

SPOTlight: Seeded NMF regression to Deconvolute Spatial Transcriptomics Spots with Single-Cell Transcriptomes

Marc Elosua Bayes, Paula Nieto, Elisabetta Mereu,
Ivo Gut, Holger Heyn



cnag

centre nacional d'anàlisi genòmica
centro nacional de análisis genómico



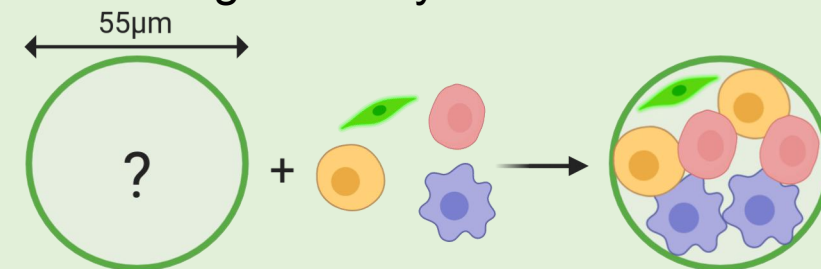
upf.

Universitat
Pompeu Fabra
Barcelona

CNAG-CRG, Centre for Genomic Regulation (CRG) -
Single-Cell Genomics and Biomedical Genomics groups
Universitat Pompeu Fabra (UPF), Barcelona, Spain.

Introduction

- Spatially resolved gene expression profiles are key to understand tissue organization and function.
- Array-based spatial transcriptomics (ST) is an unbiased and high-throughput approach to map genes within their spatial context with its main trade-off being the loss of single-cell resolution.
- scRNAseq enables the profiling of thousands of single-cell transcriptomes without preserving the spatial context and potentially introducing recovery biases of cell composition.



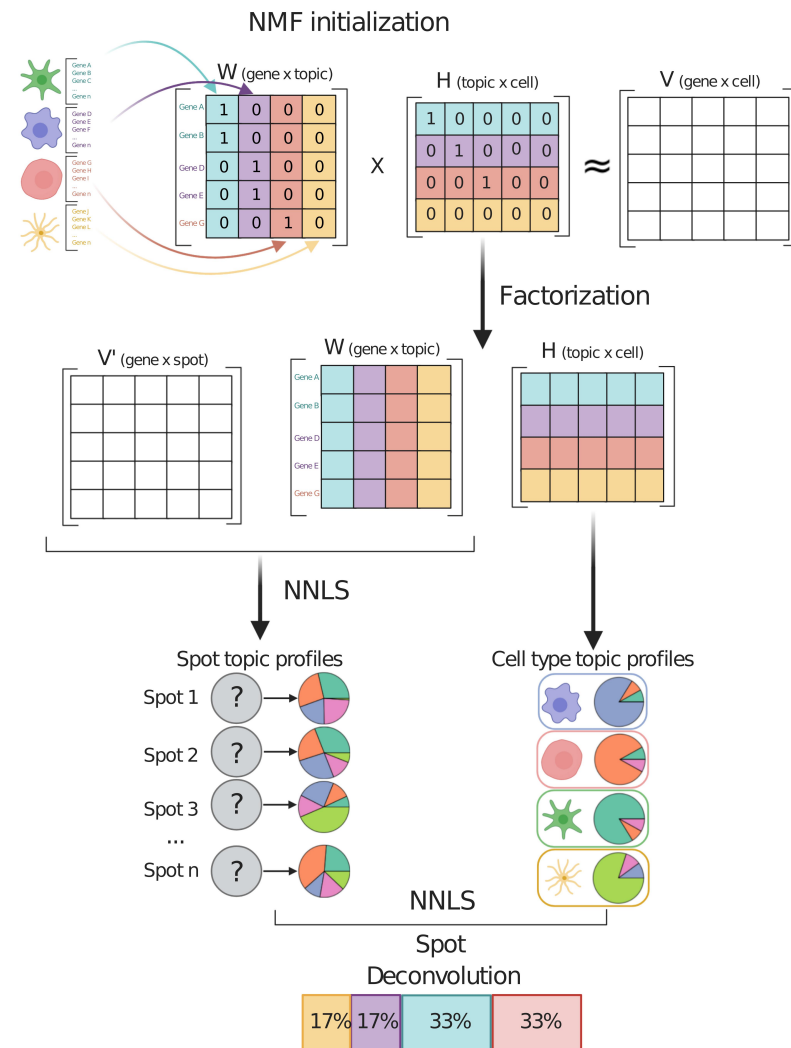
<https://www.biorxiv.org/content/10.1101/2020.06.03.131334v1>

