

# Gene Expression Network Analysis in Emerging Model Organisms

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## ABSTRACT

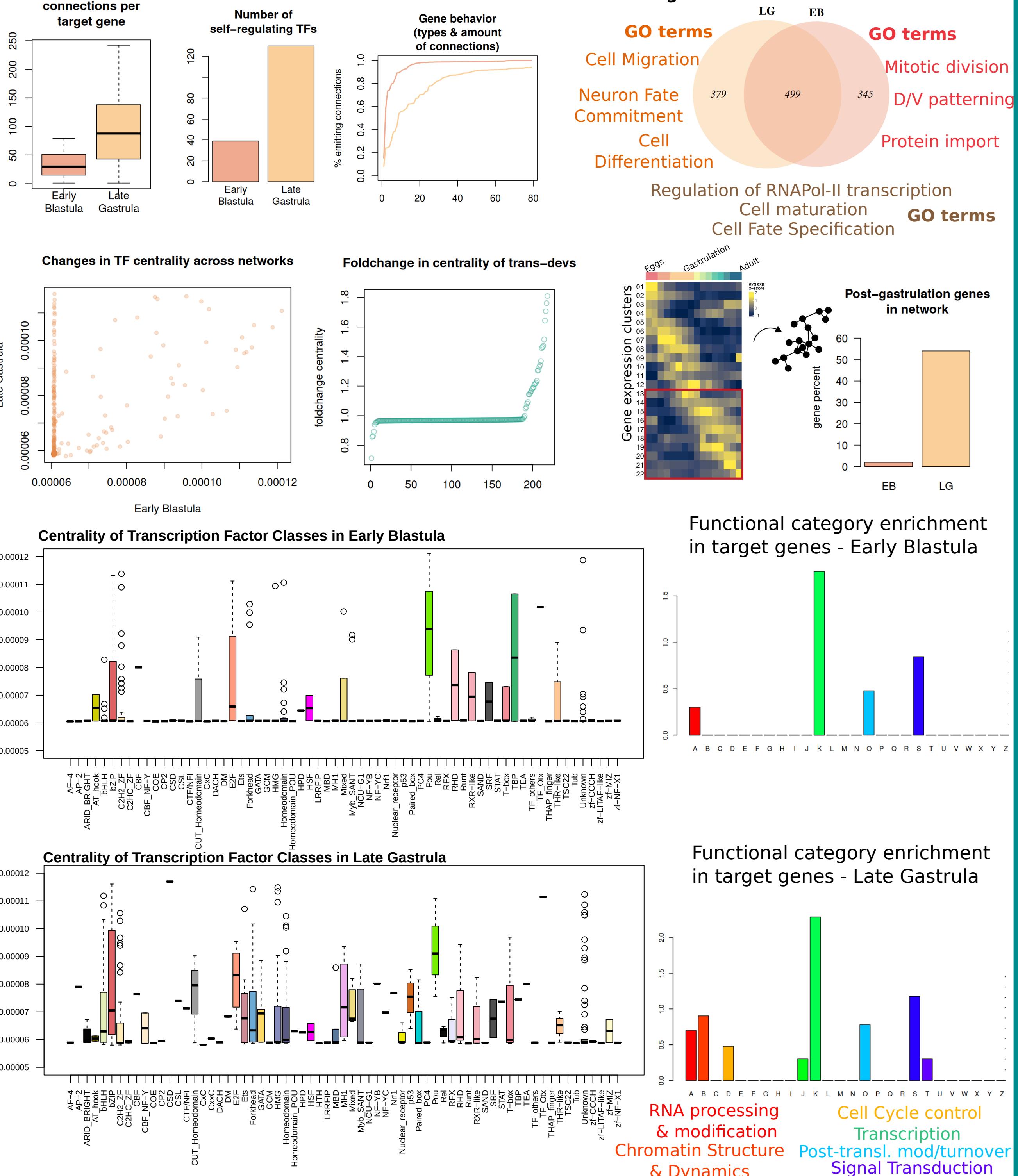
The advent of multi-Omics and single cell technologies has extended quantitative molecular biology onto many species across the tree of life, uncovering novel cell type diversity in a wide range of understudied organisms. Current efforts focus on the definition of cell type gene programmes -genes working together to regulate cell type differentiation and maintenance, that can be used to identify cell types and their relationships between them. Here we extend the idea of using Network Analysis to characterise the gene expression programmes of cell types. We demonstrate that Network Analyses with transcriptomics and chromatin data are effective at generating biological hypotheses for further validation in both bulk and single cell analyses. For the latter, methods for gene expression aggregation and normalisation at the cell type level allow the application of well-established tools such as Weighted Gene Coexpression Analysis or ANANSE, while benefiting from the resolution and high granularity of single cell data. Using standard graph tools, network structure information can be further crossed with gene annotation to extract information of biological relevance.

