Machine learning for integrating imaging, anatomo-pathological and omics data to predict outcome of patients treated with immunotherapy

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Orsay inter-unit seminar

10/05/2023

Outline

1. **Introduction:** predict the outcome of metastatic non-small cell lung cancer patients treated by immunotherapy

2. **Unimodal approaches:** extract relevant features from each modality

3. **Multimodal approach:** handle missing modalities with late fusion strategies

Lung cancer in France

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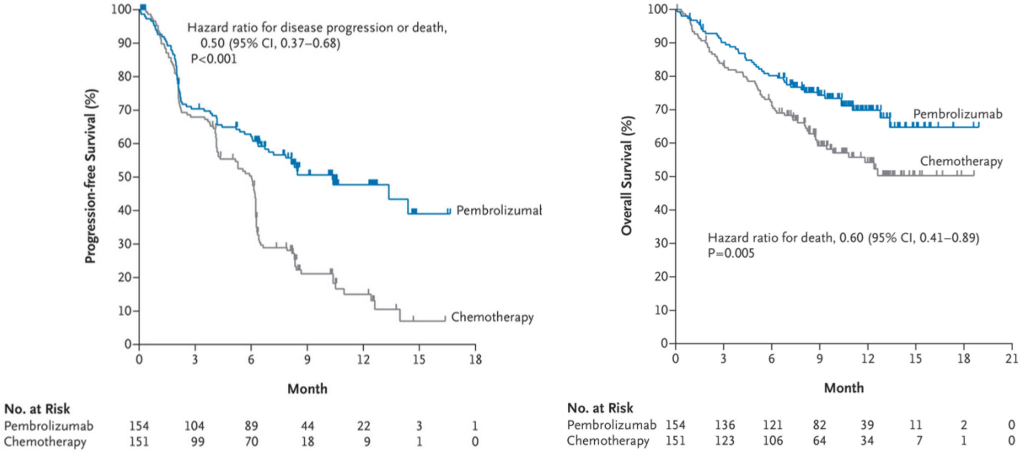

KEYNOTE-024 trial, chemotherapy vs pembrolizumab for ≥ 50% PD-L1 advanced NSCLC patients (Reck et al. 2016)

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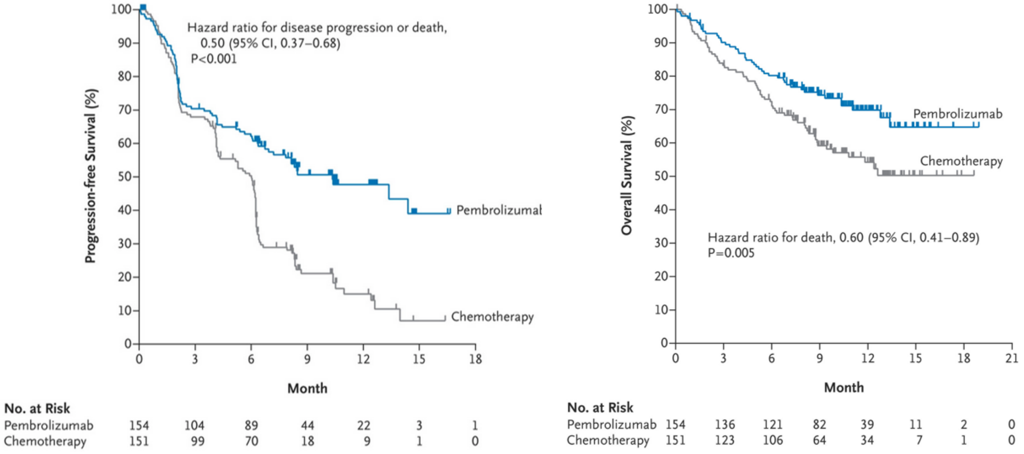

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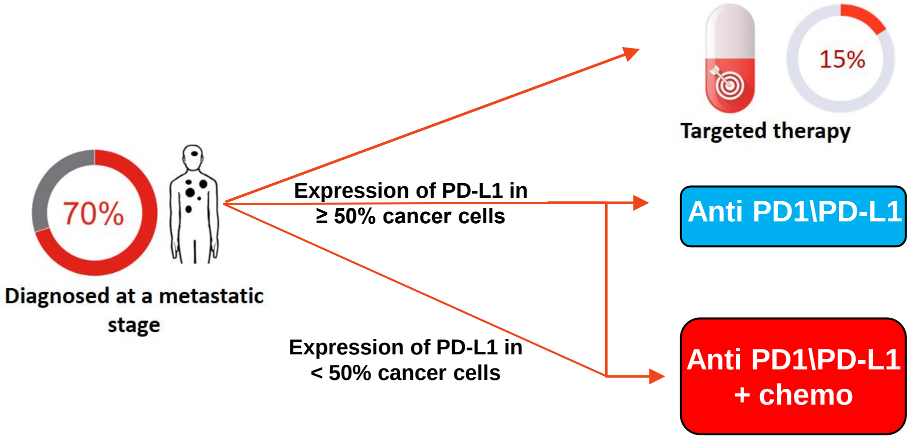

Targeted therapy

Diagnosed at a metastatic stage

Expression of PD-L1 in ≥ 50% cancer cells

Anti PD1\PD-L1

Expression of PD-L1 in < 50% cancer cells

Anti PD1\PD-L1 + chemo

Standard-of-care for advanced NSCLC in Europe

Standard-of-care still needs to be optimized

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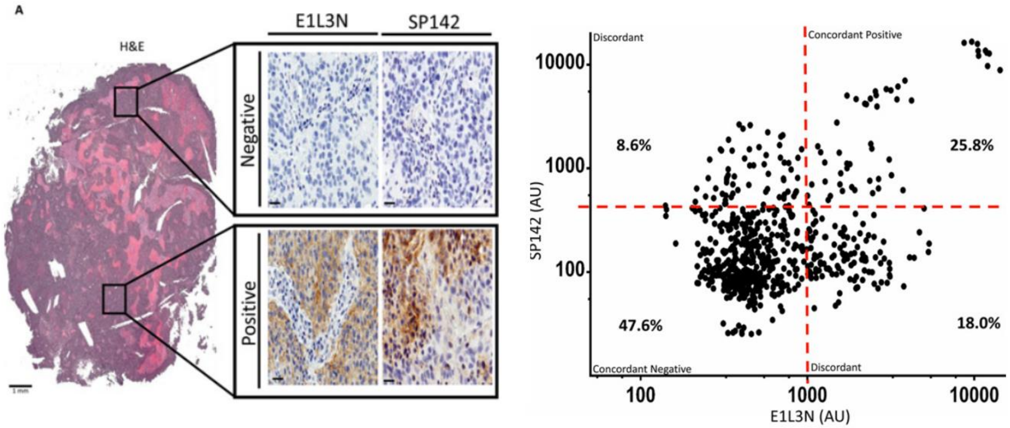

Heterogeneity of expression of PD-L1 and variation with antibody use (Maclaughlin et al. 2016).

