Deconvolution of Transcriptomic Data Shows Biologically and Clinically Relevant Signals in Pancreatic Tumors

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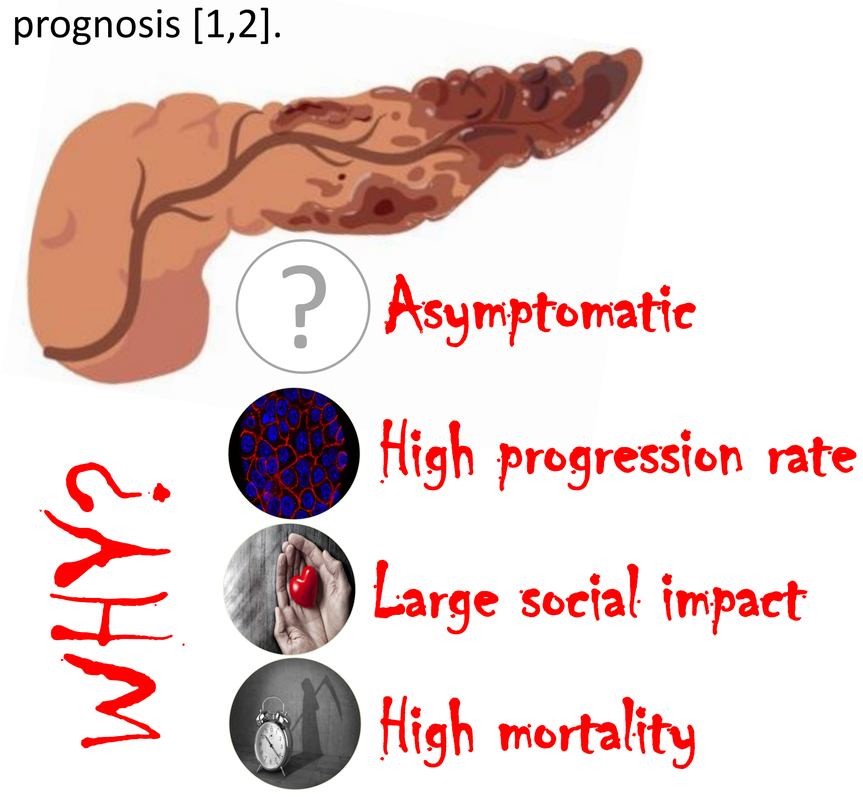
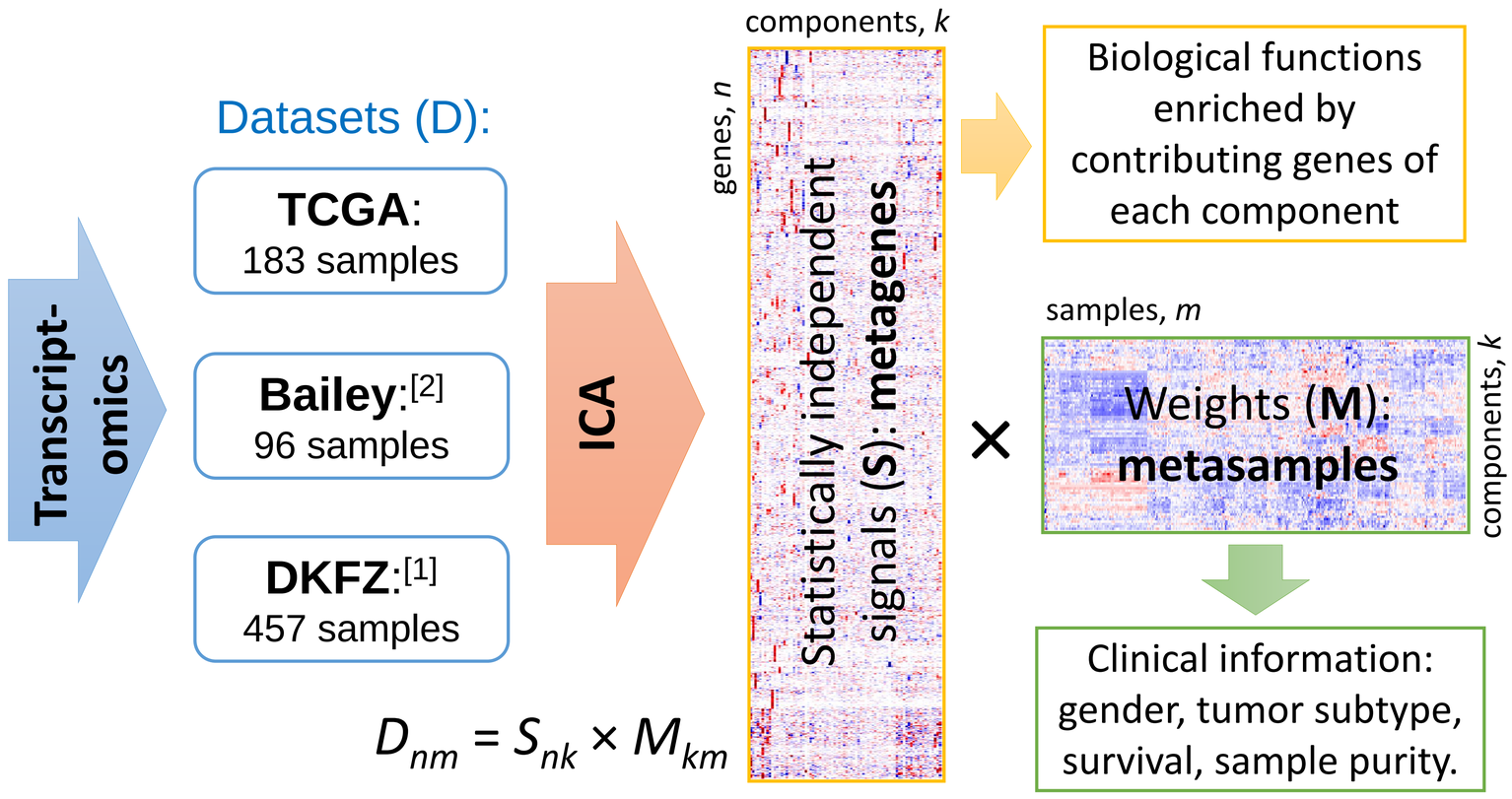
Pancreatic cancer is a significant **challenge** to oncology. The early stages of the disease are **asymptomatic**, which limits diagnosis and treatment of the neoplastic process and thus lead to bad survival prognosis [1,2].