## CASE 1 characterising cis regulation during hemichordate gastrulation

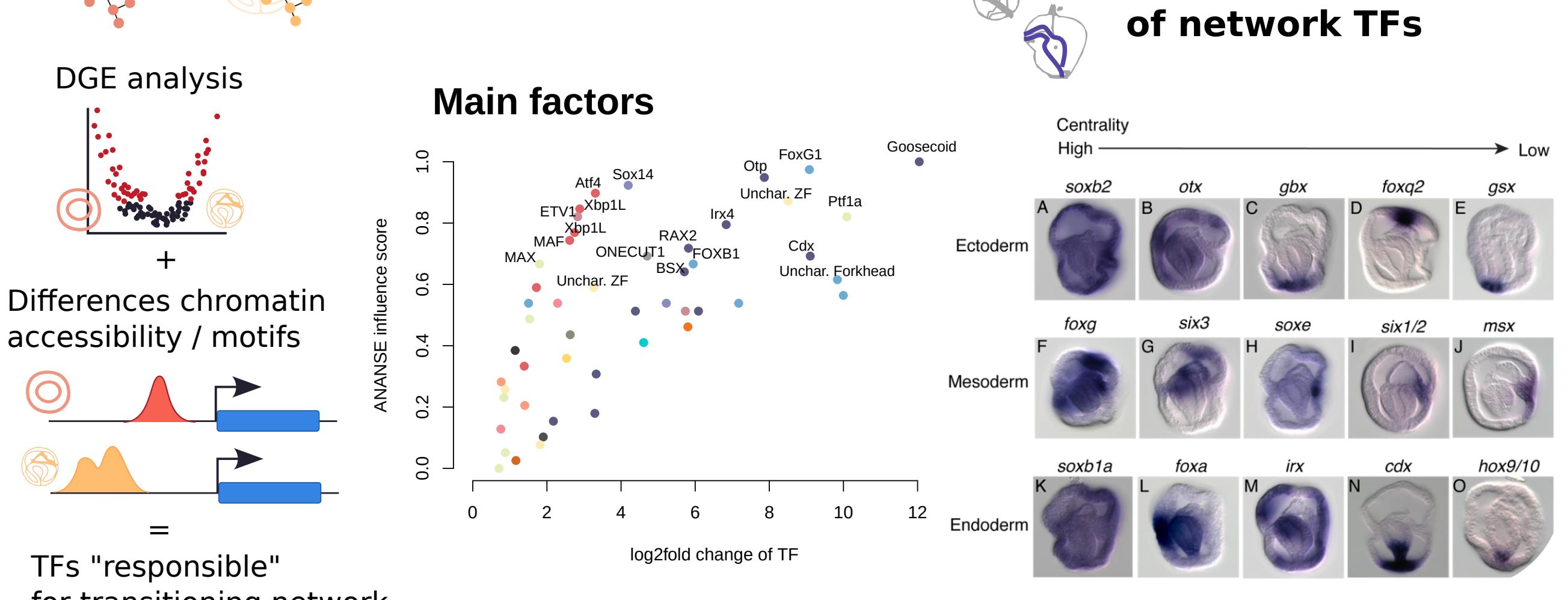
Alberto Perez-Posada, Che-Yi Lin, Ching-Yi Lin, Yi-Chih Chen, Jr-Kai Yu, Yi-Hsien Su, Juan J. Tena