Supervised Machine Learning for biomarker discovery

- Build a function f which takes as input baseline variables and predicts the patient's outcome

- We want f to minimize the error between the predicted outcome and the true observed one for all the patients of our cohort

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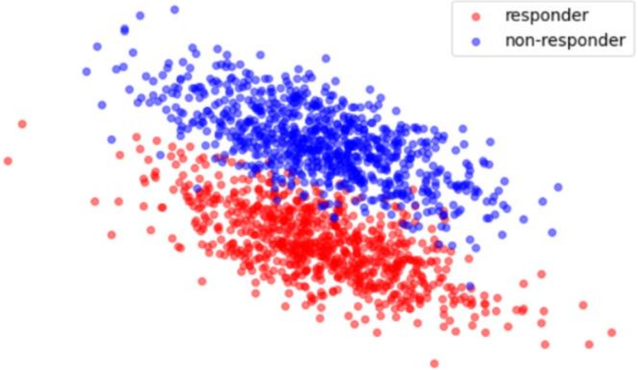

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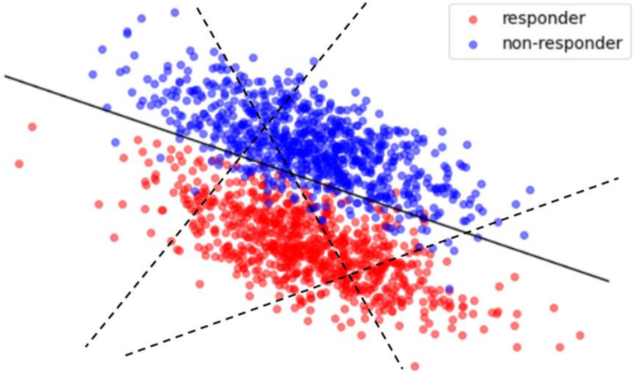
$$f(x_1, x_2) = \hat{\beta}_0 + \hat{\beta}_1 x_1 + \hat{\beta}_2 x_2 = \hat{y}$$



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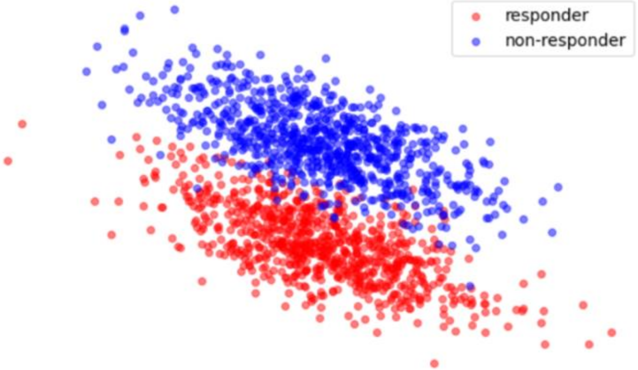

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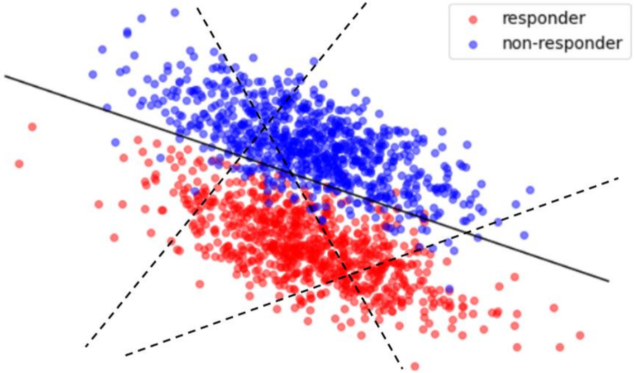

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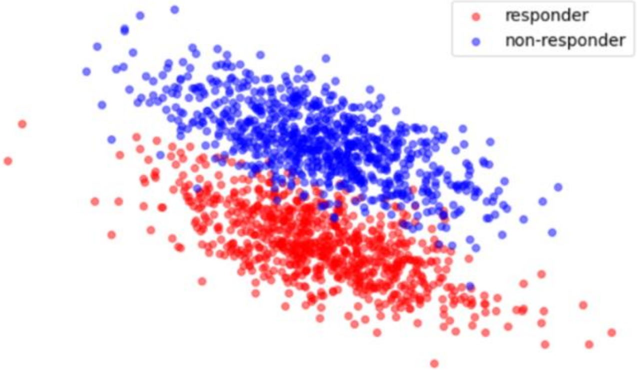

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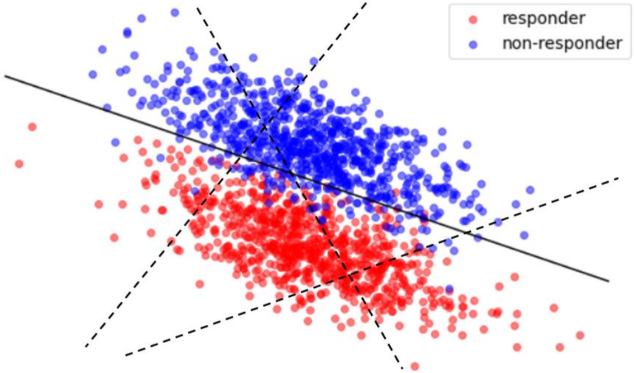

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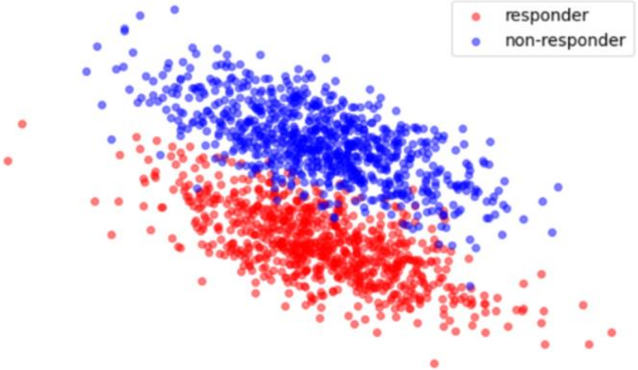

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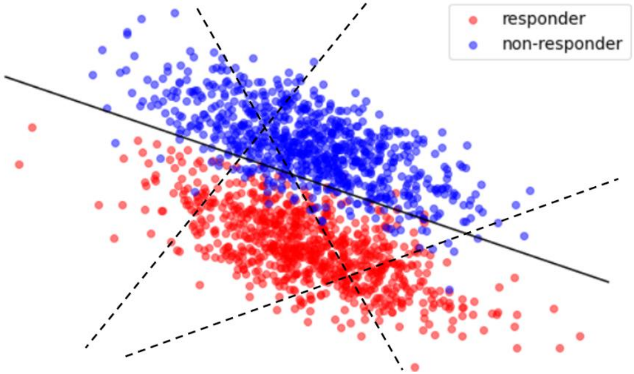

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❸ Make new hypotheses on the mechanisms modulating treatment response and motivate further experiments

TIPIT: multimodal Machine Learning for powerful predictions

- A wide variety of data modalities can now be collected for many patients at baseline

- They offer complementary views of the disease at different scales (molecular, tissular, whole-body…)

