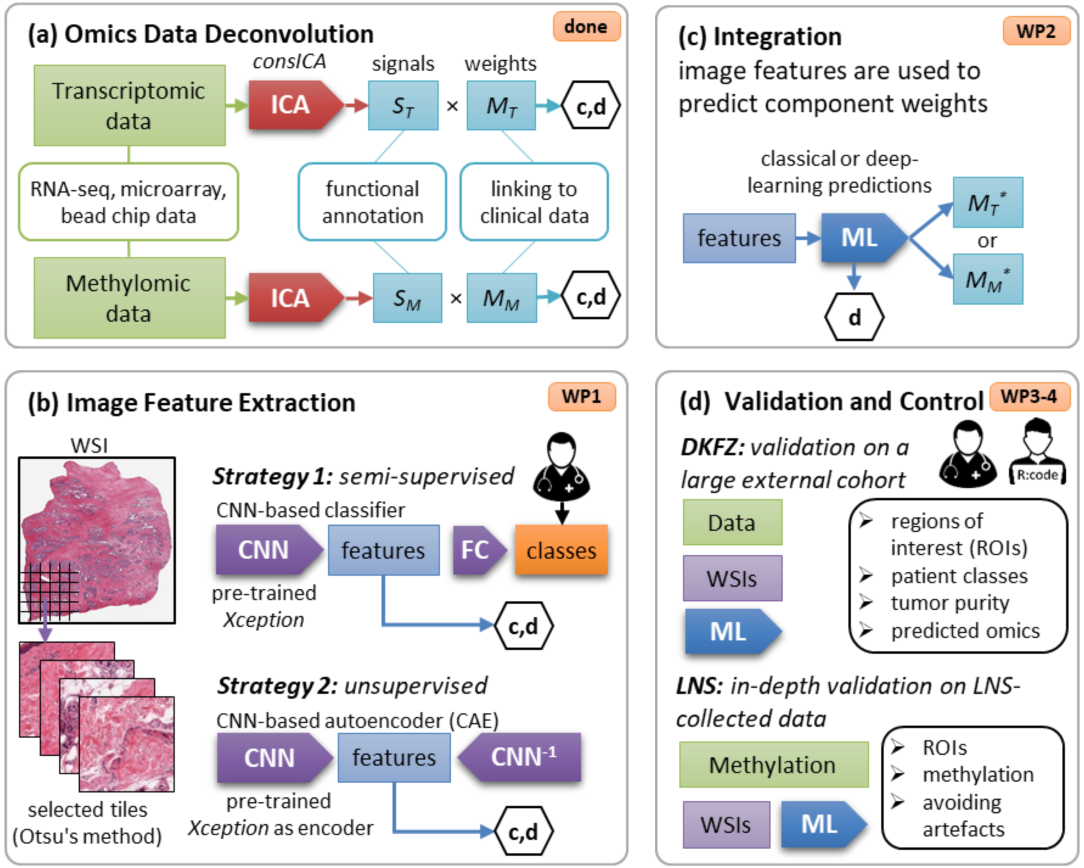
Observation

ICA results of mRNA expression data from TCGA-PAAD cohort



MEDEA: Project Overview

LUXEMBOURG INSTITUTE OF HEALTH



(a) Omics Data Deconvolution

done

consICA

signals

weights

Transcriptomic data

ICA

S_T × M_T

c,d

RNA-seq, microarray, bead chip data

functional annotation

linking to clinical data

Methylomic data

ICA

S_M × M_M

c,d

(c) Integration

WP2

image features are used to predict component weights

classical or deep-learning predictions

features

ML

M_T^*

or

M_M^*

d

(b) Image Feature Extraction

WP1

WSI

Strategy 1: semi-supervised

CNN-based classifier

CNN

features

FC

classes

pre-trained *Xception*

c,d

selected tiles (Otsu's method)

Strategy 2: unsupervised

CNN-based autoencoder (CAE)

CNN

features

CNN^{-1}

pre-trained *Xception* as encoder

c,d

(d) Validation and Control

WP3-4

DKFZ: validation on a large external cohort

R:code

Data

WSIs

ML

- regions of interest (ROIs)
- patient classes
- tumor purity
- predicted omics

LNS: in-depth validation on LNS-collected data

Methylation

WSIs

ML

- ROIs
- methylation
- avoiding artefacts

CAE: convolutional autoencoder; **CNN**: convolutional neural network; **FC**: fully-connected network or layer; **ICA**: independent component analysis; **ML**: machine learning; **ROI**: region of interest; **WSI**: whole slide image.

