DANISH SINGLE-CELL NETWORK NEWSLETTER

JANUARY - 2024

THIS MONTH'S HIGHLIGHTS:

Single-cell joint profiling of multiple epigenetic proteins and gene transcription

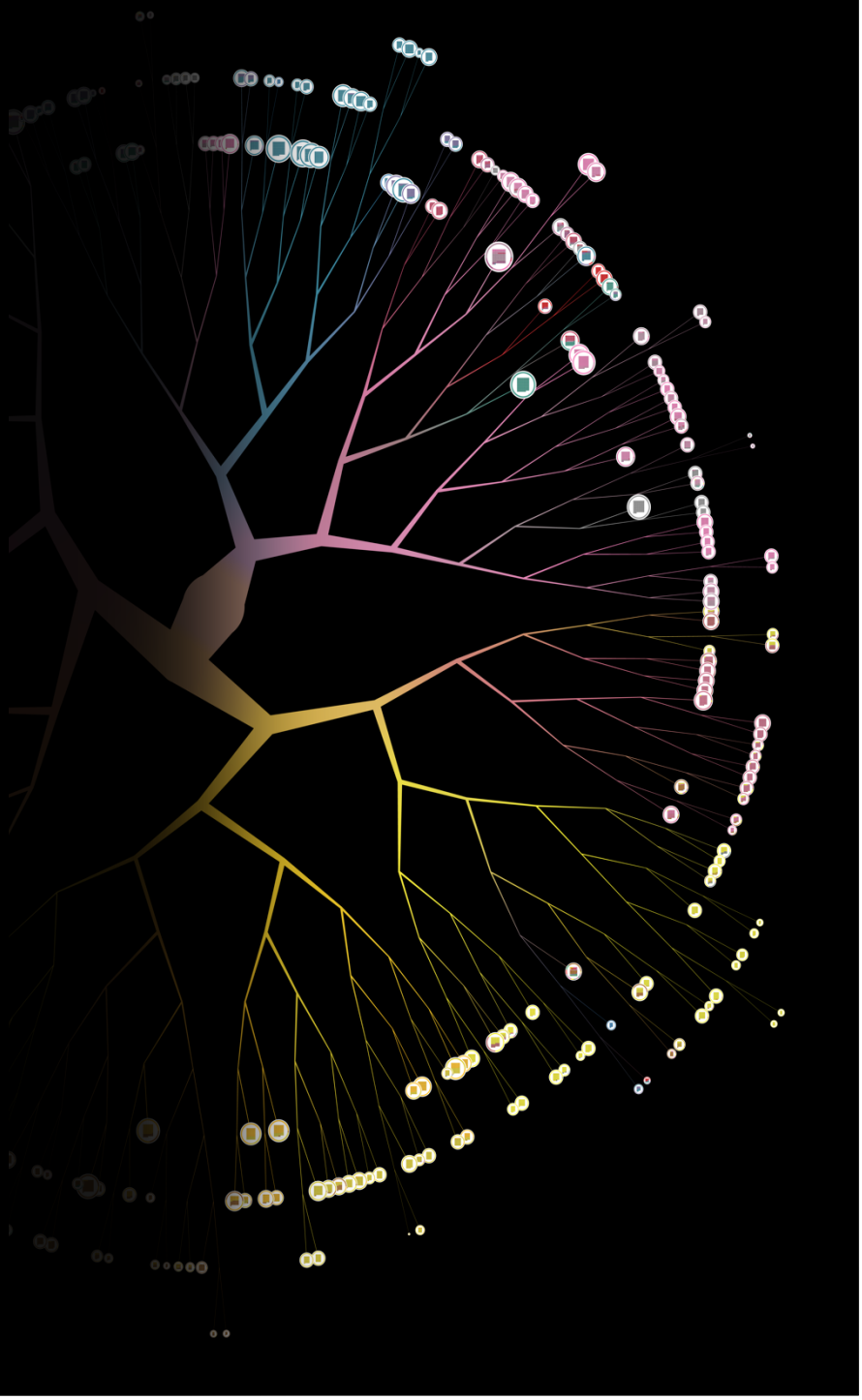
Xiong, H., et al.

SinCMat: A single-cell-based method for predicting functional maturation transcription factors

Barvaux, S., Okawa, S., del Sol, A.