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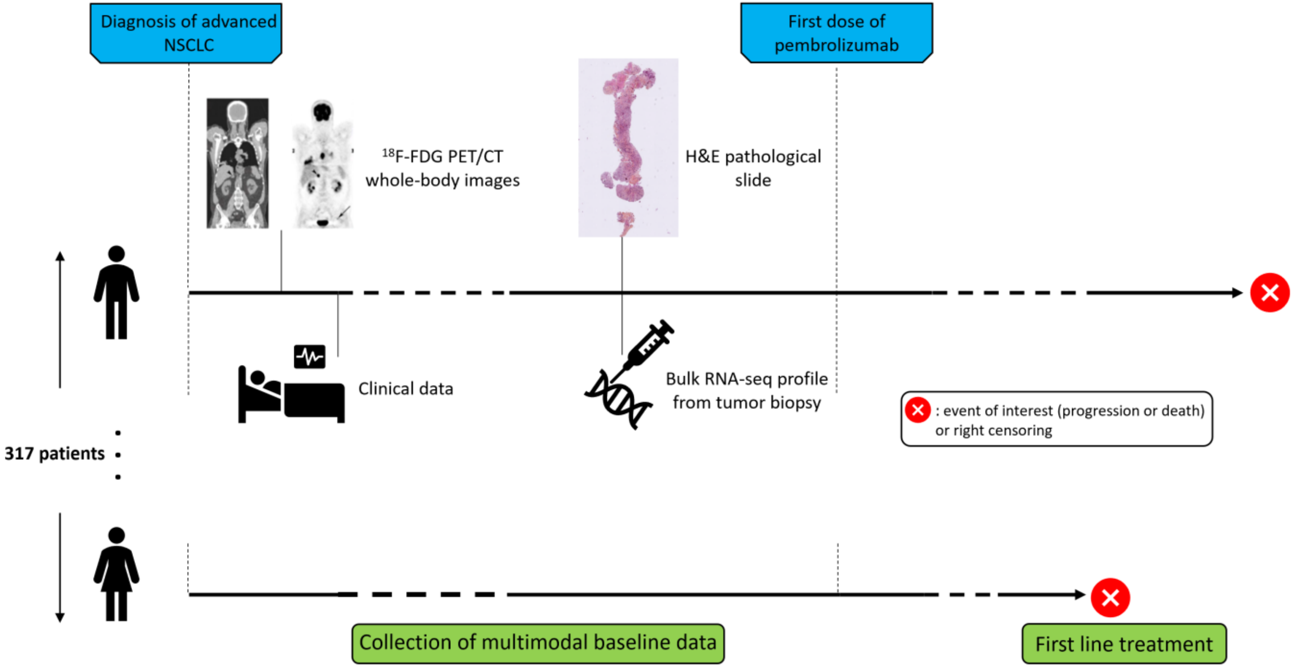

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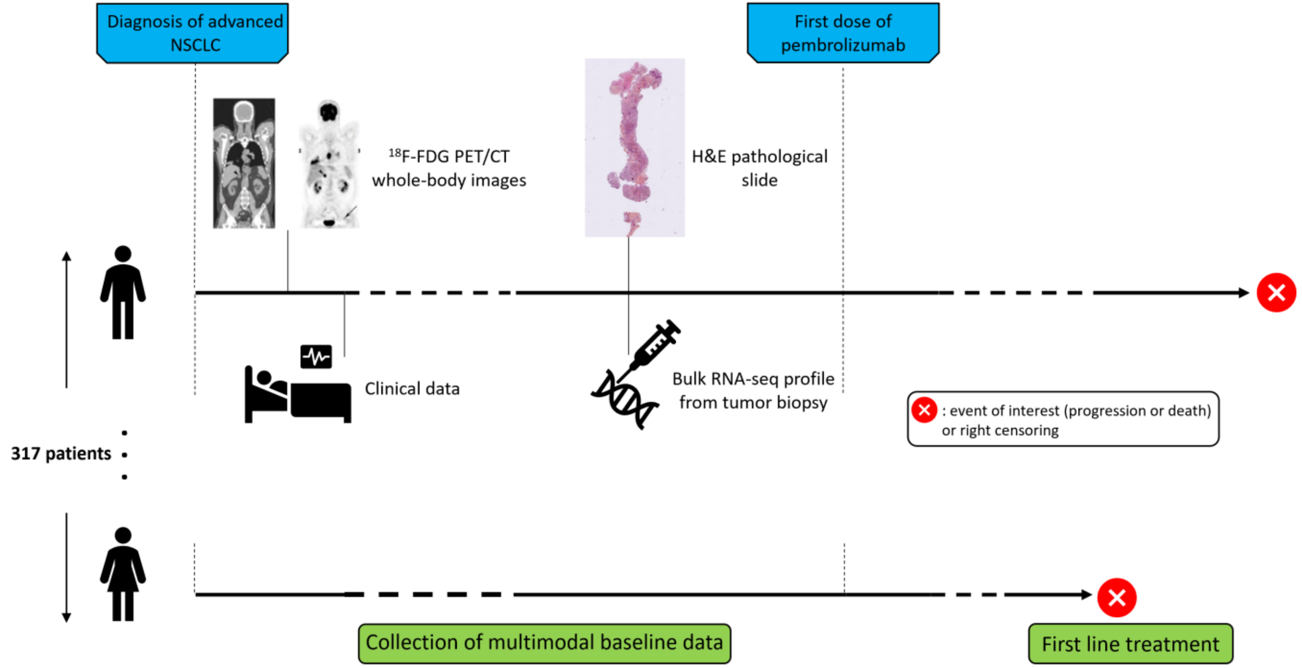

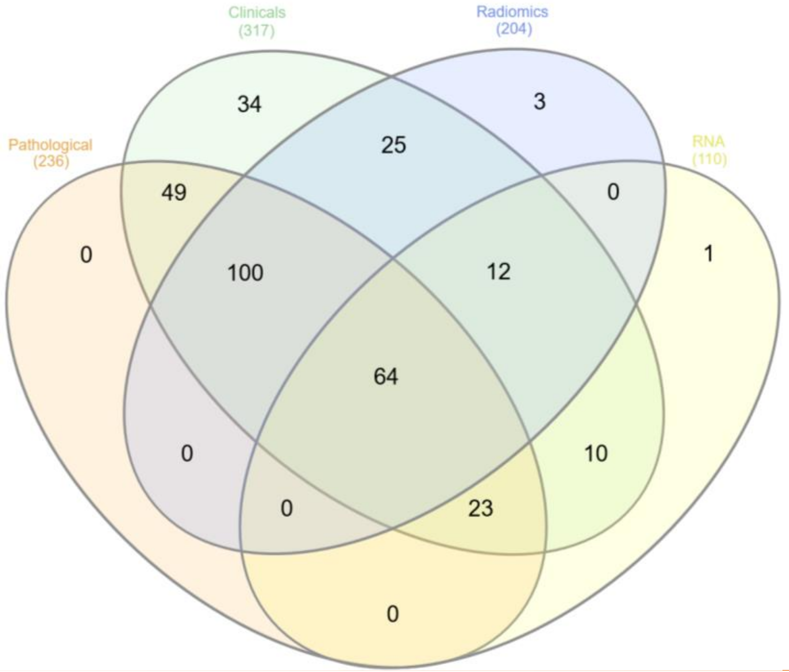

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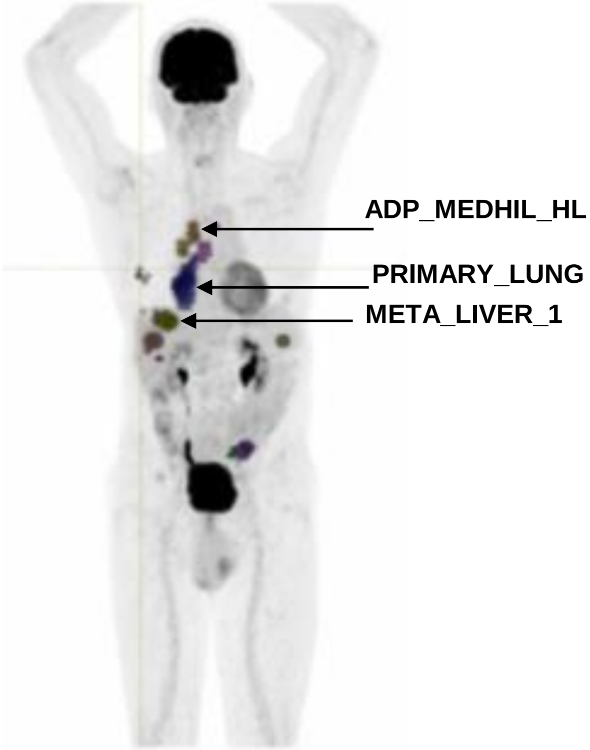
Medical imaging data & radiomics analyses

18F-FDG PET scans characterize the molecular heterogeneity of each metastasis as well as the spread of the disease in the whole-body



18F-FDG PET scan at baseline for a metastatic NSCLC patients. Segmentation and annotation of each lesion

