Introduction to single-cell sequencing and group project

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CSAMA 2019, 17th edition
Why do we want to sequence single cells?
My favourite discovery by single-cell sequencing

A Public BCR Present in a Unique Dual-Receptor-Expressing Lymphocyte from Type 1 Diabetes Patients Encodes a Potent T Cell Autoantigen

Rizwan et al. Cell 2019
Isolation of single cells and sequencing protocols

Svensson et al. 2018
Cell barcode and unique molecular identifier (UMI)

Sequencing data preserves information:

- Which cell did the sequenced transcript belong to? → cell barcode
- How many times did one transcript get sequenced? → UMI
Whole gene vs. 3’ or 5’ sequencing

Depending on the library preparation and sequencing protocols that you are using, you will get different coverage of mRNA molecules.

A typical mRNA molecule:

- **5’ G —PPP—**
  - coding sequence
  - AAAAAA<sub>150-250</sub> 3’

- **whole gene coverage: Smart-seq2**
- **3’ coverage: DropSeq, 10x Genomics**
- **5’ coverage: 10x Genomics immune profiling**
Overview of single-cell topics during CSAMA

- Wednesday morning: Lectures (Simon Anders, Davide Risso)
- Thursday afternoon: Group work on single-cell sequencing techniques (Katharina Imkeller)
- Friday afternoon: Lab on analysis of single-cell sequencing data (Simon Anders, Davide Risso)
Group project: Understanding the technical aspects of single-cell sequencing

Aims of the workshop

▶ Understand the molecular biotechnology behind single-cell sequencing.
▶ How do we get from mRNA molecule to sequencing read?
▶ Which method to choose for a specific question?
▶ Why do we model the data differently for different sequencing approaches?

▶ 4 groups, 4-6 participants per group
▶ Group work during Thursday lab, 13h30-16h30.
▶ Presentation of results to the whole course on Friday, 13h30.
▶ Please register on the list at front desk (limited space)!
The material for the group project is here...
https://github.com/Bioconductor/CSAMA/tree/2019/lab/group_project_scseq

GROUPS

- SMART-seq2
- Drop-seq and 10x Genomics 3’
- 10x Genomics 5’ including VDJ sequencing
- SPLiT-seq