PPML-Omics: A privacy-preserving federated machine learning method protects patients' privacy in omic data

Zhou, J. et al.



COVER IMAGE
Author: Katarina Dragicevic, University of Copenhagen
Hierarchical clustering of neurons

UNIVERSITY OF COPENHAGEN

UPCOMING EVENT

4th Danish Single Cell Meeting: Technology towards Cell Biology and Medicine

https://event.sdu.dk/danishscsym2024/conference

Time and place: May 2nd-3rd 2024; Auditorium O100, University of Southern Denmark

Registration deadline: 19-04-2024
Poster abstract submission deadline: 19-04-2024
Short talk abstract submission deadline: 11-04-2024

UNIVERSITY OF COPENHAGEN

Single-cell joint profiling of multiple epigenetic proteins and gene transcription

Xiong, H., *et al. Science Advancers* (2024). https://doi.org/10.1126/sciadv.adi3664

In this newsletter edition, we introduce uCoTarget, an innovative method enabling simultaneous and high-throughput measurements of multiple epigenetic modalities. uCoTarget's unique design, compatible with the standard Illumina sequencing platform, eliminates the need for specialized microfluidic devices and comes at an impressively low cost of $0.01 per cell in major biochemical reagents. With scalability to 1 million single cells, uCoTarget allows the joint measurement of five histone modifications simultaneously, and its versatility suggests potential expansion to more epigenomic modalities. The method's efficacy is demonstrated in exploring the single-cell dynamics during HSPC differentiation, shedding light on the intricate epigenomic landscape.

In comparison to existing technologies, uCoTarget stands out for its enhanced convenience and efficiency in multimodality profiling. Unlike some other technologies, uCoTarget does not necessitate the production of specific recombinant nanobody fusion proteins, offering easy coprofiling of multiple epigenetic proteins in a single experiment. Noteworthy is the upgraded version, uCoTargetX, which facilitates the simultaneous measurement of RNA along with multiple histone modifications, promising a powerful tool for analyzing multimodal heterogeneities.

However, it is essential to acknowledge certain limitations, including data sparsity in current single-cell epigenomic approaches and potential variations in read counts within single cells. Despite these challenges, uCoTarget holds promise for higher-dimensional reconstruction of the genome-epigenome-transcriptome-proteome landscape in single cells, providing valuable insights into regulatory mechanisms. Furthermore, we anticipate that uCoTargetX may find application in constructing human cell atlases, uncovering unbiased epigenetic principles in deregulated cell lineages associated with human diseases.

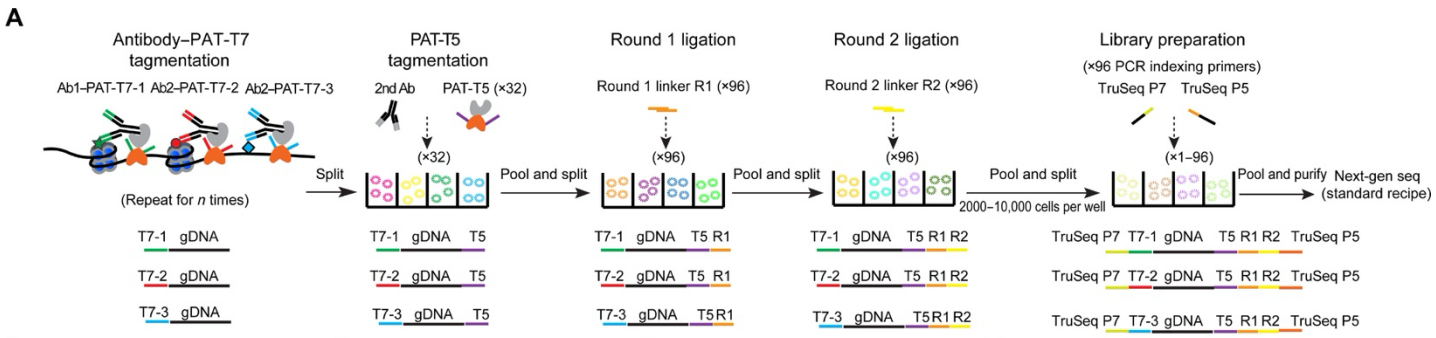


Figure 1. The design of single-cell uCoTarget.