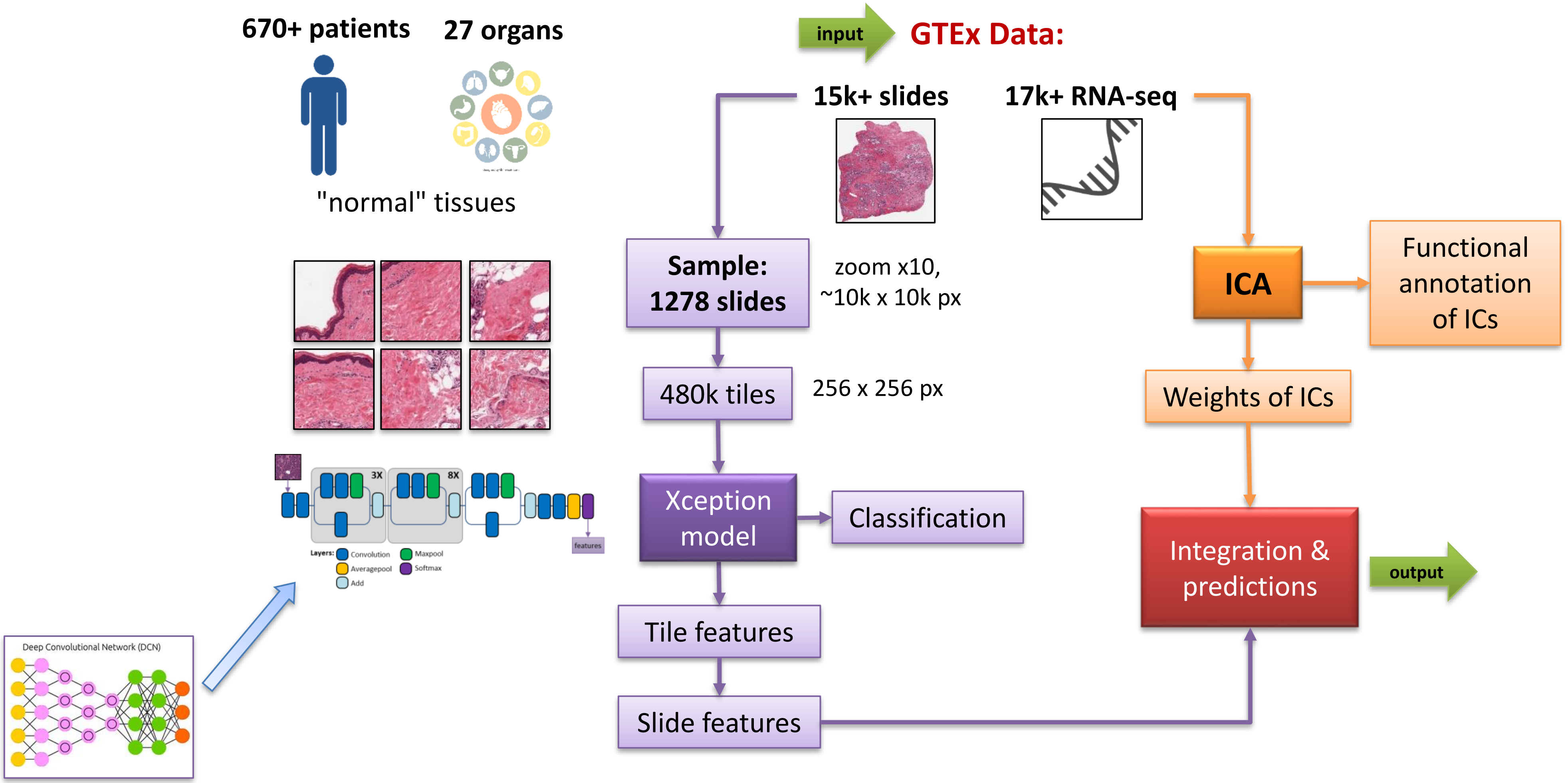
(a) Deconvolution of the omics data using developed tool *consICA*. This method was already developed and applied to entire GTEx (mRNA), TCGA (mRNA and meDNA), and DKFZ (mRNA) cohorts.