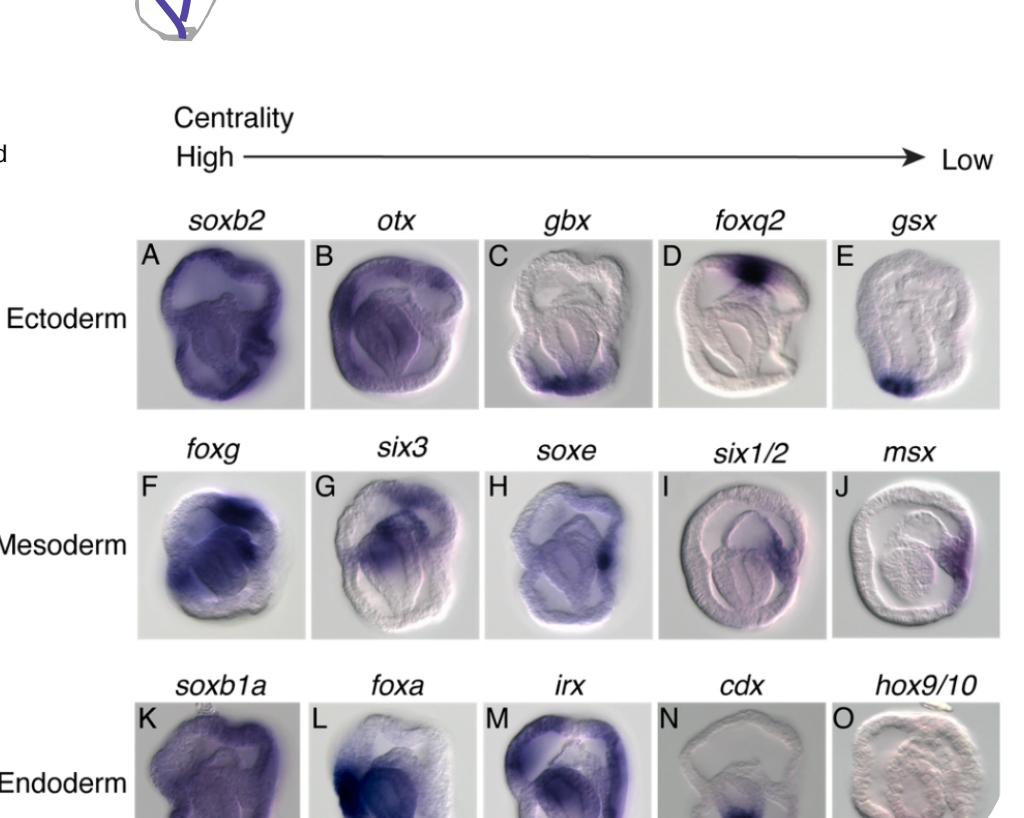
RNA-seq and ATAC-seq of Early Blastula and Late Gastrula was used to generate networks of TF/target genes using ANANSE. We filtered out sparse interactions and focused on common/exclusive target genes and TF activity within the network.