Extraction of radiomic features for machine learning (at the lesion and the whole-body levels)

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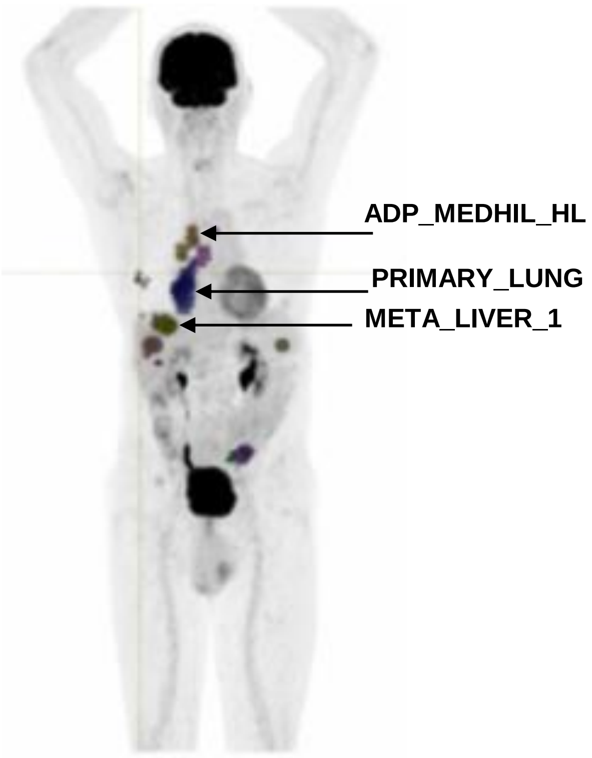

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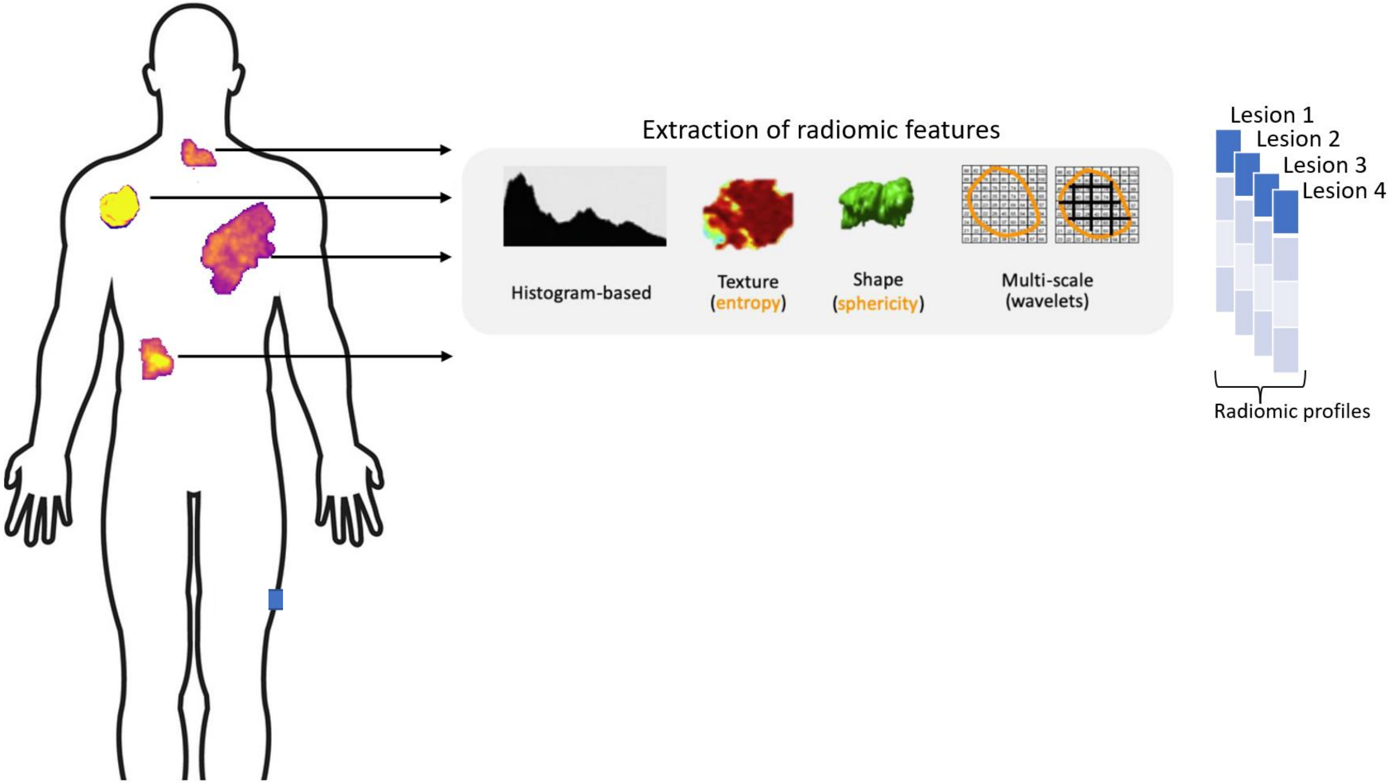

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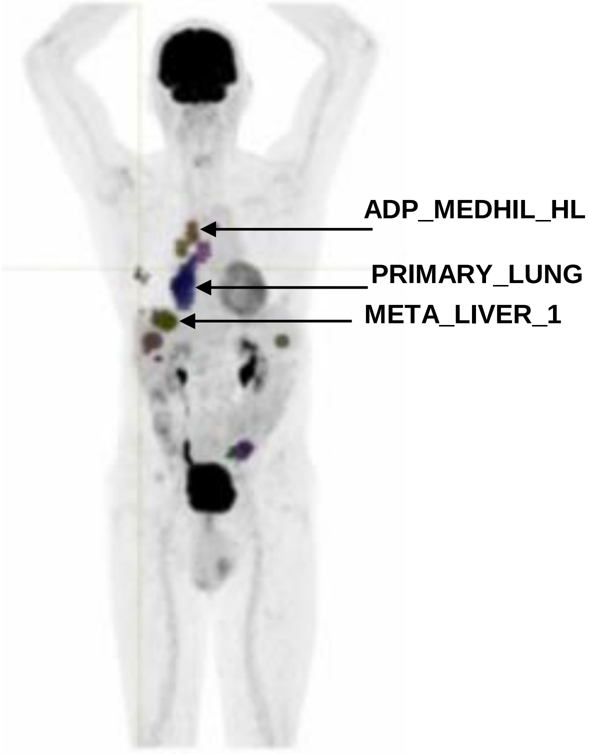

