**DATE: Day 19 Month 4 Year 2026**

# SUMMARY of
## FY2025 RESEARCH RESULTS REPORT
## For International Collaborative Research with IPR, The University of Osaka

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| **Research Title** | | **Deep learning for capturing signal-dependent enhancer heterogeneity at the single cell level** |
| **Applicant** | **Name** | **Ken Murakami** |
| | **Affiliation** | **Research Institute of Molecular Pathology, Alexander Stark Group** |
| | **Present Title** | **Computational Postdoc** |
| **Research Collaborator (Host PI)** | | **Mariko Okada** |

**Summary**

To elucidate transcriptional regulatory mechanisms underlying cellular responses to external stimuli, it is essential to identify transcription factors and regulatory DNA elements at single-cell and single-gene resolution. Conventional approaches often depend on manually defined genomic regions and motif enrichment analysis, which can introduce strong researcher-dependent bias. Although recent deep learning-based methods attempt to infer regulatory motifs from DNA sequence and gene expression data, improved predictive performance does not necessarily guarantee accurate estimation of motif importance.

To overcome this limitation, we developed a novel machine learning framework based on policy gradient methods to evaluate the effects of transcription factor binding motifs on target gene expression using single-cell multi-omics and DNA sequence information. Our method integrates scMultiome data, which simultaneously capture gene expression and chromatin accessibility at the single-cell level, with reference genome sequences, and predicts the probability that each gene is highly expressed in each cell from DNA sequences and single-cell ATAC-seq signals at ATAC peak regions surrounding the gene.

We evaluated the performance of the proposed method using publicly available human peripheral blood cell scMultiome data and compared it with existing approaches, including CellOracle, LINGER, MIRA, and SCENIC+. Benchmarking against transcription factor–target gene pairs in the CollecTRI database demonstrated that our method achieved significantly higher predictive accuracy than all methods tested.

These results indicate that our framework provides a powerful new approach for identifying transcription factor–gene regulatory relationships from single-cell multi-omics data. In future work, we plan to apply this method to the analysis of stimulus responses in mouse hippocampal cells to better understand dynamic transcriptional regulation in complex tissues.

***Deadline: May 11, 2026**
***Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.**
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***This summary will be published on the web.**