

# DANDRITE Topical Seminar

## Deciphering the epigenetic landscape of the brain: Innovations in chromatin profiling with single-cell nano-CUT&Tag

In the past years profiling of the epigenome with single-cell resolution has brought novel insights into functions of the regulatory chromatin, transcription factors and gene regulatory networks. These advances were mainly driven by single-cell ATAC-seq profiling of the accessible chromatin. However, the functions of regulatory chromatin elements such as enhancers or promoters is determined not only by DNA accessibility, but also by the histone modification status among others.

We have recently developed a method to profile histone modifications with single-cell resolution from thousands of cells at the same time – single-cell CUT&Tag. Now, we went one step further and developed a novel improved technology - nano-scCUT&Tag that make it for the first time possible to multimodally profile three epigenetic modalities including open chromatin and two histone modifications from thousands of single cells. Nano-scCUT&Tag uses a new set of nanobody-Tn5 transposase fusion proteins to target multiple epigenetic modalities at the same time. In addition to being multimodal, nano-scCUT&Tag has lower input requirements, yields more fragments per cells and improves clustering resolution over previous generation of scCUT&Tag.

We have applied nano-CUT&Tag to the juvenile mouse central nervous system and uncovered unprecedented epigenetic heterogeneity. The obtained multimodal profiles can be used to deconvolute the individual cell identities in the brain and generate high quality multimodal epigenetic profiles. Moreover, we used nano-CUT&Tag to uncover the dynamics of the chromatin during a differentiation process in vivo across a pseudotime trajectory. We then leveraged the relationship between chromatin opening and enhancer activation to define chromatin velocity and predict the lineage progression during differentiation. Altogether, nano-scCUT&Tag provides unprecedented insights into chromatin regulatory landscape in the mouse CNS.

Hosted by Taro Kitazawa (DANDRITE) and co-hosted by Lei Cheng (CellIX).



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Date: **Monday 2 September 2024**  
Time: **13:00 – 14:00**  
Venue: **Nucleus, 1871-120**  
Address: **Universitetsbyen 81, 8000 Aarhus**

**OPEN TO ALL INTERESTED.**