<https://github.com/MarcElosua/SPOTlight>

Objectives

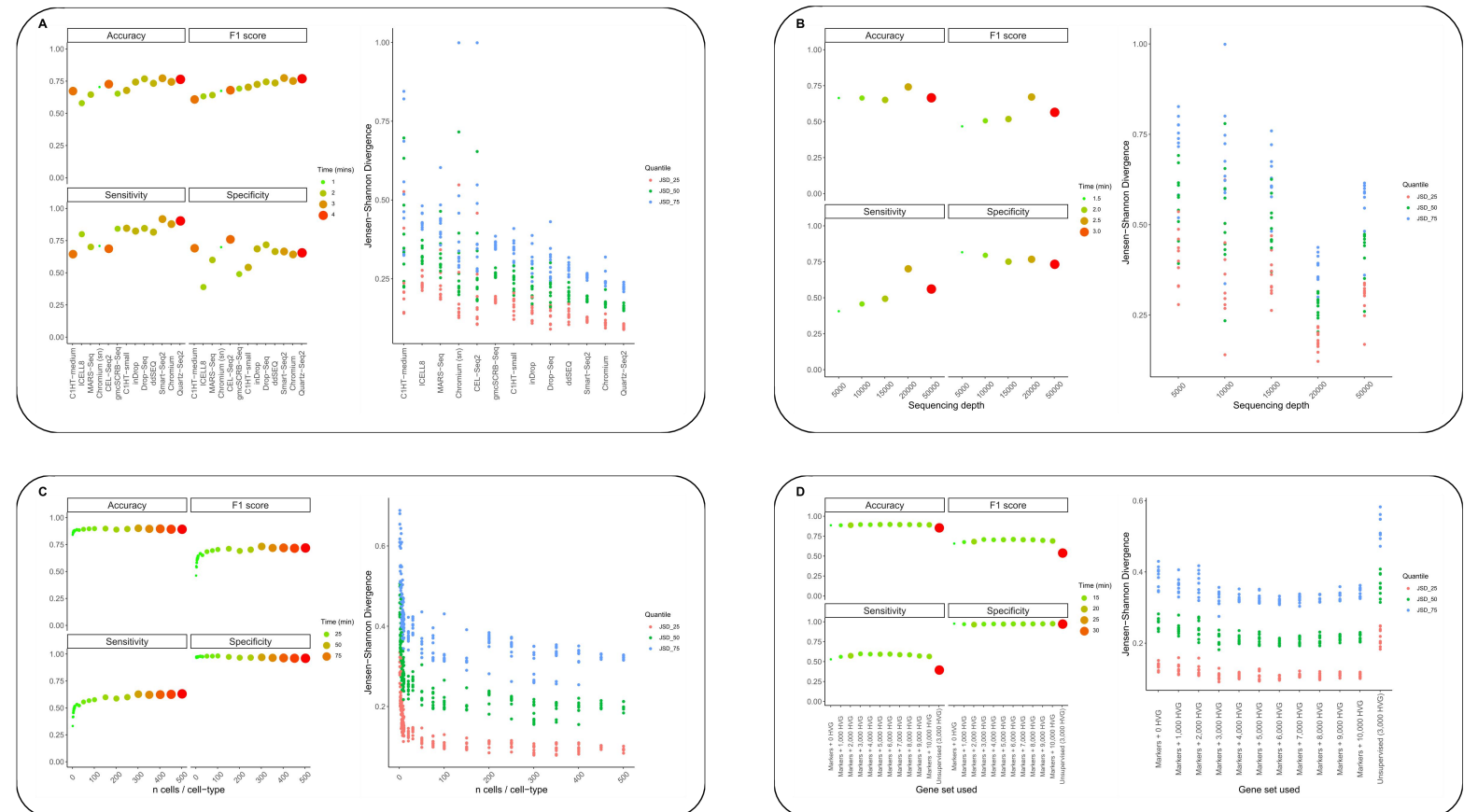
- To develop a framework integrating spatial transcriptomics and scRNAseq data modalities.
 - To benchmark the performance in different technical settings.
 - To validate the results in biologically relevant models.

