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Systematic Characterization of Cell Types by Transcriptional Profiling

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How can different cell types be systematically characterized? This question has been around since the unit of life, the cell, was first observed. In the present study, the genetic codes and molecular fingerprints that rule specific cell types within different organs of the larva of *Drosophila melanogaster*, as well as within the nervous system of different species of metazoans, were deciphered.

First, by applying a cutting-edge technique, scRNAseq, the *Drosophila melanogaster* larval brain cell atlas was constructed. Main cell types were identified: neurons, neural progenitor cells, glial cells, undifferentiated neurons and non-neural cells. But, are these cell populations in the brain stable in extreme life situations? Upon starvation, it was shown that the brain retained its overall composition; however, cell-type specific effects were observed.

Second, transcriptional profiling can be applied to a specific cell type to unravel different cell populations within a group. Hence, neuronal diversity, across different nervous systems within the tree of life, was investigated. Historically, neurons were classified based on the expression of neurotransmitters following Dale's principle: "one neuron – one neurotransmitter". In the present study, neurons were shown to coexpress marker genes for different neurotransmitters, suggesting a different scenario: "one neuron – multiple neurotransmitters".

Finally, cell fate determination and identification of cell type specific marker genes can also be addressed by transcriptomic analysis. To understand the different events that trigger the establishment of sensory neurons in the peripheral nervous system of *Drosophila melanogaster* larva, whole organ transcriptome and differential expression analysis were performed. Two main transcription factors, *proboscipedia* and *twin of eyegone,* were shown to be likely involved in cell fate determination and maintenance of the sensory neurons in the external chemosensory organs.

Altogether, these results illustrated the power of transcriptional profiling for a systematic characterization of diverse cell types. An approach that can be easily extended and adapted to solve different biological questions, by comparing different structures, and even different species.

Jury:

- Prof. Dr. Simon Sprecher (thesis supervisor)
- Prof. Dr. Patrick Tschopp (external co-examiner)
- Dr. Boris Egger (internal co-examiner)
- Prof. Dr. Jörn Dengjel (president of the jury)