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

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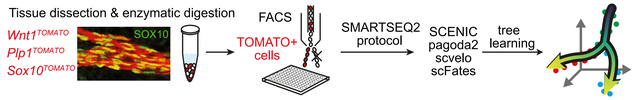
Der Wissenschaftsfonds.

Scientific quests

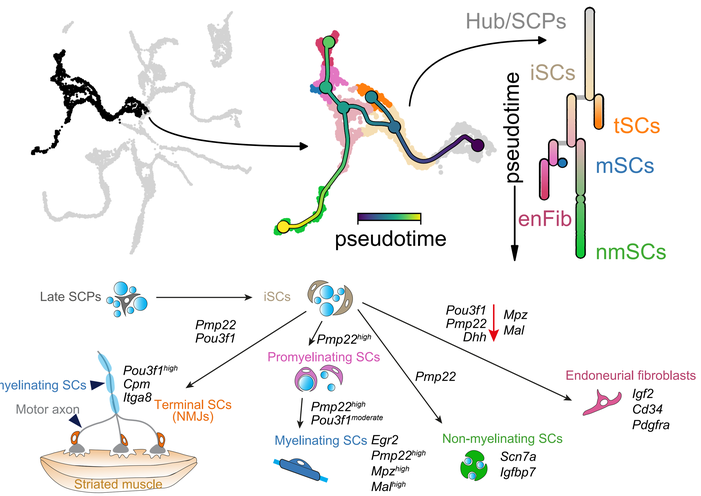
- What are the molecular portrait of NC & SCPs lineages?
- What is the structure of cell fate decision?
- Are SCPs multipotent neural crest-like cell state?

