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consICA: a package for parallel consensus ICA of multi-omics data and interpretation of the results

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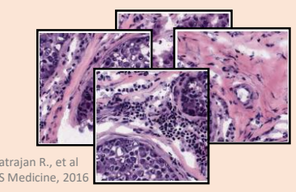
Challenges

Experimental data (RNA-seq)

- Technical heterogeneity
- Sample composition
- Clonal evolution in cancer


http://abrf.masonlab.net/


Natrajan R., et al PLoS Medicine, 2016

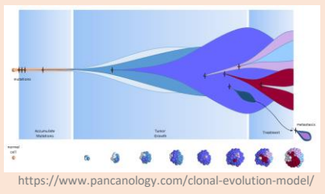
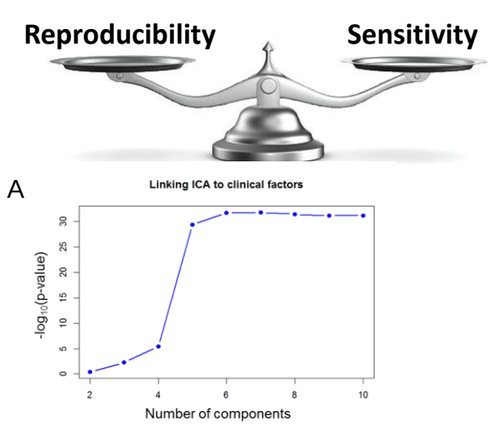

https://www.pancanology.com/clonal-evolution-model/

FIGURE 1. Sources of biases that limit comparison between transcriptomics data of cancer patients.



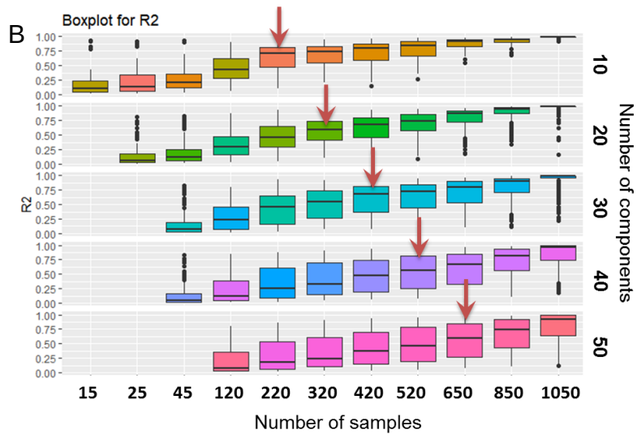


FIGURE 3. (A) Detection of a confounding factor (gender) by ICA. (B) The stability of ICA increases with growth of the dataset and decreases with increase of the number of components.

