

Schwann cell precursors represent a neural crest-like hub state with biased multipotency

Swann cell precursors represent a neural crest-like hub state with biased multipotency
Swann Faure*¹, Maria Eleni Kastriti*¹, Dorothea von Ansen*¹, François Lallemand², Saida Hadjab², Igor Adameyko¹

¹Medical University of Vienna - Center for Brain Research, Dpt. of Neuroimmunology, Wien, Austria,

*: equal contribution

²Karolinska Institute, Department of Neuroscience, Stockholm, Sweden



FWF

Der Wissenschaftsfonds.



Scientific questions

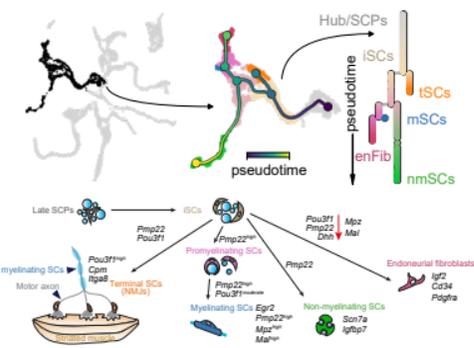
- What are the molecular portrait of NC & SCPs lineages?
- What is the structure of cell fate decision?
- Are SCPs multipotent neural crest-like cell state?

Data sampling & analysis

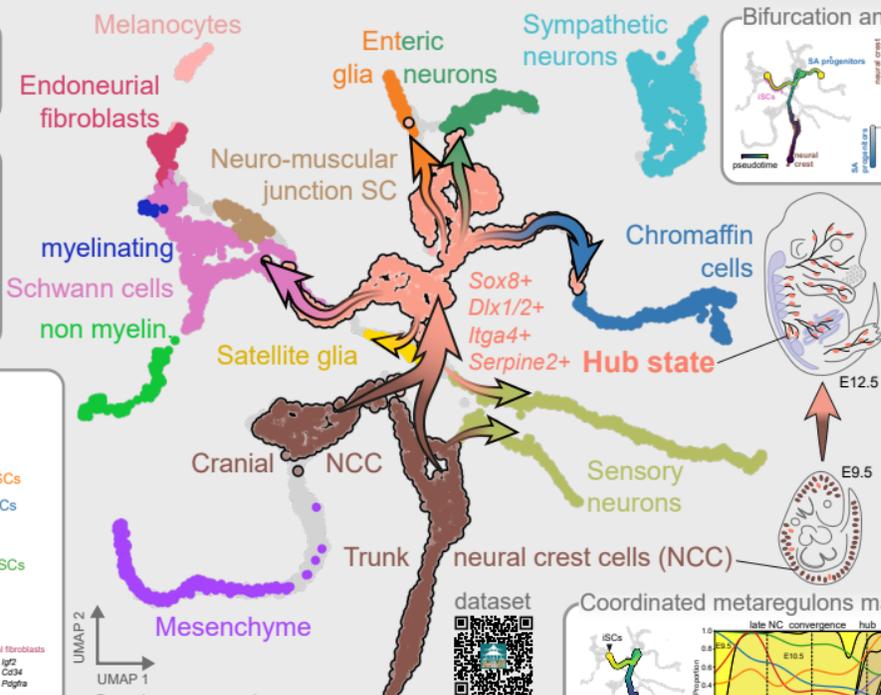


- Cells are sampled using lineage tracing over various embryonic stages and locations, and were sequenced using SmartSeq2.
- From the count matrices were generated the differentiation tree and CytotRACE measurements. From spliced/unspliced matrices were generated RNA velocity mapping.

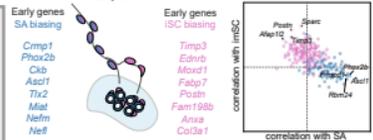
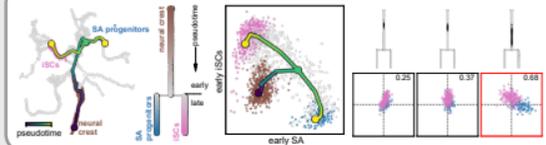
Investigation of SC heterogeneity



- Focused trajectory analysis shows transcriptional and regulatory paths towards myelinating, non-myelinating, neuro-muscular junction terminal SCs and endoneurial fibroblasts.
- *Pou3f1*, known to play a crucial role in myelination, emerged as a candidate biasing factor towards terminal neuro-muscular junction SCs.

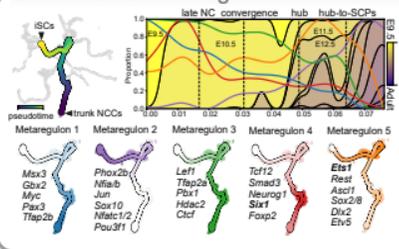


Bifurcation analysis reveals early biasing



- Hub cells contains several bifurcations toward terminal fates such as ChC, enteric glia/neurons, and iSCs.
- DE analysis is performed to identify branch specific genes, which are then further classified according to their pseudotime activation: before fork=early, after fork=late
- In all bifurcations, the following phenomenon occurs:
 - (1) co-activation of branch-specific gene modules prior to the fork/bifurcation
 - (2) repulsion of these modules while reaching the fork
 - (3) commitment after the bifurcations

Coordinated metaregulators maintain the NC-like state in hub cells



- The "hub"/SCPs might be defined as a cell state with re-activation of metaregulon 5, characterized by *Ets1*
- Metaregulators 1 and 3 are linked to neural crest properties and cell reprogramming.
- Metaregulon 2 is linked to the terminal differentiation of Schwann cells.
- The "hub" state is distinct in terms of regulation from the majority of the neural crest cells where metaregulators 1 and 3 are dominating.

Spatio-temporal aspects