(b) Image analysis and feature extraction starts with a pre-trained *Xception* model and uses weakly supervised training to fine-tune model's parameters. Two strategies will be compared in the project: strategy 1 is a semi-supervised one using CNN-based classifier and strategy 2 – completely unsupervised using CAE. *Xception* will be used as an initial estimation of the encoder's parameters.

(c) Integration of ICA-weights and image features will be done either by a classical ML-approach (linear regression or random forest regression) or by a FC neural network.

(d) A thorough validation of the results include (i) validation of an external pancreatic cancer cohort (DKFZ) and collection and (ii) in-depth analysis of in-house (LNS) samples of glioma patients. The expertise of the Co-PI (pathologist) will be used to validated predictions and the PI and his team will control that the WSI-features are sensible and not artefacts.

Preliminary Results



670+ patients

27 organs

"normal" tissues

input

GTEx Data:

15k+ slides

17k+ RNA-seq

Sample: 1278 slides

zoom x10, ~10k x 10k px

480k tiles

256 x 256 px

Xception model

Classification

Tile features

Slide features

ICA

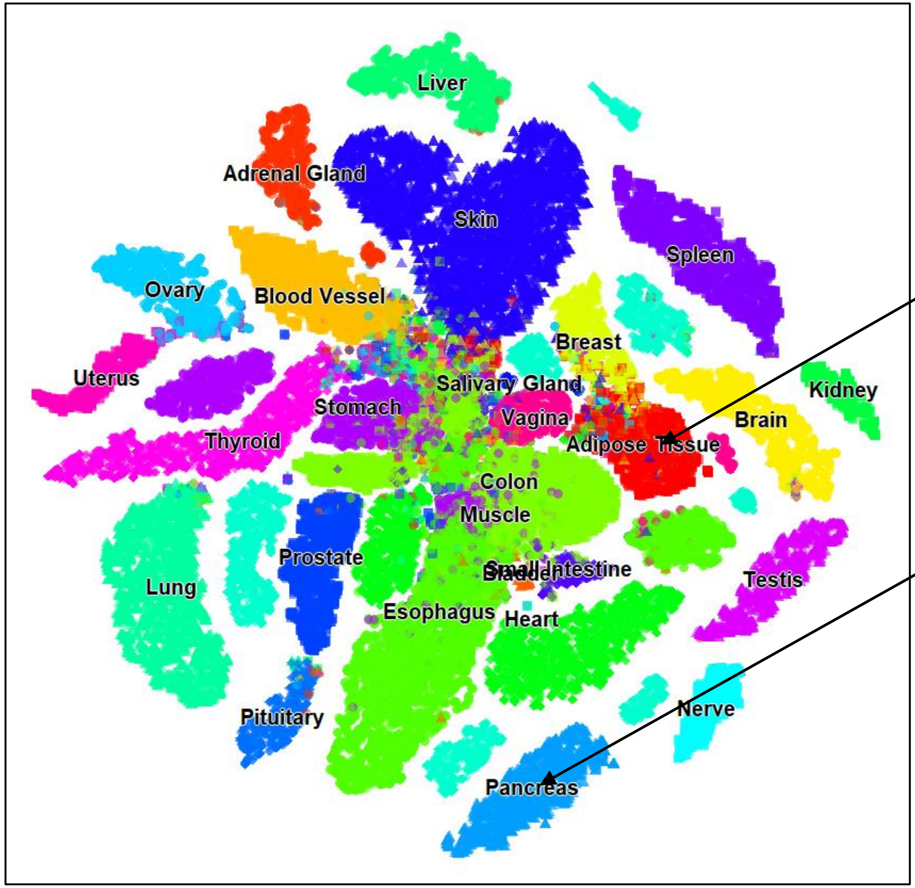
Functional annotation of ICs

Weights of ICs

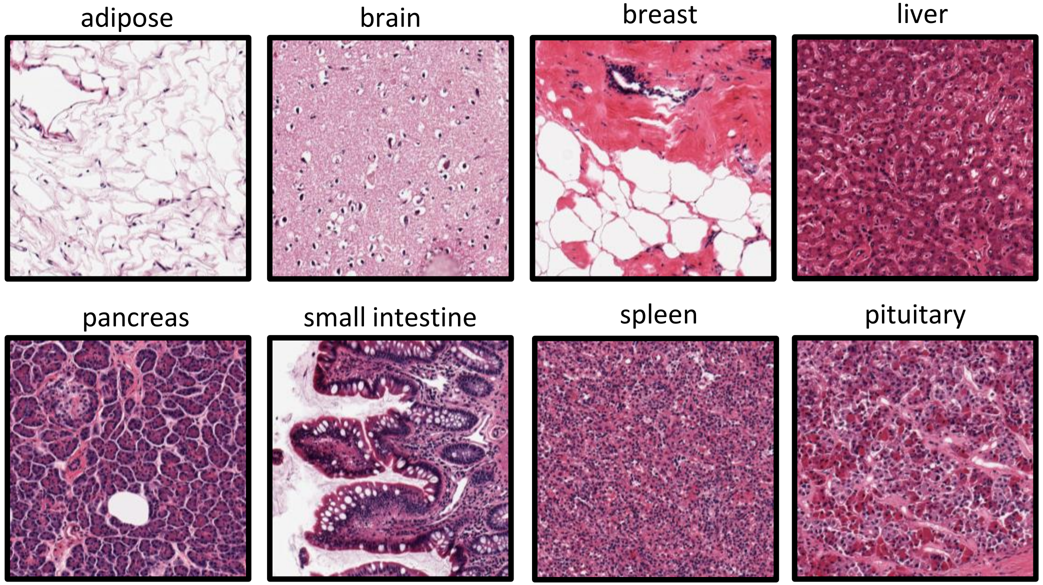
Integration & predictions

output

Tile-level Feature Extraction



Examples of tiles classified with top certainty and co-localized with class medoids