Method

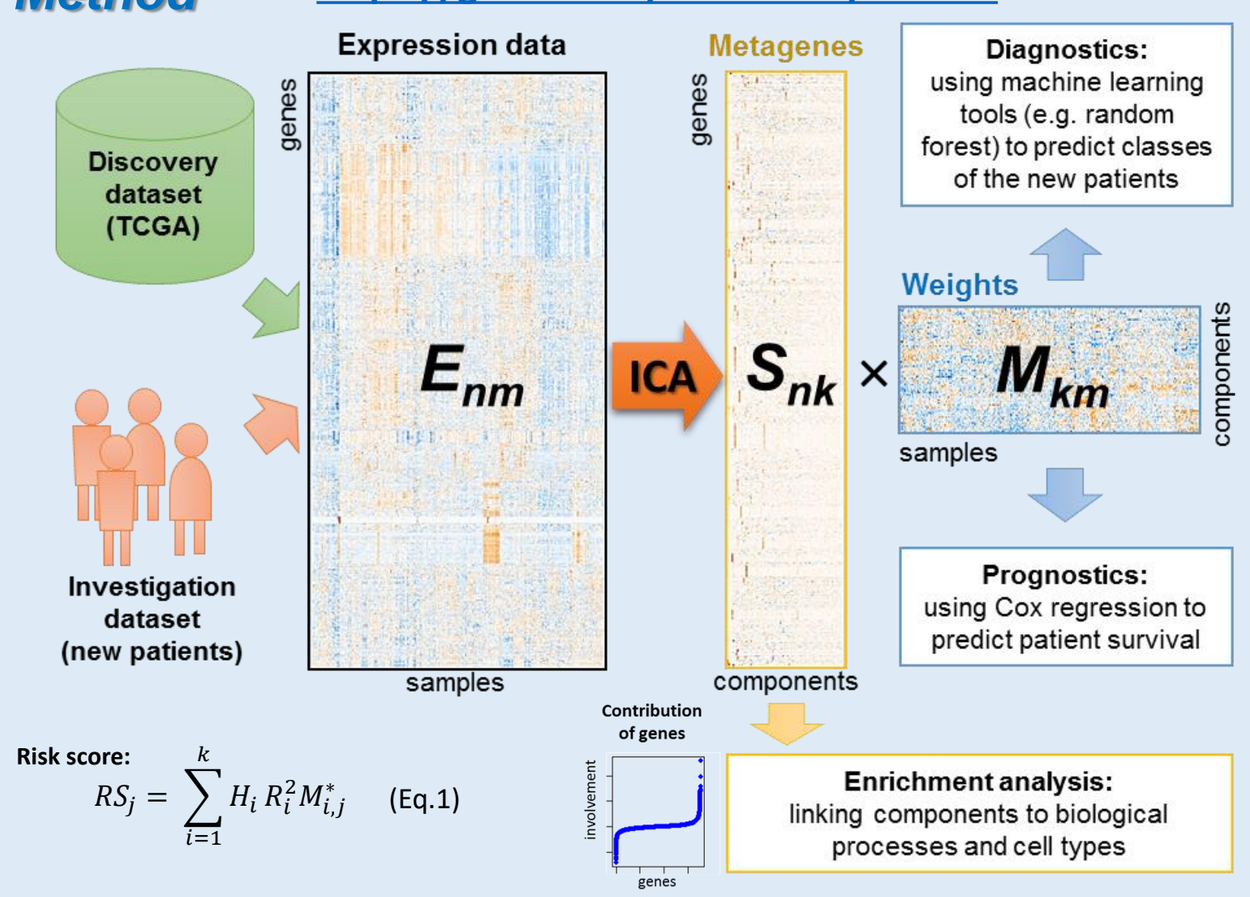
https://gitlab.com/biomodlih/consica

SKCM (melanoma)
Discovery: 472
Validation: 44
Investigation: 5

GBM/LGG (gliomas)
Discovery: 701
Validation: 325
Investigation: 58

LUAD/LUSC (lung cancers)
Discovery: 1128
Validation: 490
Investigation: 36

PAAD (pancreas cancers)
Discovery: 457
Validation: 96
Investigation: 183



Risk score:
$$RS_j = \sum_{i=1}^{k} H_i \, R_i^2 M_{i,j}^* \quad \text{(Eq.1)}$$

FIGURE 2. ICA decomposes combined gene expression matrix from multiple bulk samples into meaningful signals in the space of genes (metagenes, **S**) and weights in the space of samples (weight matrix, **M**). Biological processes and signatures of cell subtypes can be found in **S**, while **M** could be linked to patient groups and patient survival (Cox regression and Eq.1).