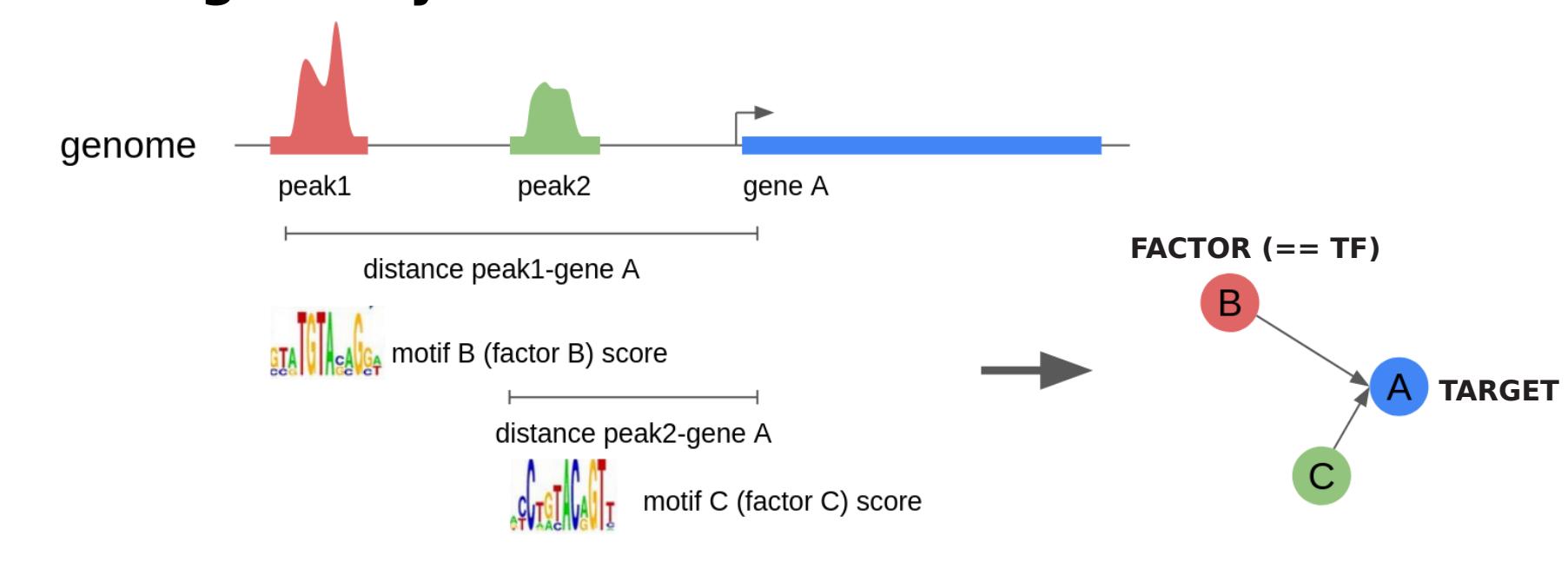
## ANANSE INFLUENCE



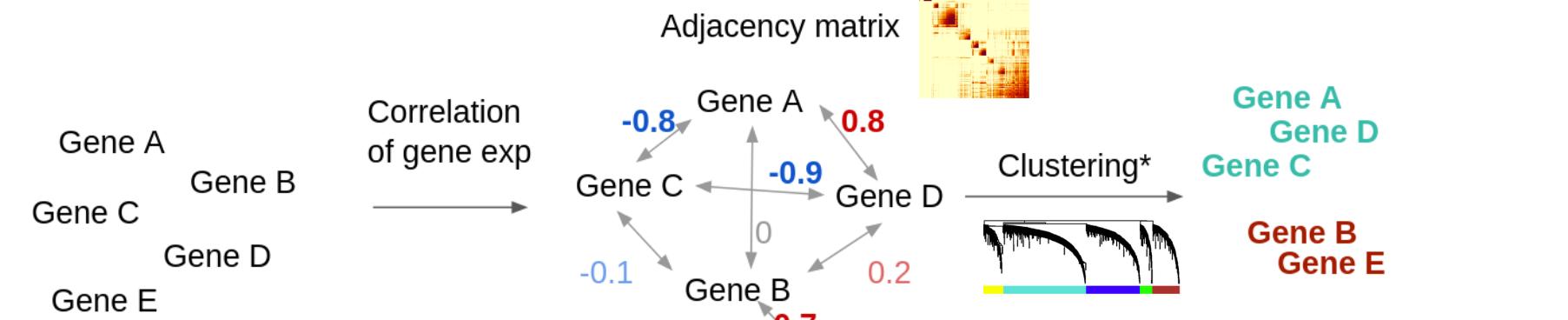
## In situ hybridisation of network TFs



## Cis-Regulatory interactions: ANANSE Xu et al., 2021

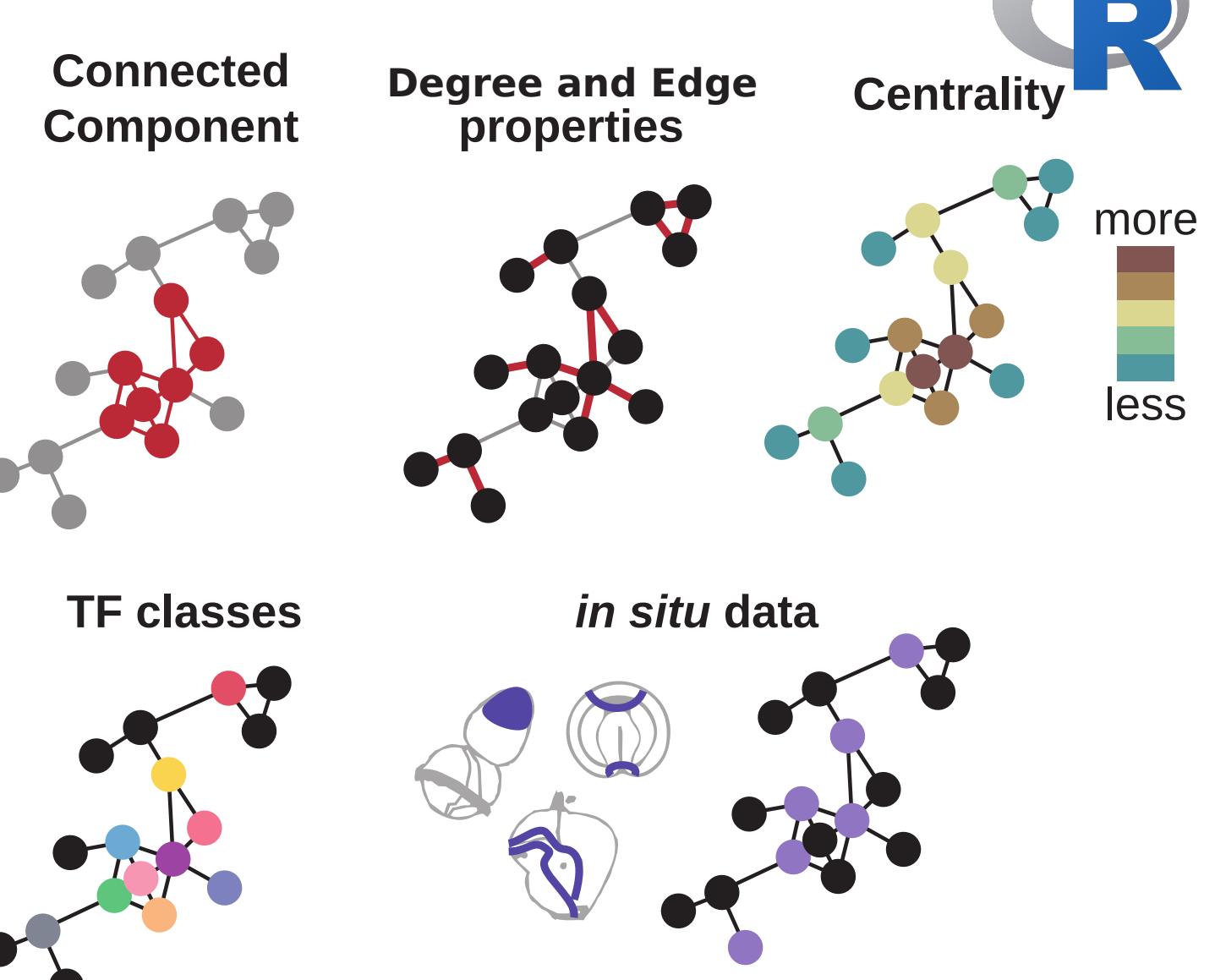


## Gene Coexpression: WGCNA Langfelder & Horvath, 2008



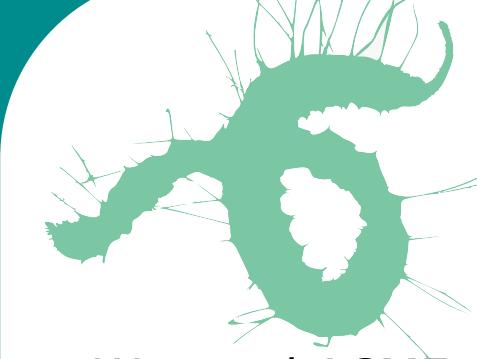
\*clustering if: **strong relation (positive or negative)**  
**topological overlap:** If A and C share many neighbours, A and C's score of connection is **weighted** to be higher.

