Single Cell Transcriptomics

Newsletter December 2020

Paper 1

Liu, Y *et al*. High-Spatial-Resolution Multi-Omics Sequencing via Deterministic Barcoding in Tissue *Cell, 2020 Nov.*

In this paper the authors present DBiT-seq - deterministic barcoding in tissue for spatial omics sequencing. This NGS-based technique allows to measure whole mRNA transcriptome as well as the expression of 20 - 100 proteins in a spatial resolution of 10 µm per pixel. The technique is also applicable to formaldehyde-fixed tissue slides. The approach they are using here is to spatial barcode biomolecules directly in the tissue instead of capturing them on a solid-phase substrate. They developed a microfluidic device which is easy and intuitive to use. The workflow of the new method is depicted in figure 1. Spatial information is obtained from the distinct combination of barcodes A_i and B_j (i = 1–50, j = 1–50) that are delivered through the 50 parallel microchannels of the devices. In this work they applied DBiT-seq on mouse embryos and showed that single-cell RNAseq data can be integrated with DBiT-seq data and used for rapid cell type identification.

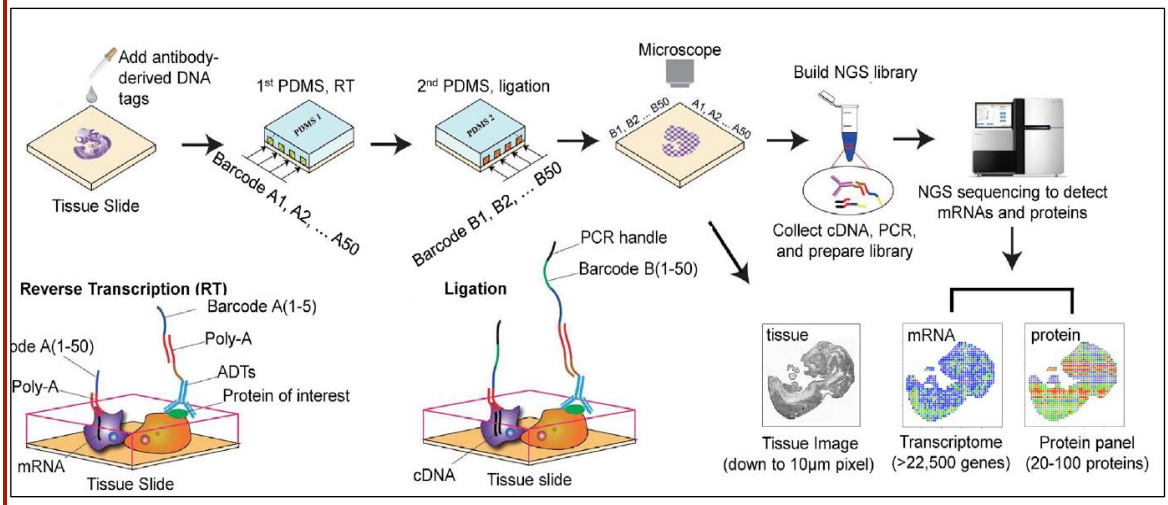

Figure 1: Schematic workflow of DBiT-seq

Paper 2

Klimm, F *et al.* Functional module detection through integration of single-cell RNA sequencing data with protein–protein interaction networks *BMC Genomics, 2020 Nov.*

In this study the authors present scPPIN, a method for the integration of single-cell RNA sequencing data with protein-protein interaction networks (PPINs). So far PPINs have been only integrated with bulk RNA sequencing data. With scPPIN it is possible to detect active modules (groups of proteins with similar biological functions) in different cell types. The new method consists of the following steps: clustering of scRNA-seq data, identifying DEGs, constructing node-weighted PPINs and finding the maximum-weight connected subgraphs with an exact Steiner-tree approach (Fig 2). Thus, based on the DEGs in a cell cluster, subnetworks of the PPINs are identified that are enriched in these cells. These active modules reveal interaction partners that are not differentially expressed but have a crucial biological function (e.g., as receptors) for the cell cluster. These proteins are only detectable by the combination of single-cell data and PPINs and therefore reveal biology beyond a standard DEG analysis. The technique is applicable to a wide range of organisms and tissues. In this work they apply scPPIN on human liver spheroids

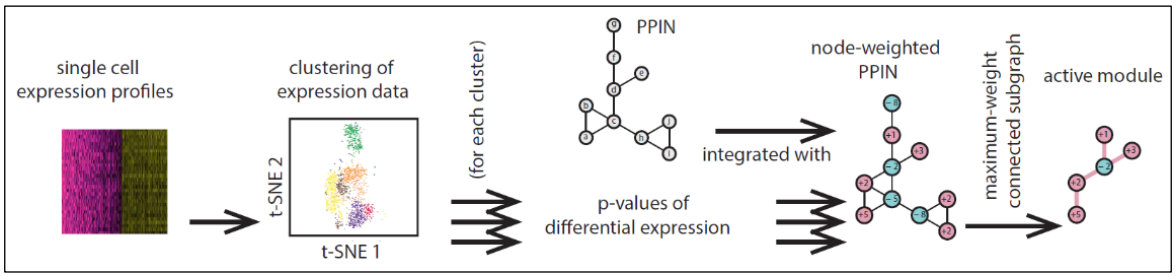

Figure 2: Analysis steps of scPPIN

Paper 3

Cao, J *et al.* A human cell atlas of fetal gene expression *Science, 2020 Nov.*

This study displays a major effort in single-cell RNA sequencing of human fetal tissues. They applied three-level single-cell combinatorial indexing for gene expression (sci-RNAseq3) to 121 human fetal samples originating from 15 organs. The final analysis included more than 4 million single cells and led to the identification of 77 main cell types (Fig 3). The fetal samples ranged from 72 to 129 days in estimated postconceptual age. Cell type annotation was conducted by matching the human gene expression data to corresponding tissues in mouse cell atlases. They highlight that the integration of mouse and human data was notably easy. Moreover, the large body of analyzed organs allowed them to integrate cell types distributed across tissues. For blood cells this resulted in a multiorgan map with developmental trajectories of cell states. This study comes along with the study on chromatin accessibility (Domcke et al.) on fetal human tissues.