SinCMat: A single-cell-based method for predicting functional maturation transcription factors

Barvaux, S., Okawa, S., del Sol, A. *Stem Cell Reports* (2024). https://doi.org/10.1016/j.stemcr.2023.12.006

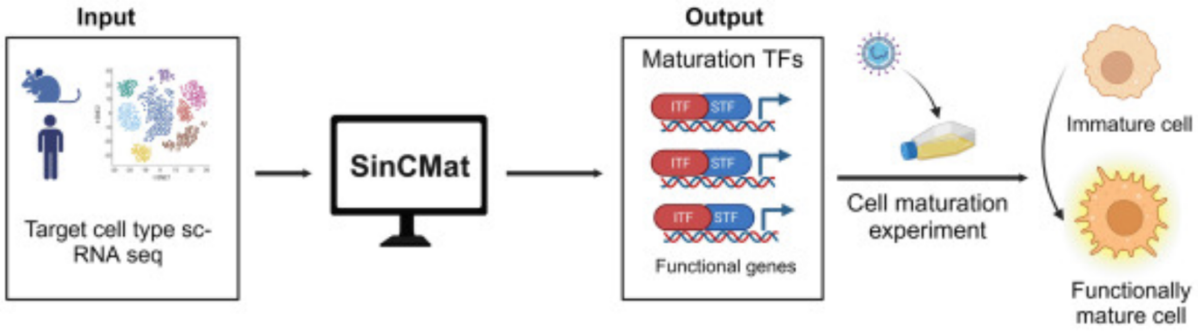


Figure 2. The workflow of SinCMat. From scRNA-seq data of target cell, SinCMat identifies TFs required for functional maturation.

In this latest breakthrough, researchers tackle a crucial challenge in regenerative medicine: the systematic production of fully mature and functional cells for clinical applications. Current differentiation and reprogramming protocols often fall short in achieving complete cellular maturation. Existing computational approaches primarily focus on cell identity conversion, neglecting the complex process of functional cell maturation.

Introducing SinCMat, the first computational method tailored for predicting functional maturation transcription factors (TFs) in any cell type using single-cell RNA sequencing (scRNA-seq) data. SinCMat, following a stepwise maturation model, integrates cell identity and maturation factors. It effectively identifies maturation TFs by leveraging the co-targeting properties of identity TFs (ITFs) and signal-dependent TFs (STFs) on functional genes. To support the community, researchers have developed SinCMatDB, a manually curated database for known maturation TFs, used to assess SinCMat's performance.

Applied extensively to adult mouse and human cell types, SinCMat accurately recapitulates known maturation TFs and uncovers novel candidates. The tool's versatility is demonstrated in case studies involving post-mitotic cells and progenitors/stem cells (SCs). Unlike traditional reprogramming TFs, SinCMat is specifically designed for maturation TF prediction, serving as a valuable complement to existing computational methods. Researchers can use SinCMat to prioritize functional maturation TFs for one-step reprogramming experiments or enhance missing functionalities in in-vitro-engineered cells. Importantly, SinCMat's applicability extends to various tissues and organs, making it a promising tool for addressing current challenges in cell engineering.

Accessible through a user-friendly web application, SinCMat eliminates the need for computer programming knowledge. With a simple requirement of scRNA-seq data for the target cell, researchers can effortlessly apply SinCMat to any mouse or human cell type of interest. SinCMat is poised to be a valuable platform, contributing to the progress of regenerative medicine by addressing the complexities of functional cell maturation in diverse tissues and organs.

PPML-Omics: A privacy-preserving federated machine learning method protects patients' privacy in omic data

Zhou, J. et al. *Science Advances* (2024). https://doi.org/10.1126/sciadv.adh8601

In recent research, scientists have introduced PPML-Omics, a sophisticated solution aimed at addressing privacy concerns arising from machine learning models in omic data analysis. This novel approach employs a decentralized differential private federated learning algorithm, showcasing prowess in preserving patient privacy across diverse omic data tasks. Notably, PPML-Omics exhibits versatility by seamlessly integrating with various machine learning models, including FCN, Auto-encoder, and DenseNet-121, making it a versatile tool applicable to a range of biological challenges.