## Network Analyses and Applications:

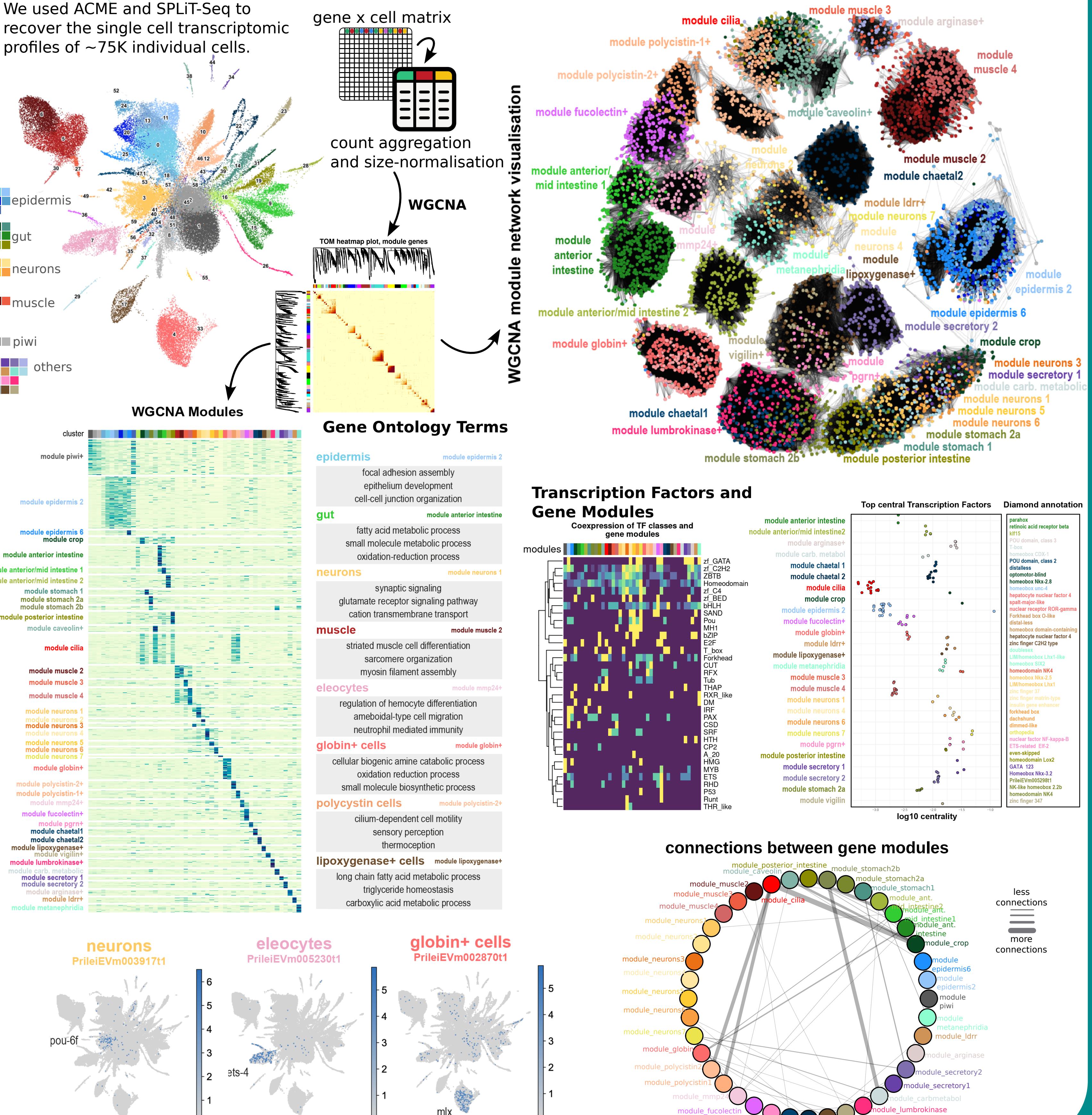


## CASE 2 unravelling cell type diversity and pluripotency in annelids

Patricia Alvarez-Campos, Helena Garcia-Castro, Elena Emili, Alberto Perez-Posada, David Salamanca-Diaz, Vincent Mason, Nathan Kenny, Duygu Ozpolat, Jordi Solana