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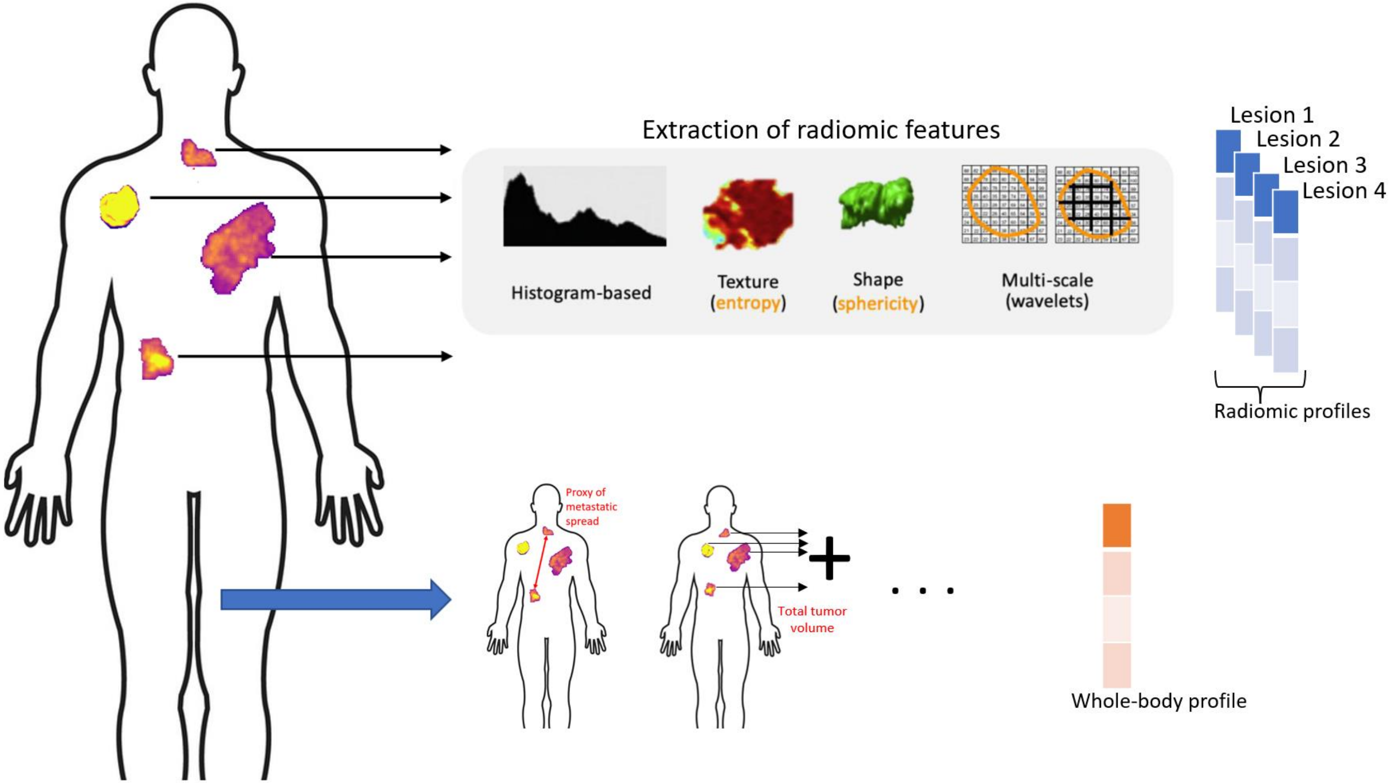

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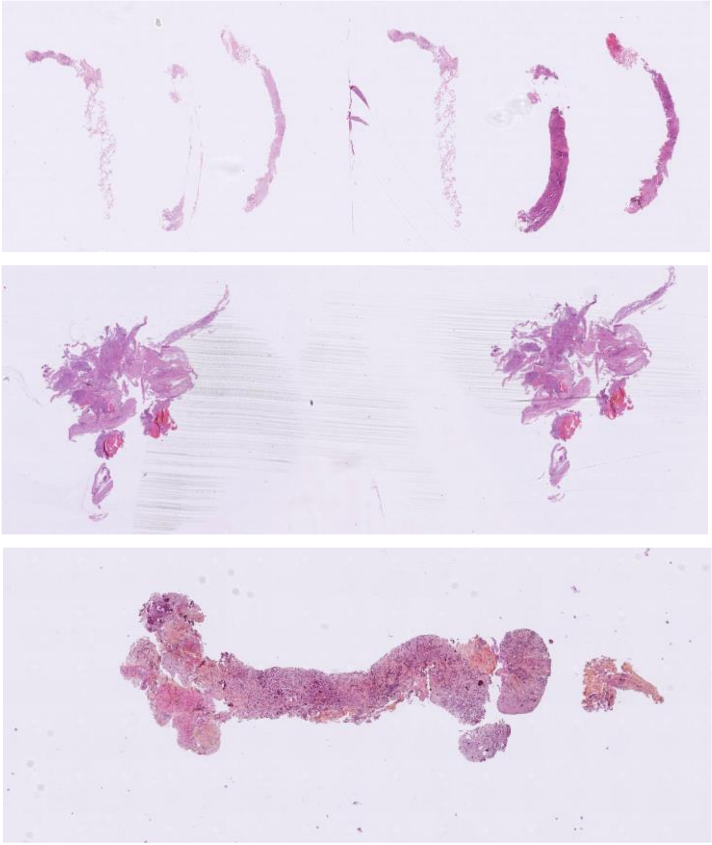
H&E pathological slides & pathomics analyses



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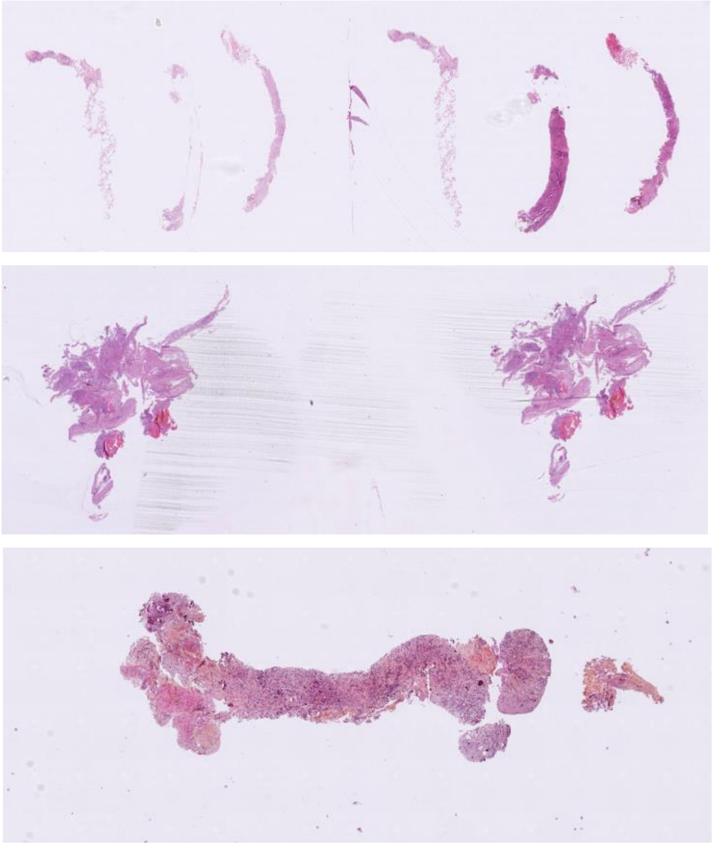

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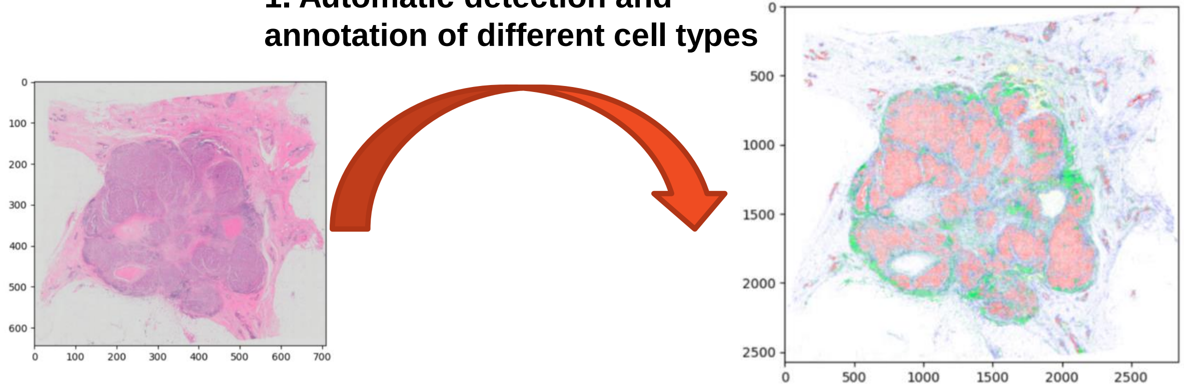

