Cell fate determination

Within the field of developmental biology one goal is to understand how a particular cell (or embryo) develops into the final cell type (or organism), essentially how a cell's fate is determined. Within an embryo, 4 processes play out at the cellular and tissue level to essentially create the final organism. These processes are cell proliferation, cell specialization, cell interaction and cell movement. Each cell in the embryo receives and gives cues to its neighboring cells and retains a cell memory of its own cell proliferation history. Almost all animals undergo a similar sequence of events during embryogenesis and have, at least at this developmental stage, the three germ layers and undergo gastrulation. While embryogenesis has been studied for more than a century, it was only recently (the past 15 years or so) that scientists discovered that a basic set of the same proteins and mRNAs are involved in all of embryogenesis. This is one of the reasons that model systems such as the fly (Drosophila melanogaster), the mouse (Muridae), and the leech (Helobdella), can all be used to study embryogenesis and developmental biology relevant to other animals, including humans. The fate map of the nematode (Caenorhabditis) can be analyzed down to the cellular level. This is due no cell mixing during development.

Investigating cell fate decision and subpopulation specification in the context of the neural lineage is fundamental to understanding neurogenesis and neurodegenerative diseases. The differentiation process of neural-tube-like rosettes in vitro is representative of neural tube structures, which are composed of radially organized, columnar epithelial cells and give rise to functional neural cells. However, the underlying regulatory network of cell fate commitment during early neural differentiation remains elusive.

RESULTS: In this study, we investigated the genome-wide transcriptome profile of single cells from six consecutive reprogramming and neural differentiation time points and identified cellular subpopulations present at each differentiation stage. Based on the inferred reconstructed trajectory and the characteristics of subpopulations contributing the most toward commitment to the central nervous system lineage at each stage during differentiation, we identified putative novel transcription factors in regulating neural differentiation. In addition, we dissected the dynamics of chromatin accessibility at the neural differentiation stages and revealed active cis-regulatory elements for transcription factors known to have a key role in neural differentiation as well as for those that we suggest are also involved. Further, communication network analysis demonstrated that cellular interactions most frequently occurred in the embryoid body stage and that each cell subpopulation possessed a distinctive spectrum of ligands and receptors associated with neural differentiation that could reflect the identity of each subpopulation.

CONCLUSIONS: Our study provides a comprehensive and integrative study of the transcriptomics and epigenetics of human early neural differentiation, which paves the way for a deeper understanding of the regulatory mechanisms driving the differentiation of the neural lineage [1)].

1)

Shang Z, Chen D, Wang Q, Wang S, Deng Q, Wu L, Liu C, Ding X, Wang S, Zhong J, Zhang D, Cai X, Zhu S, Yang H, Liu L, Fink JL, Chen F, Liu X, Gao Z, Xu X. Single-cell RNA-seq reveals dynamic transcriptome profiling in human early neural differentiation. Gigascience. 2018 Nov 1;7(11). doi: 10.1093/gigascience/giy117. PubMed PMID: 30239706.