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2023 - Present Assistant Professor, Sungkyunkwan University (SKKU)
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2022-2023 Principal Researcher, Edgene Incorporation, Korea
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Research Interests:
Mitochondrial Genome Editing, Mouse Disease Model, Gene Therapy, Nucleic Acids Detection

Selected Publications:

1. Comprehensive phenotypic assessment of mitochondrial ND5 nonsense mutation in mice, ***Experimental and Molecular Medicine***, 2024, *in press*

2. Engineering TALE-linked deaminases to facilitate precision adenine base editing in mitochondrial DNA, ***Cell***, 2024, 187(1), 95-106, e26

3. Precision mitochondrial DNA editing with high-fidelity DddA-derived base editors, ***Nature Biotechnology***, 2023, 41, 378-386

4. Enhanced mitochondrial DNA editing in mice using nuclear-exported TALE-linked deaminases and nucleases, ***Genome Biology***, 2022, 23, 211

5. Mitochondrial DNA editing in mice with DddA-TALE fusion deaminases, ***Nature Communications***, 2021, 12, 1190

Precision Mitochondrial Genome Editing in Animal

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Abstract

Mitochondrial DNA genome editing presents a vast opportunity for creating animal models of human genetic disorders caused by pathogenic mutations in the mitochondrial genome. It also may provide therapeutic choices for those diseases using DdCBEs or TALED, which consist of the split bacterial toxin DddAtox, transcription activator-like effector (TALE), and uracil glycosylase inhibitor (UGI), and TadA8e, an engineered adenine deaminase. Here I present a mouse model harboring human mitochondrial pathogenic missense mutation and knockout mutation in the MT-ND5 gene. Using the DdCBE enzyme, I could successfully generate model mice with targeted C-to-T or base editing in the murine mitochondrial DNA, demonstrating severe phenotypes like in human diseases. Further, the utility of mitochondrial base editors has been limited by off-target activity in both mitochondrial DNA, nuclear DNA, and even RNA in cytosol. Therefore, I present engineered base editing proteins, HiFi-DdCBE and engineered TALED, by protein engineering to avoid off-target activity for organellar DNA in human cells and animals.