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Extraction of pathomics features for machine learning. Illustration with a breast cancer slide with lymphocytes (green), connective cells (blue) and neoplastic cells (red) (Marvin Lerousseau)

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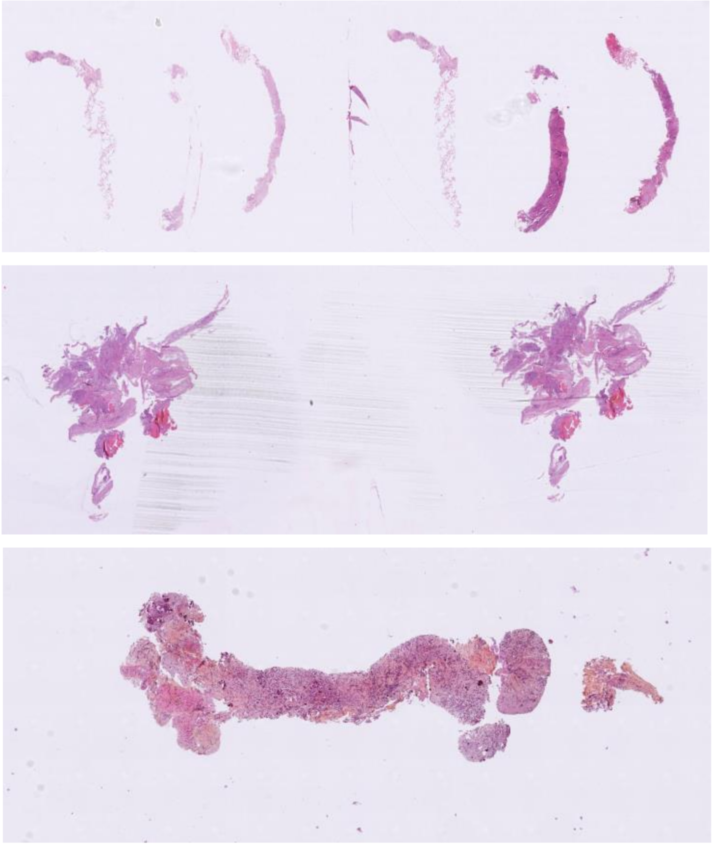

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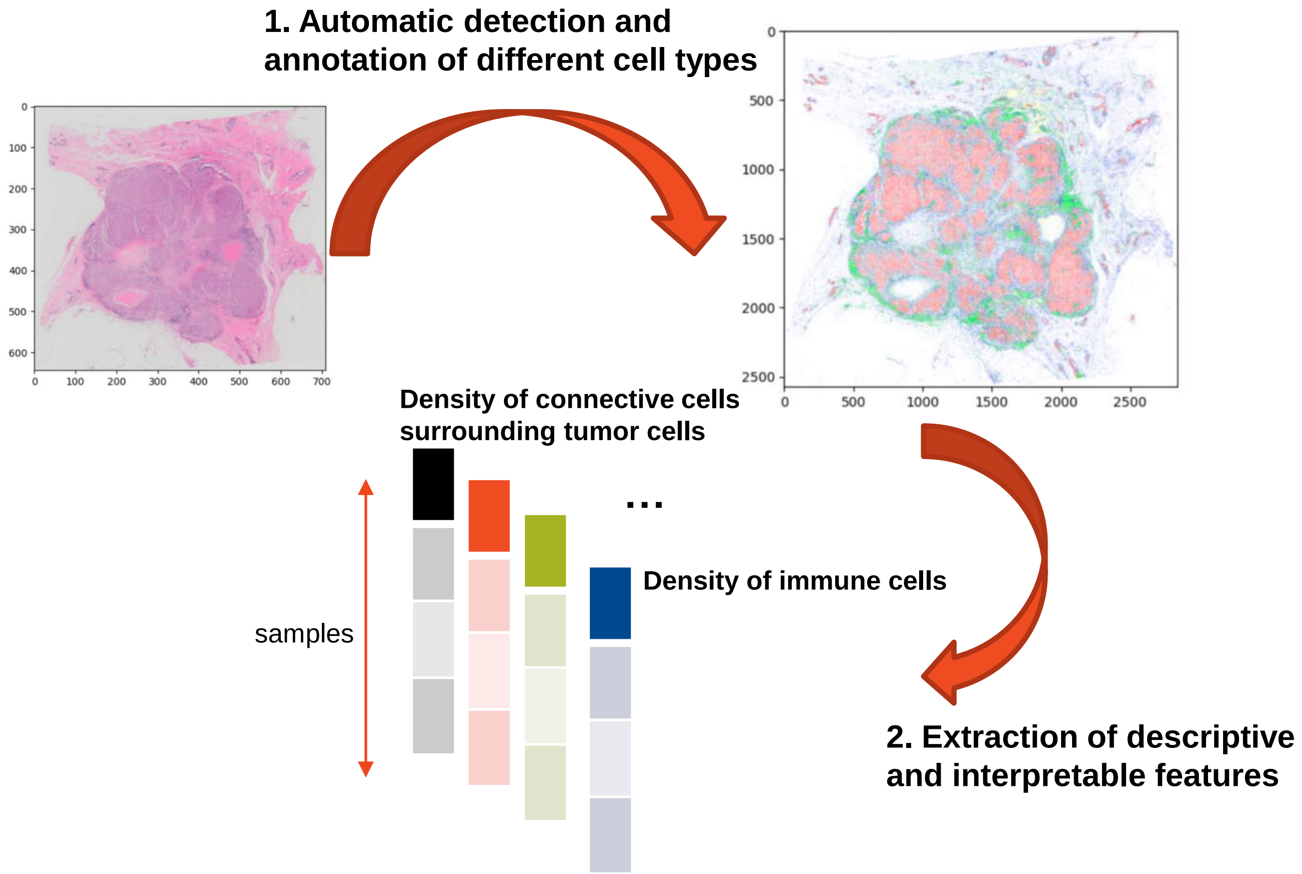

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Density of connective cells surrounding tumor cells

Density of immune cells

samples

2. Extraction of descriptive and interpretable features

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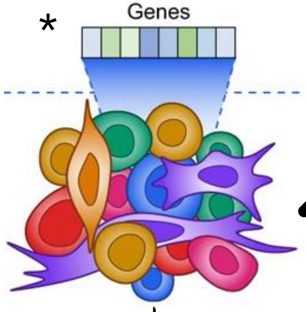
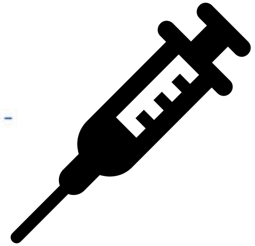
Bulk RNAseq: handle highly dimensional data

*

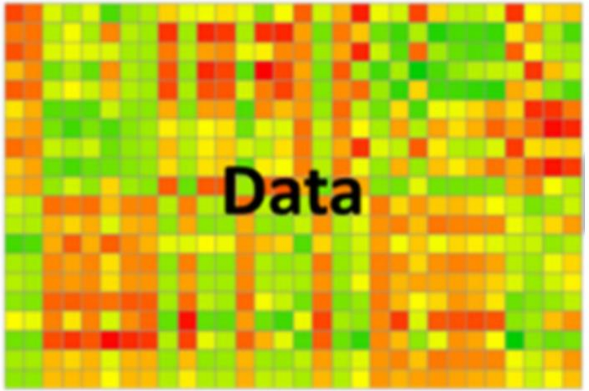




Solid biopsy of one patient

$\sim 2 \times 10^4$ protein-coding genes

110 samples



* Liao *et al.* Nature Communications 2022

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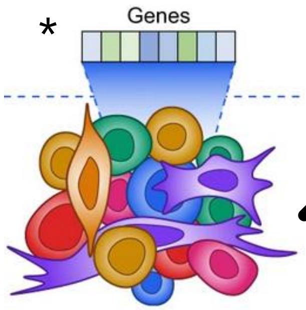