Method



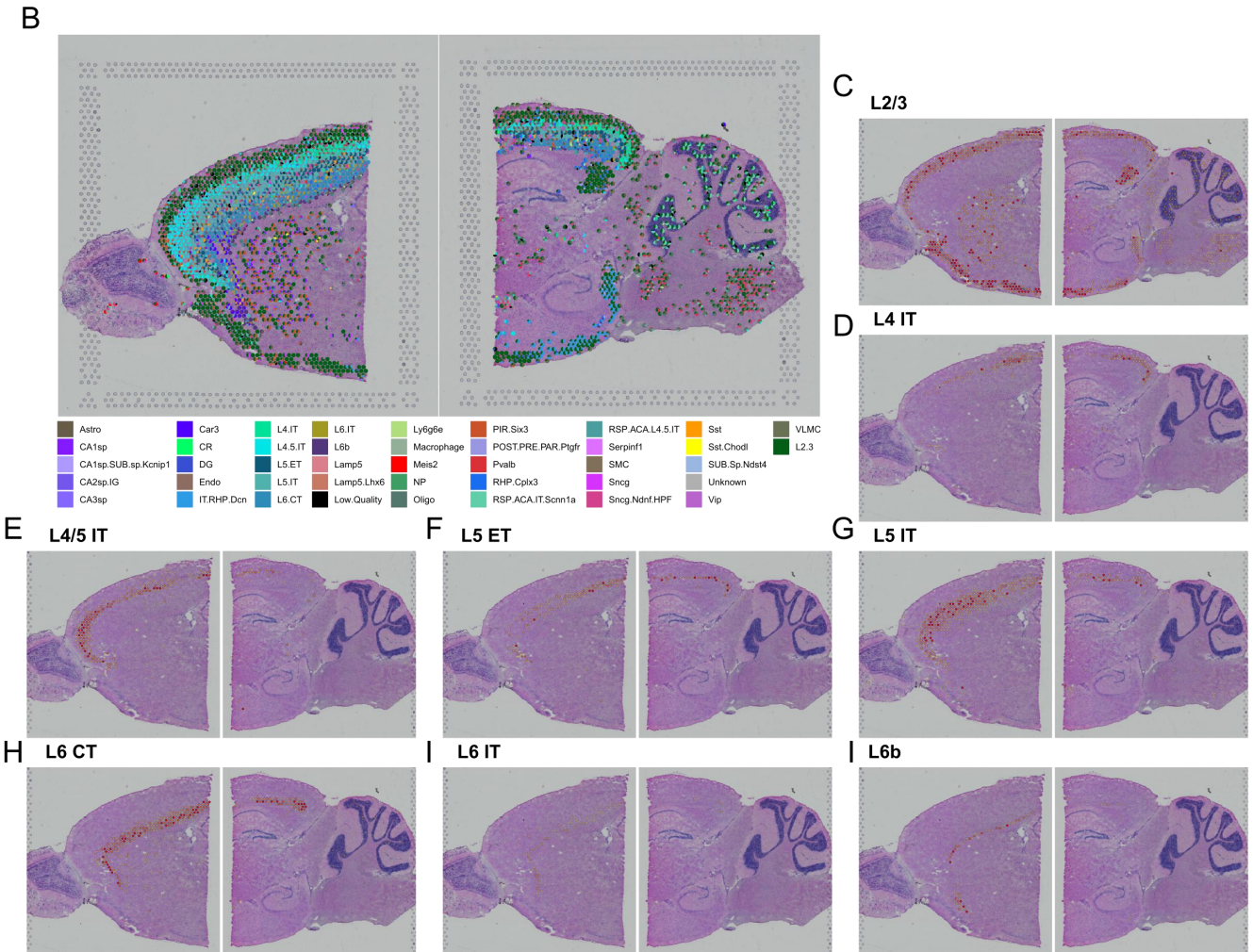