Independent component analysis transforms the data into a matrix product of statistically independent transcriptional signals and their weight.



$$D_{nm} = S_{nk} \times M_{km}$$

Research goals:

1. Identify **pathophysiological processes** affecting survival of patients with pancreatic cancer.
2. Characterize **tumor purity** in unsupervised manner.
3. **Predict survival** of new patients.

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

Risk score (RS) is calculated as the weighted sum on scaled rows of ***M*** and Cox log hazard ratio (*H*). Stability of the components (R^2) is also considered.

https://gitlab.com/biomodlih/consica

1 Components identified by ICA were annotated by biological functions (GO) and linked to survival using Cox regression as is described in [3].

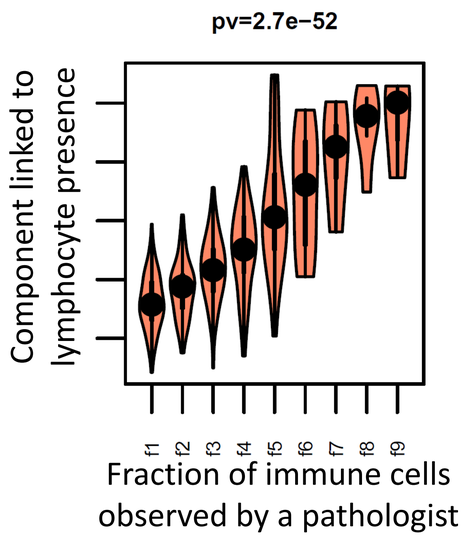
Increased risk:
- **keratinization**
- **cell cycle**
- response to hypoxia
- neoangiogenesis
- cornification
- activation of ERK-signaling

No effect:
- immune response
- gender
- axon development

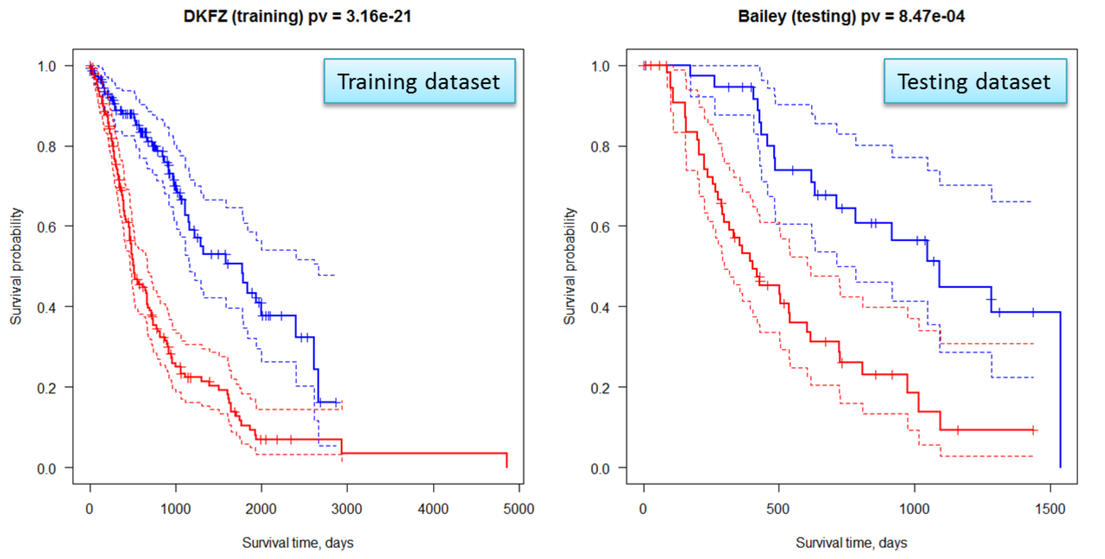
Reduced risk:
- hormone secretion activity (normal function)
- digestion
- antigen binding

Unlike in melanoma [3], no direct link was found between immune response and survival: perhaps due to a dual / antinomic effect.

2 ICA was able to detect transcriptional signals specific to stroma and tumors. Abundance of normal pancreas tissue as well as immune cells was detected in an unsupervised manner and correlated to an independent observation of an immuno-histopahthologist. For Bailey dataset such correlation was observed with *in silico* predictions.



3 Here we combined DKFZ (training) and Bailey (testing) datasets. ICA was performed on the joint data. Risk scores (RS) were calculated as in [3] and visualized:



Conclusions:

- Pathophysiological **processes** that affect survival in patients with pancreatic cancer are **cell proliferation** and **keratinization**. No strong effect of immune components on survival was detected.
- **Tumor purity** was characterized. It strongly correlated with independent observations of immune cells in DKFZ cohort and in silico estimation in Bailey dataset.
- **Risk score** calculated for the testing dataset (Bailey) strongly correlated with the survival (p-value < 0.001).

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References

1. Bauer et al., International Journal of Cancer, 2018, 142(5):1010-21
2. Bailey et al., Nature, 2016, doi:10.1038
3. Nazarov et al., BMC Genomics, 2019, 12(1):132