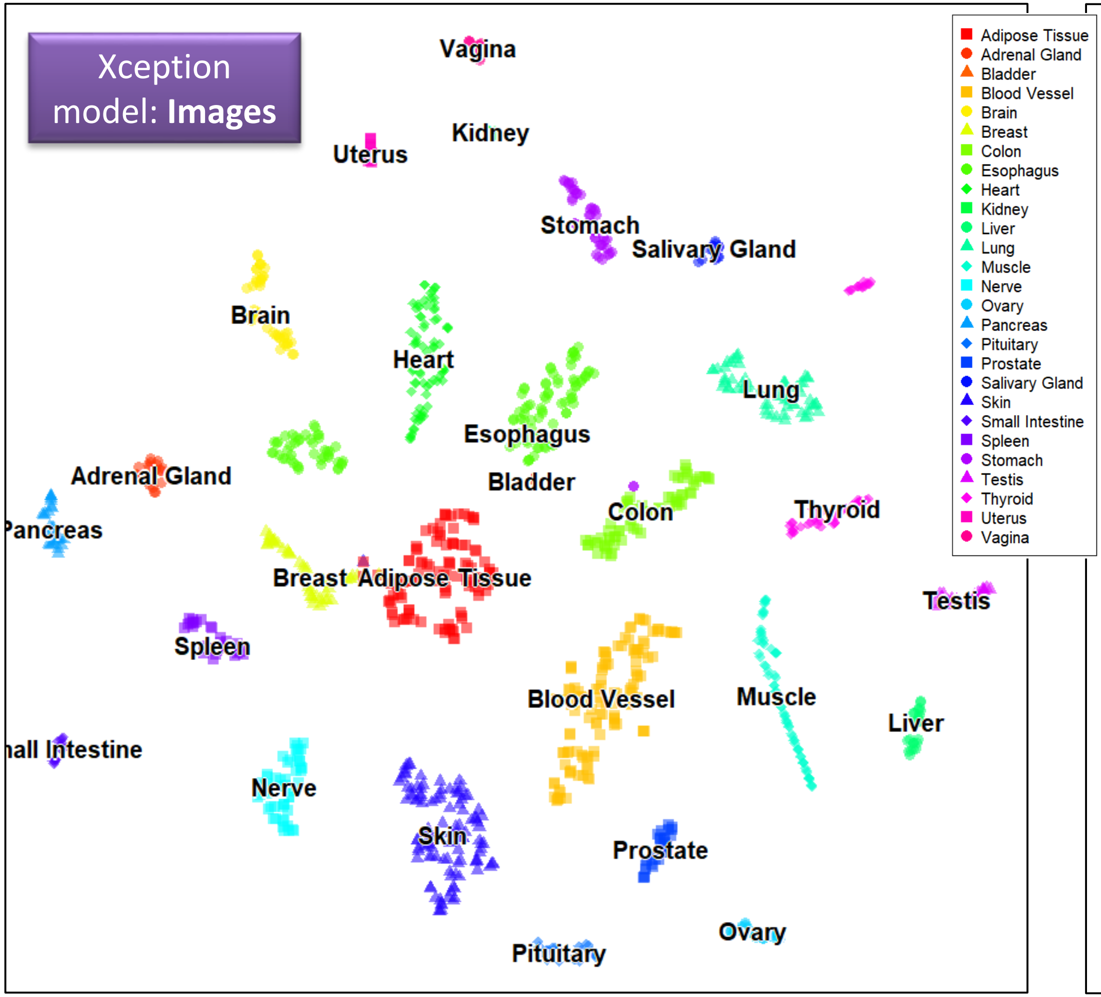


Xception, after parameter fine-tuning on organ classification