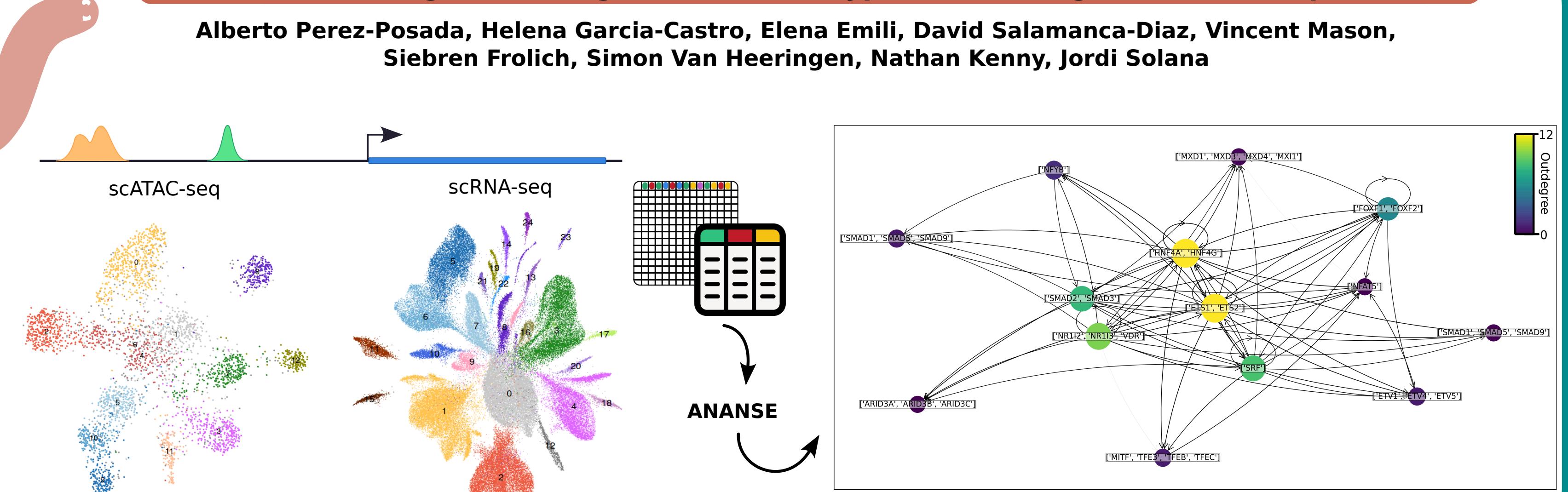
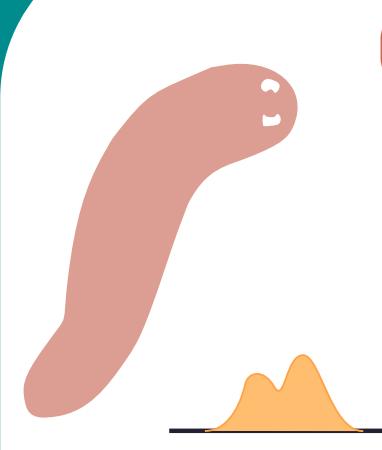


We used ACME and SPLiT-Seq to recover the single cell transcriptomic profiles of ~75K individual cells.



## CASE 3 uncovering the cis-regulation of cell types at the single cell level in planarians

Alberto Perez-Posada, Helena Garcia-Castro, Elena Emili, David Salamanca-Diaz, Vincent Mason, Sieben Frolich, Simon Van Heeringen, Nathan Kenny, Jordi Solana



## Bibliography:

- Xu et al., 2021
- Langfelder & Horvath, 2008
- Csardi and Nepusz, 2006
- Perez-Posada et al., 2022
- Garcia-Castro et al., 2021

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>> Using network metrics such as degree, centrality, and connected components, together with functional gene annotation, can help i) identify co-expressed genes from the same gene regulatory networks, and ii) provide quantitative information about the gene networks of cell types. Overall, network analysis can widen our perspective of what genes and gene interactions contribute to the regulatory program of cell types.