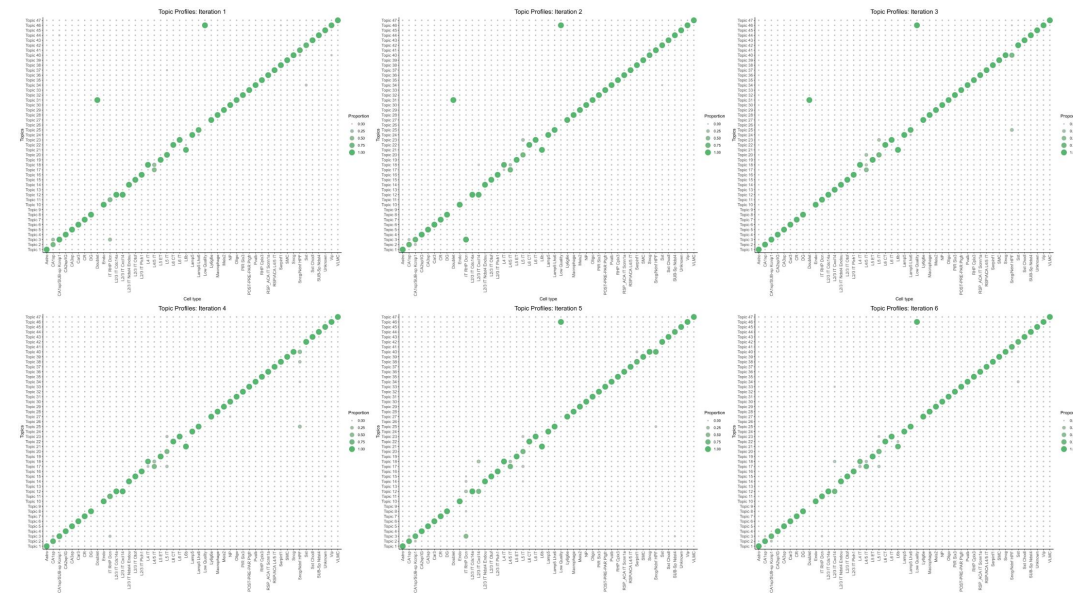
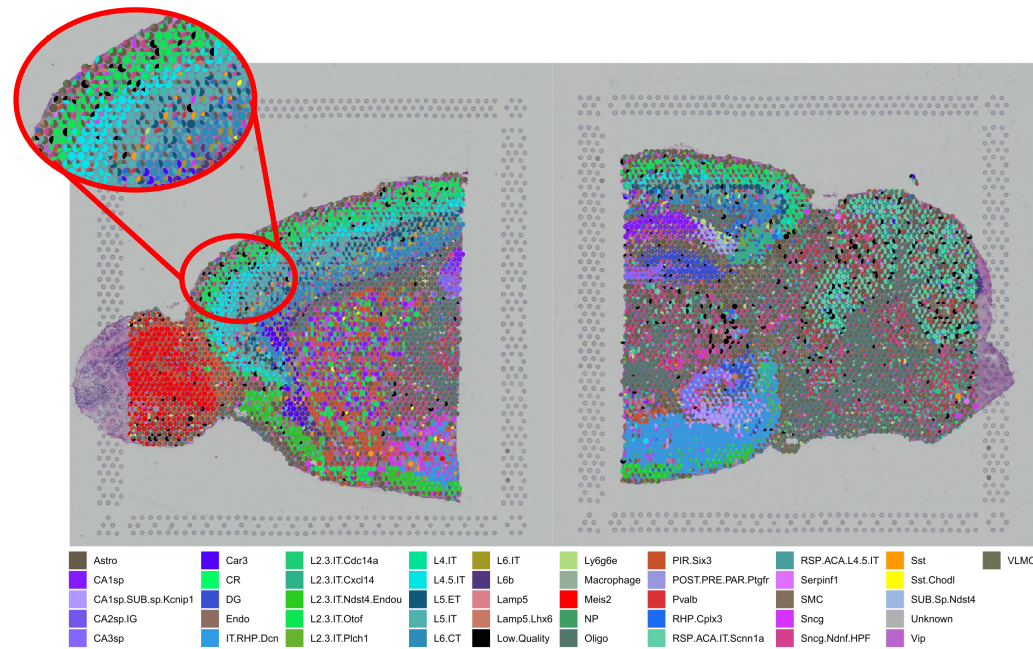
Results