task, transform each tile to ~150 non-zero features.

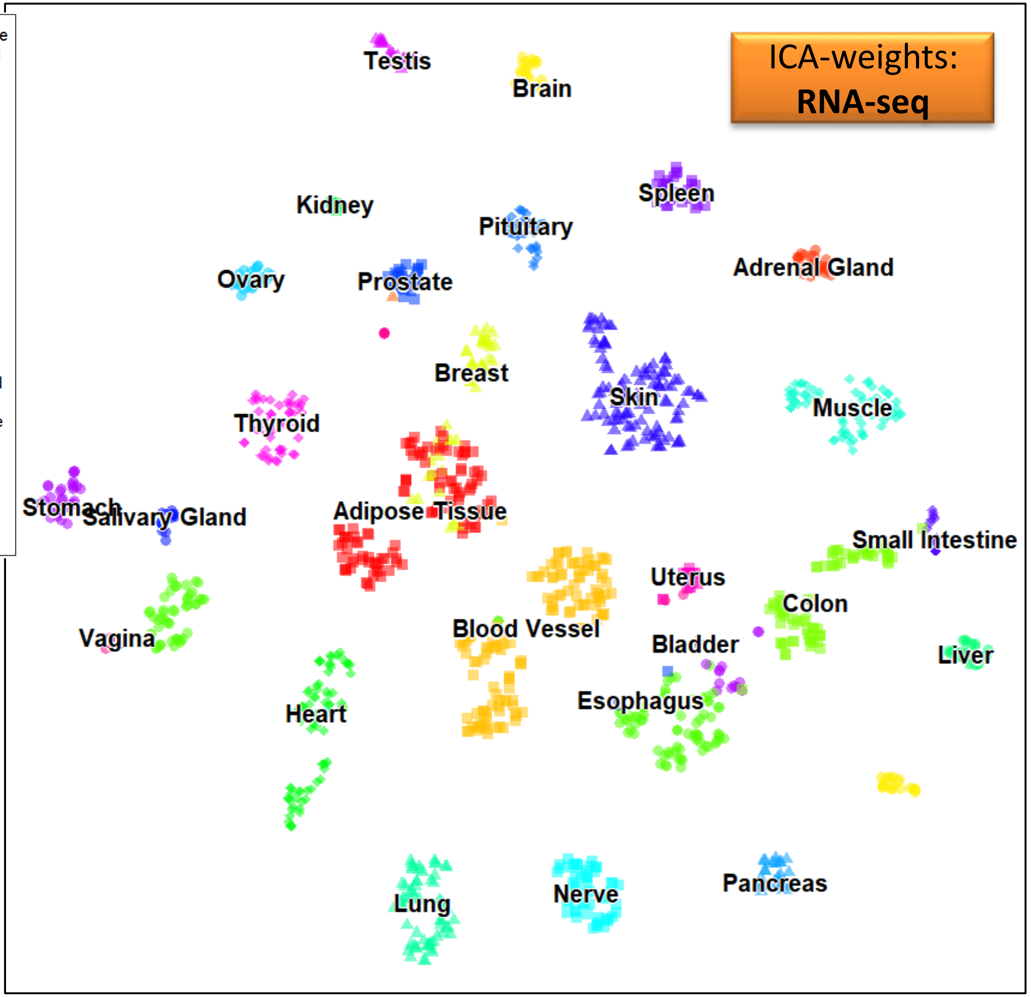
Further analysis:

These features were summarized to slide-level. Only 50% top-correlated tiles were preserved (can be further improved later…)

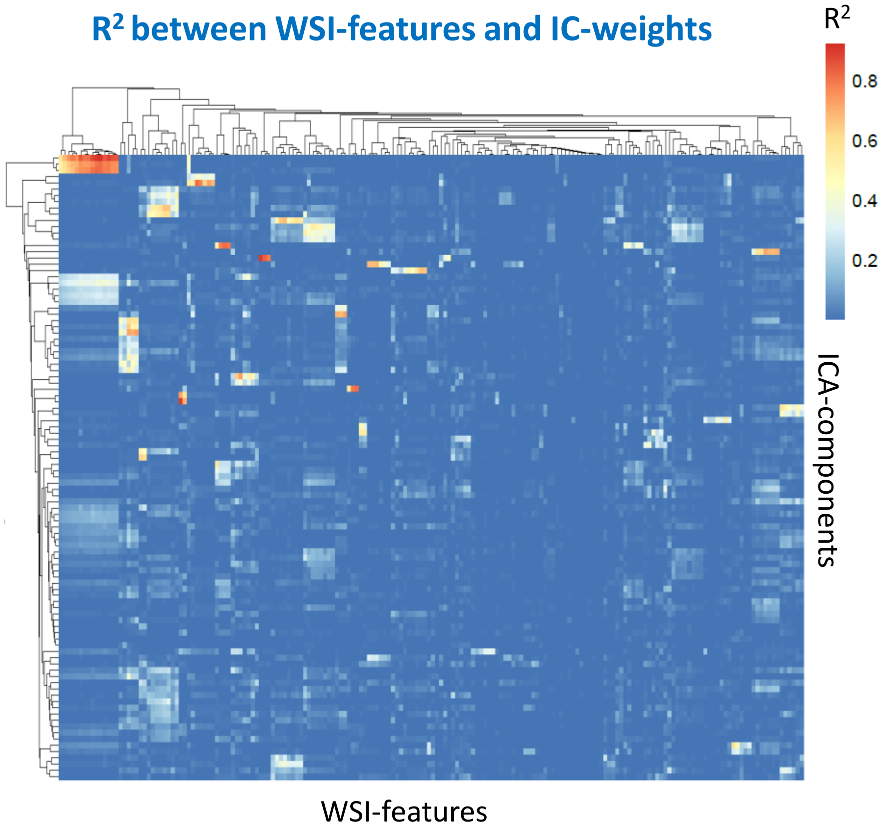
Slide-level Analysis and ICA

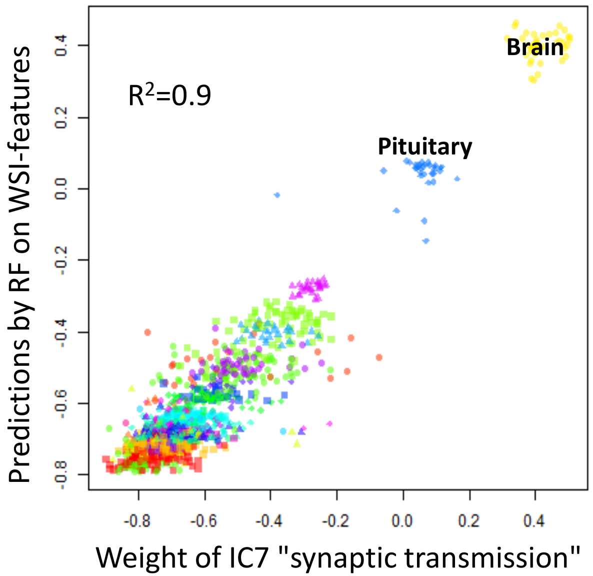


🟥	Adipose Tissue
●	Adrenal Gland
▲	Bladder
■	Blood Vessel
●	Brain
▲	Breast
■	Colon
●	Esophagus
◆	Heart
■	Kidney
●	Liver
▲	Lung
◆	Muscle
■	Nerve
●	Ovary
▲	Pancreas
◆	Pituitary
■	Prostate
●	Salivary Gland
▲	Skin
◆	Small Intestine
■	Spleen
●	Stomach
▲	Testis
◆	Thyroid
■	Uterus
●	Vagina



Predictions


R^2 between WSI-features and IC-weights


Predicting IC-weight

GO:BP linked to IC7	FDR
chemical synaptic transmission	8e-28
regulation of membrane potential	8e-28
behavior	4e-22
regulation of ion transport	6e-22
synaptic vesicle cycle	3e-20
cognition	7e-20

Predicting ICA-components

- 20% of the components were predicted with R^2>0.9
- 89% – with R^2>0.5

nature COMMUNICATIONS

A deep learning model to predict RNA-Seq expression of tumours from whole slide images

Benoît Schmauch[1✉], Alberto Romagnoni[1,4], Elodie Pronier[1,4], Charlie Saillard[1], Pascale Maillé[2,3], Julien Calderaro[2,3], Aurélie Kamoun[1], Meriem Sefta[1], Sylvain Toldo[1], Mikhail Zaslavskiy[1], Thomas Clozel[1], Matahi Moarii[1], Pierre Courtiol[1,5] & Gilles Wainrib[1,5✉]

Predicting genes

- 0.4% of the genes showed R^2>0.9