Platform bias / biological processes

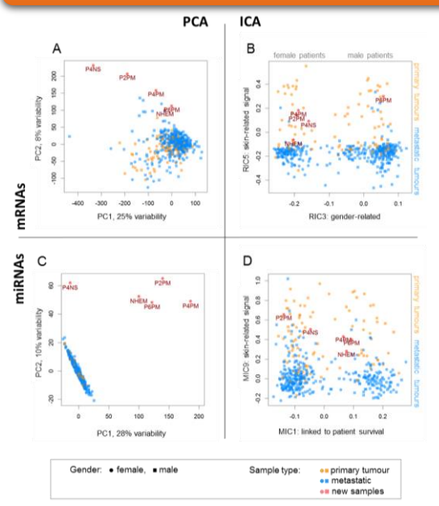


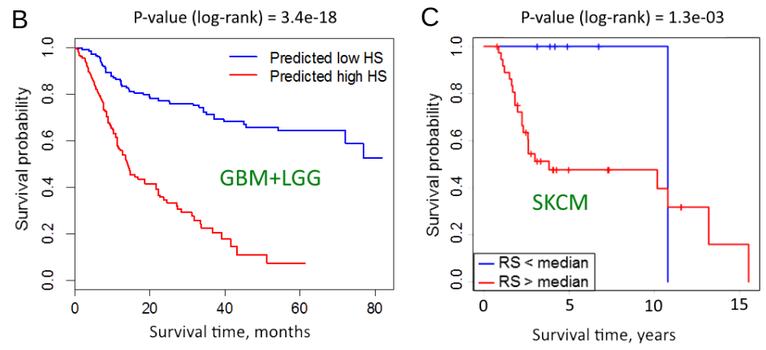
FIGURE 4. ICA-based batch correction in melanoma mRNA (A,B) and miRNA (C,D) datasets. PCA captures mainly technical factors, while ICA correctly projects new samples into the space of biologically meaningful components.

Diagnostics & prognostics

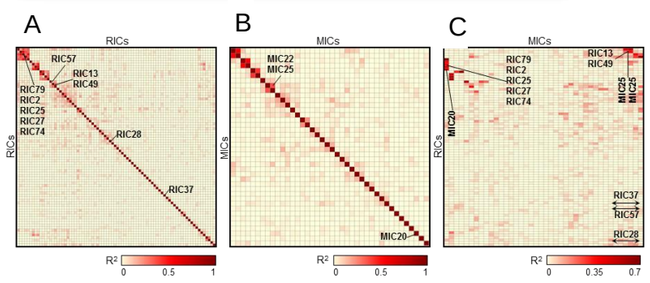
A

Actual → Predicted ↓	immune	keratine	MITF-low
immune	160	9	6
keratine	9	91	6
MITF-low	1	2	47

FIGURE 5. Example of confusion matrix for melanoma patient classification for melanoma (A). Predicted risk correlates with actual survival in independent cohorts of glioma (B) and melanoma (C) patients.



Multi-omics data integration



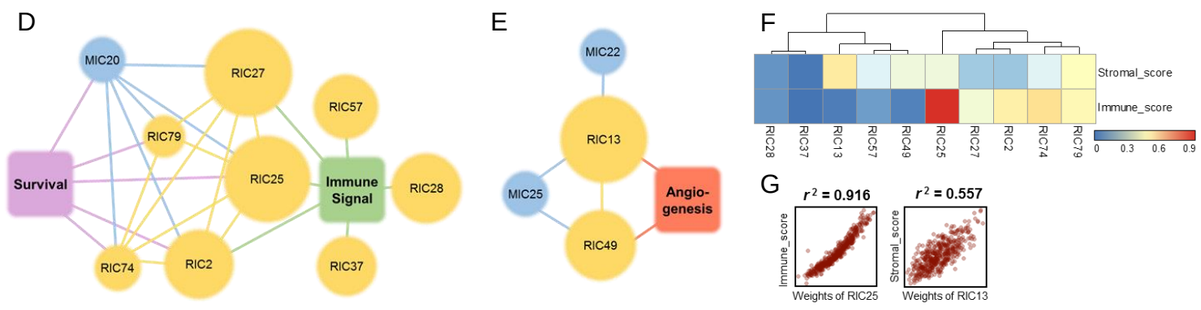


FIGURE 6. Heatmaps of r^2 between weights (**M**-matrix) of RIC-RIC (A), MIC-MIC (B) and RIC-MIC (C). Clusters of components linked to immune response (D) and to angiogenesis and stroma (E). Components were compared with ESTIMATE scores and corresponding r^2 are shown in (F). RIC25 and RIC13 components correlated best to immune and stromal scores (G).

Conclusions

- ❑ Consensus ICA **corrects technical biases** and improves comparability of the new data to the reference dataset.
- ❑ ICA provides information about **biological processes** in the new samples and allows scoring them.
- ❑ Weights of the ICA-derived components can be used to **predict patient survival and classes**, as was demonstrated on an independent datasets.
- ❑ Finally, ICA can be used for **data integration**, when several levels of omics data are available.

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References

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2. Nazarov et al., **(2019)** BMC Medical Genomics
3. https://gitlab.com/biomodlih/consica

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