Data sampling & analysis

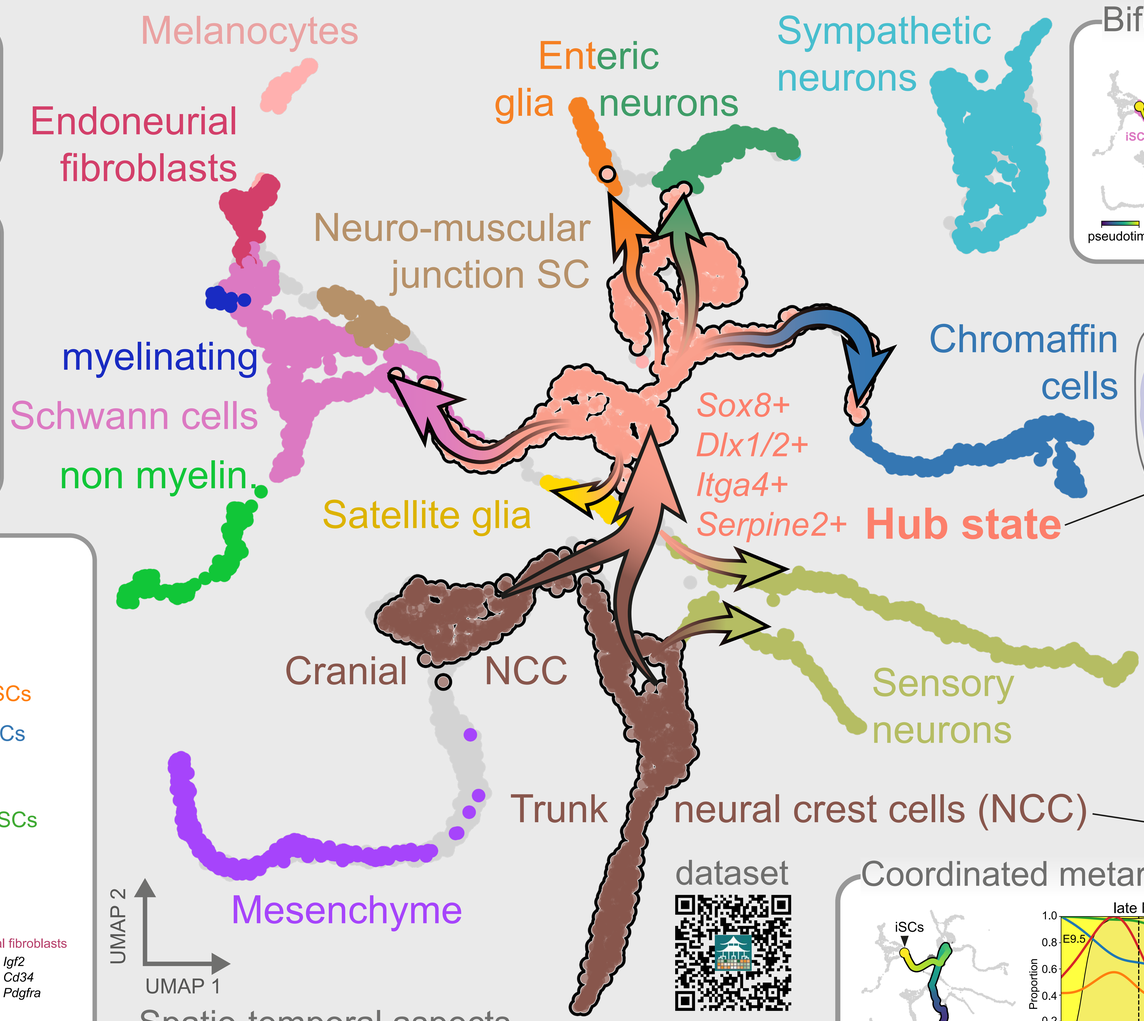


- Cells are sampled using lineage tracing over various embryonic stages and locations, and were sequenced using SmartSeq2.
- From the count matrices were generated the differentiation tree and CytoTRACE measurements. From spliced/unspliced matrices were generated RNA velocity mapping.

Investigation of SC heterogeneity

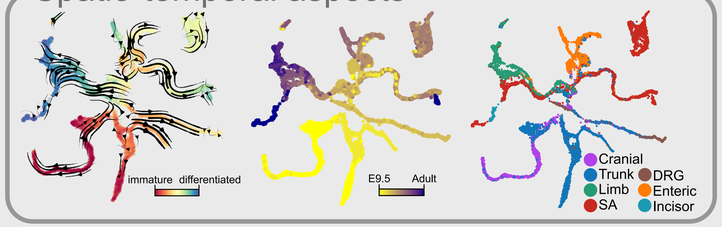


- Focused trajectory analysis shows transcriptional and regulatory paths towards myelinating, non-myelinating, neuro-muscular junction terminal SCs and endoneurial fibroblasts.
- *Pou3f1,* known to play a crucial role in myelination, emerged as a candidate biasing factor towards terminal neuro-muscular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

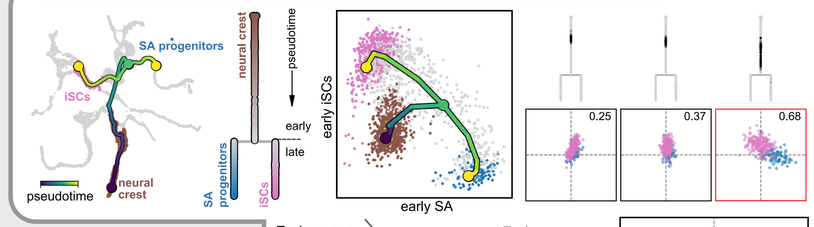


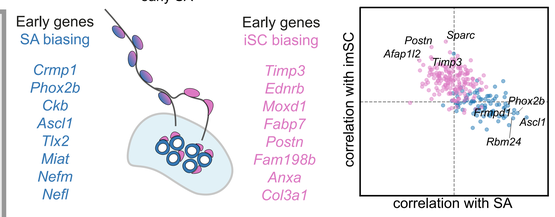
dataset

Spatio-temporal aspects



Bifurcation analysis reveals early biasing





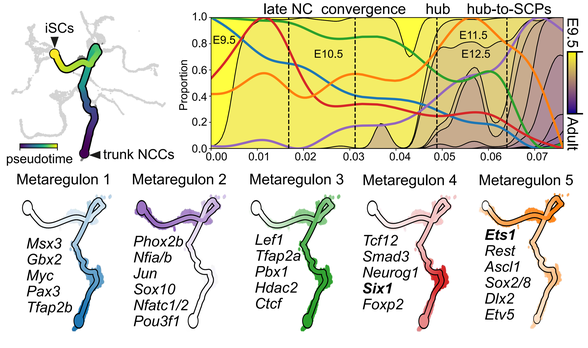
- Hub cells contains several bifurcations toward terminal fates such as ChC, enteric glia/neurons, and iSCs.
- DE analysis is performed to identify branch specific genes, which are then further classified according to their pseudotime activation: before fork=early, after fork=late
- In all bifurcations, 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 metaregulons 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*
- Metaregulons 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 metaregulons 1 and 3 are dominating.