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1. Expression of specific oncogenes

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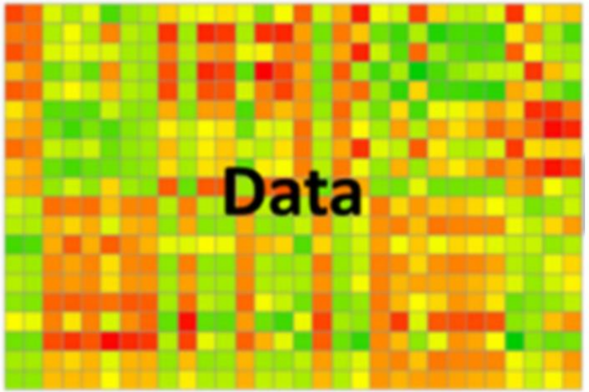

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Extraction based on prior knowledge

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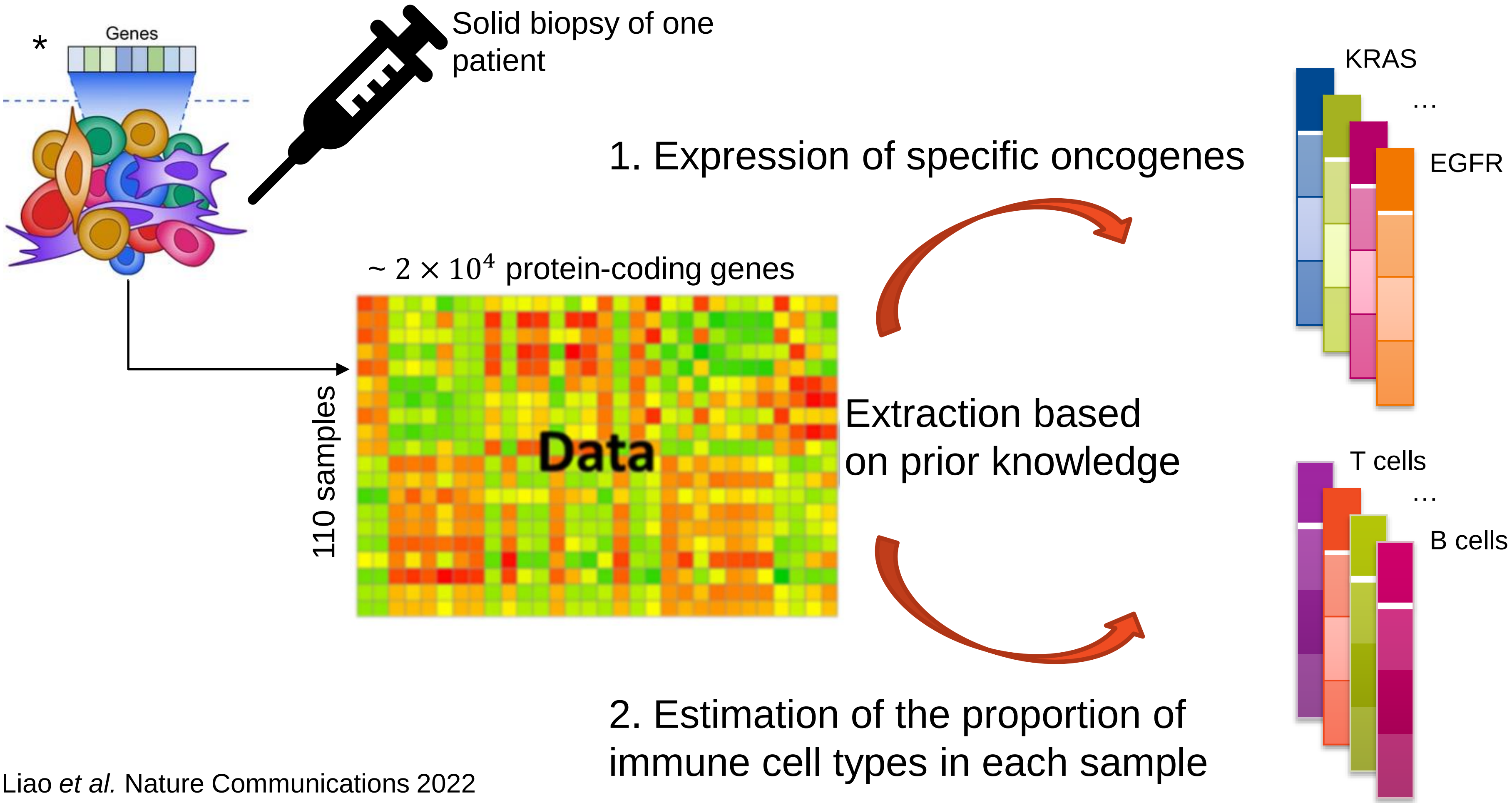

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Extraction based on prior knowledge

2. Estimation of the proportion of immune cell types in each sample

* Liao *et al.* Nature Communications 2022

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Late fusion strategy: aggregate unimodal predictions

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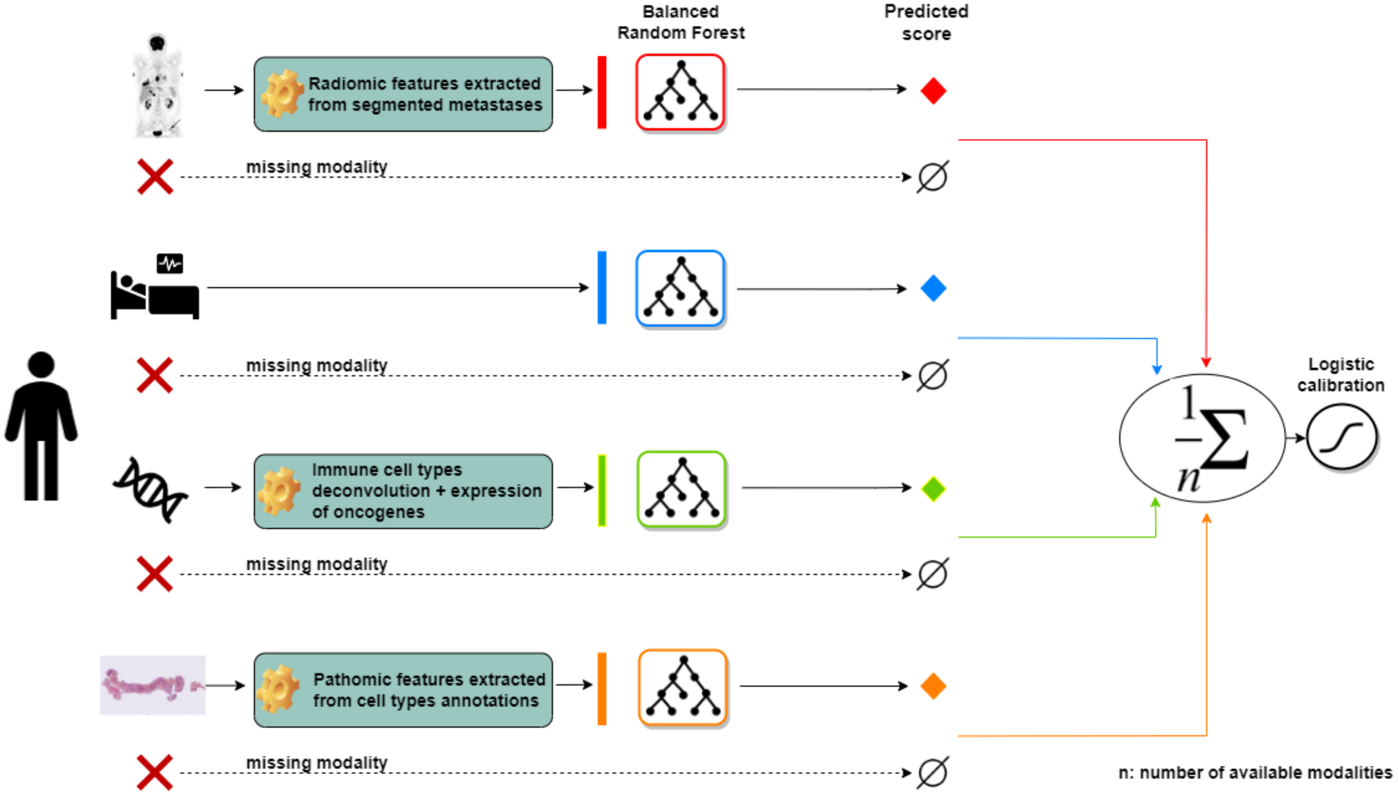

