Single cell transcriptomics reveals sequential fate selection points and mechanism of cell fate commitment of the neural crest

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Neural crest cells are transient embryonic progenitors that are often called 4th germ layer since they give rise to a large number of differentiated cell types in the body. In that regard, neural crest is a great system to study developmental architecture and molecular mechanisms of multiple fate selection. We took advantage of a single cell transcriptomics approach to address fate selection mechanisms in the neural crest. To investigate the positions of cell fate decisions we developed computational methods to reconstruct multiple-branching differentiation trajectories through principal graph modeling. The results showed that cell fate switches operate as sequential bifurcations of choices and enabled comprehensive reconstruction of gene modules associated with major neural crest differentiation patterns and waves of gene regulatory changes. Analysis of the first post-migratory bifurcation point reveals early-biasing and commitment stages of cell fate selection. Fate-specific gene modules are heterogeneously expressed in premigratory neural crest populations, followed by gradual activation and synchronization of fate-specific gene modules leading to compositional differences in pre-bifurcating cell populations. Commitment stage is characterized by mutually exclusive activation of post-bifurcation gene modules.