- 28% – R^2>0.5

Take Home Message 2

- Deep Learning Networks could be used for feature extraction
- Image features could be used to predict deconvolved signals
- Deconvolved ("clean") signals are better predicted than genes (and related GO gene sets)
- Combining molecular and his histopathological data may:
  - Help pathologists faster and more accurate classify samples
  - Improve accuracy of automatic data analysis

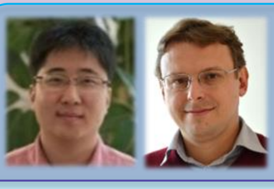
- Spatial transcriptomics, perhaps is our future ☺

Acknowledgements

LUXEMBOURG
INSTITUTE
OF HEALTH

Bioinformatics Platform
@ Data Integration and Analysis unit

R.Toth
V.Despotovic
L.Zhang
T.Koma
A.Muller



S-Y.Kim
P.Nazarov

LUXGEN

A.Aalto
Y.Zhang
B.Nosirov
T.Lukashiv

NORLUX @ DoCR

Multiomics Data Science group @ Cancer Research

Key internal collaborators

Simone Niclou

Anna Golebiewska

Michel Mittelbronn

Key external collaborators

LSRU, Uni Luxembourg
Stephanie Kreis

Institute Curie, France
Andrei Zinovyev

DKFZ, Heidelberg
Jörg Hoheisel
Andrea Bauer
Nathalia Giese

Interns / students

Maryna Chepeleva (PhD student)

Aliaksandra Kakoichankava (PhD student)

Yibioa Wang (MSc)

Thomas Eveno (MSc)

Laurene Picandet (MSc)

Fonds National de la Recherche Luxembourg

Supported by FNR Luxembourg. Grants:

- C17/BM/11664971/**DEMICS**
- C21/BM/15739125/**DIOMEDES**