1- Technical Validation



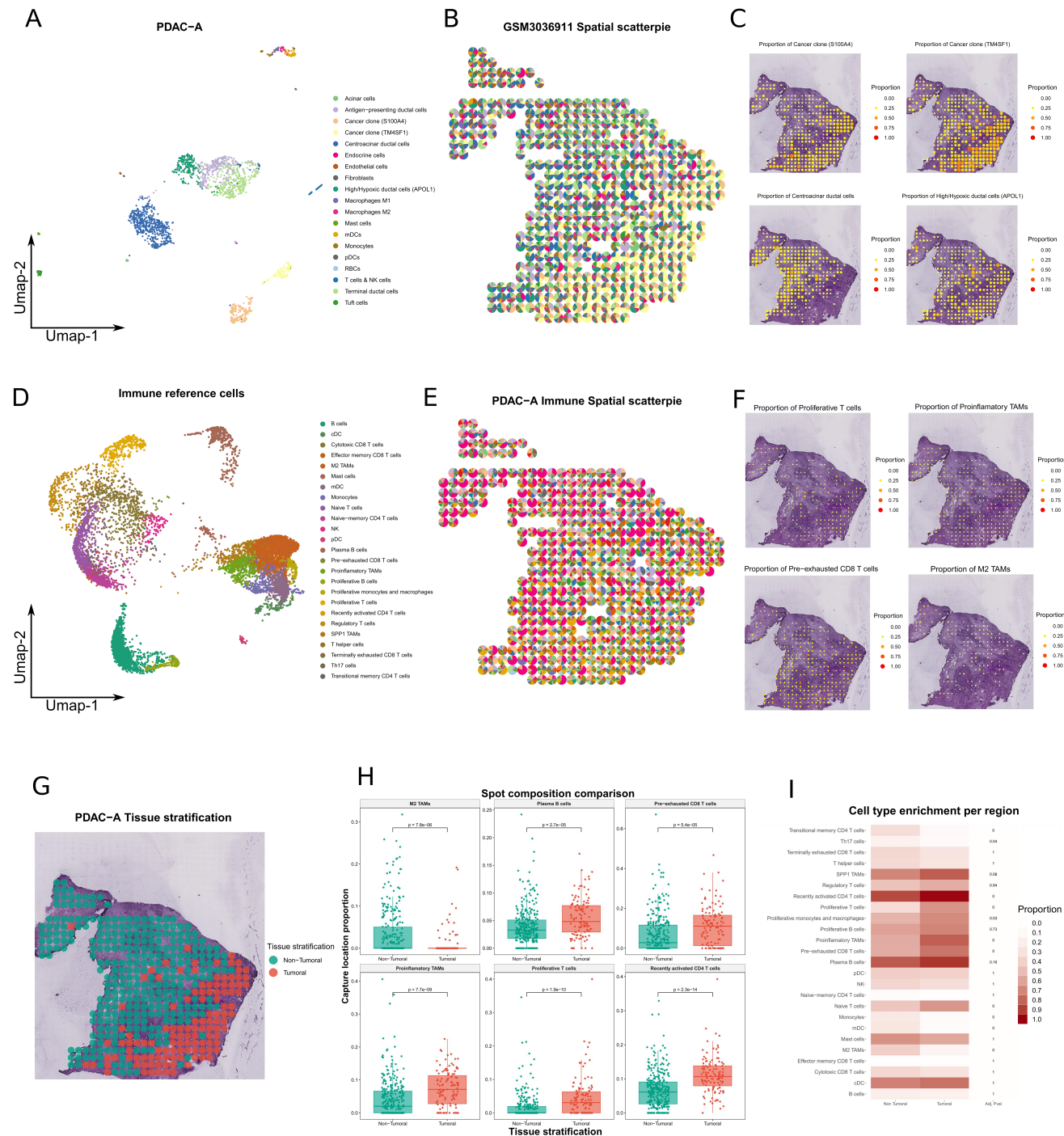
Results

2- Model tissue Validation



Results

3- Pancreatic Ductal Adenocarcinoma validation



Conclusions

- SPOTlight proved to be a robust, accurate, and sensitive tool to determine cell-type locations and a fine-grained composition of ST spots.
- We applied SPOTlight on different biological scenarios, different technology versions, and using matched and external references confirmed its broad and flexible application spectrum.
- We believe SPOTlight to be a universal tool to combine both pillars of the single-cell genomics field and to deduce cellular function and organization in situ.

1- Lein, E.S., Hawrylycz, M.J., Ao, N., Ayres, M., Bensinger, A., Bernard, A., Boe, A.F., Boguski, M.S., Brockway, K.S., Byrnes, E.J., et al. (2007) Genome-wide atlas of gene expression in the adult mouse brain. *Nature*, 445, 168–176.

2- Moncada, R., Barkley, D., Wagner, F., Chiodin, M., Devlin, J.C., Baron, M., Hajdu, C.H., Simeone, D.M. and Yanai, I. (2020) Integrating microarray-based spatial transcriptomics and single-cell RNA-seq reveals tissue architecture in pancreatic ductal adenocarcinomas. *Nat. Biotechnol.*, 38, 333–342.