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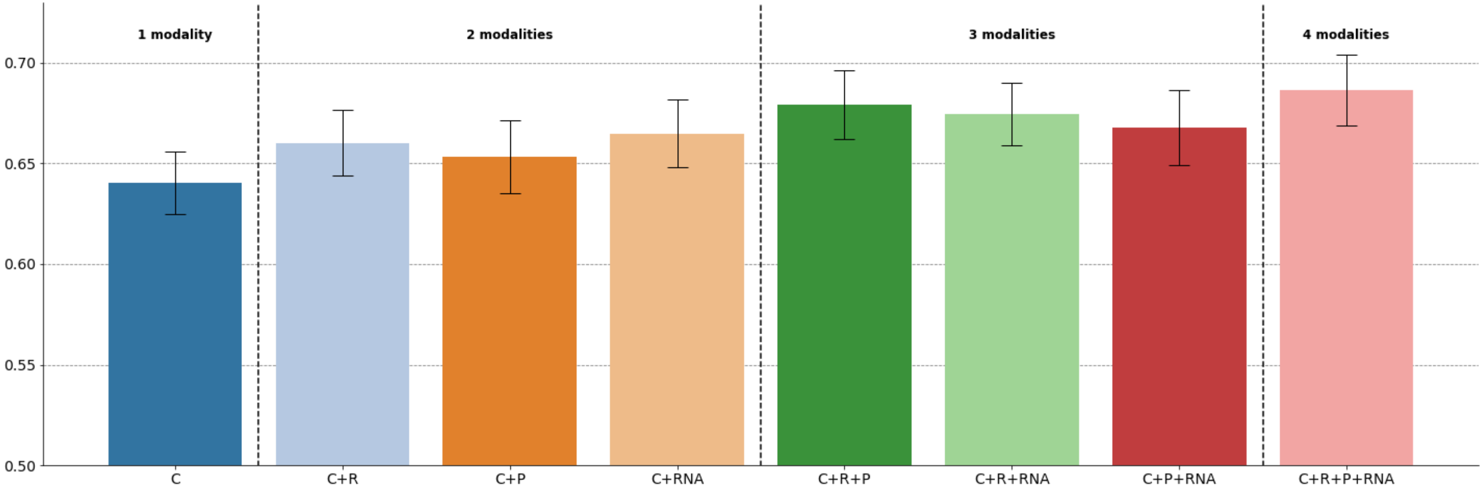

ROC AUC scores of different multimodal combinations averaged over 100 experiments

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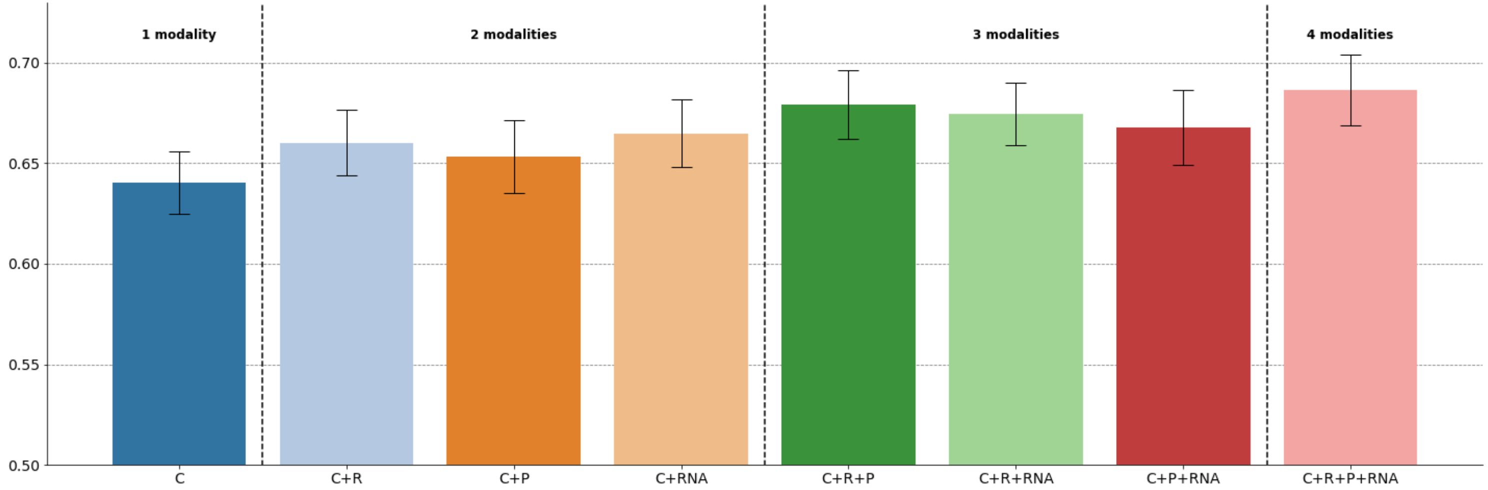

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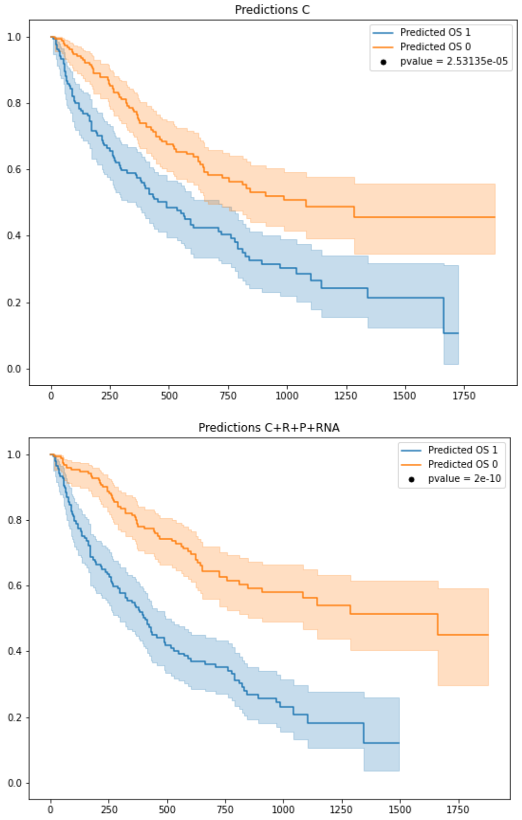

Kaplan-Meier curves comparing the two predicted classes (clinical model vs multimodal model)

Conclusions & perspectives

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3. Explore and design new features for the different modalities to use their full potential.

Acknowledgements

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