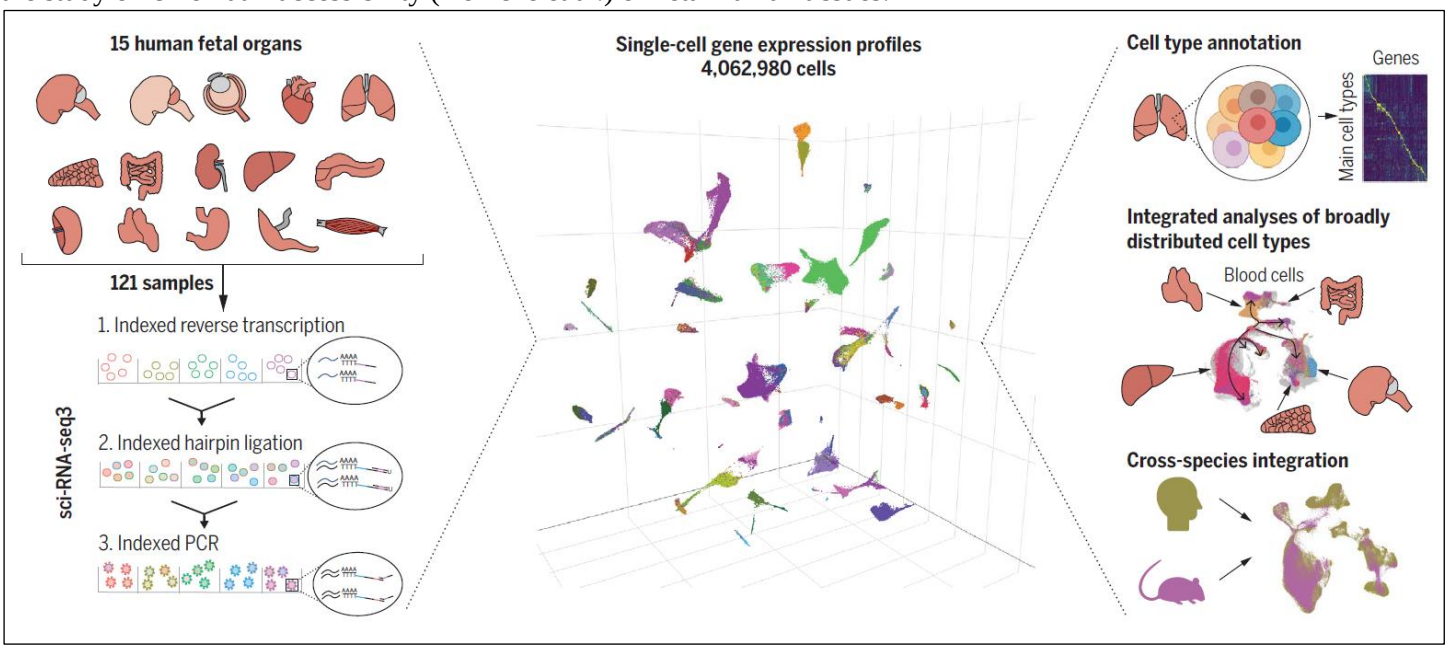

Figure 3: A human cell atlas of fetal gene expression

New papers from Danish researchers

- Selective vulnerability of supragranular layer neurons in schizophrenia Mykhailo Y. Batiuk, Teadora Tyler, Shenglin Mei, Rasmus Rydbirk, Viktor Petukhov, Dora Sedmak, Erzsebet Frank, Virginia Feher, Nikola Habek, Qiwen Hu, Anna Igolkina, Lilla Roszik, Ulrich Pfisterer, Zdravko Petanjek, Istvan Adorjan, Peter V. Kharchenko, Konstantin Khodosevich, *bioRxiv, 2020 Nov*
- Transcriptomic analysis links diverse hypothalamic cell types to fibroblast growth factor 1-induced sustained diabetes remission Bentsen MA, Rausch DM, Mirzadeh Z, Muta K, Scarlett JM, Brown JM, Herranz-Pérez V, Baquero AF, Thompson J, Alonge KM, Faber CL, Kaiyala KJ, Bennett C, Pyke C, Ratner C, Egerod KL, Holst B, Meek TH, Kutlu B, Zhang Y, Sparso T, Grove KL, Morton GJ, Kornum BR, García-Verdugo JM, Secher A, Jorgensen R, Schwartz MW, Pers TH, *Nat Commun., 2020 Sep*
- Predicting gene regulatory networks from cell atlases Andreas Fønss Møller, Kedar Nath Natarajan, *Life Sci Alliance. 2020 Nov*
- miRNA activity inferred from single cell mRNA expression, Morten Muhlig Nielsen, Jakob Skou Pedersen, *bioRxiv, 2020 Jul*
- TENET: gene network reconstruction using transfer entropy reveals key regulatory factors from single cell transcriptomic data Junil Kim, Simon T. Jakobsen, Kedar N Natarajan, Kyoung-Jae Won, *Nucleic Acids Research, 2020 Nov*

Next Single Cell Seminar

Next seminar will take place in January.

If you would like to announce anything single cell related, being it job announcement, event, your published paper, technology development etc, please contact us.

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