The research team also dives into the intricate realm of batch effects in multi-institutional omic data, a common hurdle traditionally mitigated through data combination before analysis. PPML-Omics, developed within the federated learning domain, adeptly manages batch effects by emphasizing shared biological features across disparate batches. Despite the additional computational resources required for the differential private mechanism, PPML-Omics proves to be an efficient solution for privacy-preserving omic data analysis, as evidenced by minimal computational burdens in simulated experiments.

In recognizing the inherent trade-off between privacy protection and utility, PPML-Omics introduces a flexible approach. Users gain the ability to customize privacy parameters during training, allowing for tailored privacy protection levels. While manual parameter selection may be considered a limitation, it acknowledges the diverse characteristics of biological data and the varying tolerances of different deep learning models to noise. In summary, PPML-Omics emerges as a sophisticated solution to privacy challenges in omic data analysis, exhibiting adaptability and efficiency for diverse applications in biological data research.

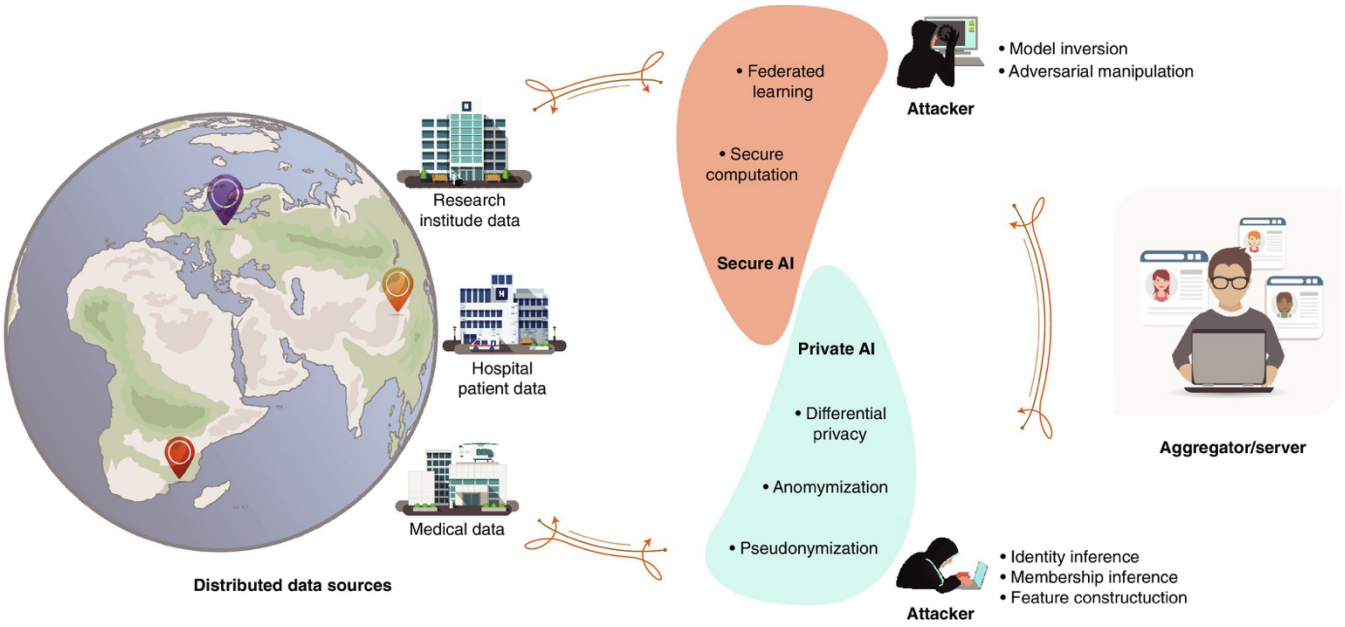


Figure 3. Schematic overview of the relationships and interactions between distributed data owners, aggregators, attackers, and techniques in the field of secure and private AI.

Next Single Cell Seminar

Time and place: 9th February 2024, Maersk Tower top floor, 7.15.92 (Link)

9:00 – 09:45

Zehra Caldwell Abay-Nørgaard, Kirkeby lab, reNEW, UCPH

Unravelling the development of the arcuate nucleus using stem cells

09:45 – 10:30

Laura Wolbeck, Khodosevich lab, BRIC, UCPH

Differential impact of maternal inflammation on neuronal progenitors in the developing neocortex

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

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