
Asia 3 Roundtable on Nucleic Acids 2024

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2023- Present Associate Editor of *Molecular Therapy*: Cell Press
2022- Present Associate Professor, Seoul National University College of Medicine
2015~2022 Assistant/Associate Professor, Department of Chemistry, Hanyang University
2012~2015 Post-doctoral Fellow, Seoul National University
2012 PhD Biophysics, Seoul National University
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Research Interests:

CRISPR, Base editing, Prime editing, Ex vivo and In vivo therapeutic editing

Selected Publications:

1. BAE* et al., "AI-generated small binder improves prime editing" (Submitted)
2. BAE* et al., "Large DNA deletions occur during DNA repair at 20-fold lower frequency for base editors and prime editors than for Cas9 nucleases" *Nature Biomedical Engineering* (Accepted).
3. BAE* et al., "Adenine base editors engineering reduces editing of bystander cytosines" *Nature Biotechnology* 39, 1426-1433 (2021).
4. BAE†* et al., "Adenine base editing and prime editing of chemically derived hepatic progenitors rescue genetic liver disease" *Cell Stem Cell* 28, 1614-1624 (2021) (†Lead Contact)
5. BAE* et al., "High-purity production and precise editing of DNA base editing ribonucleoproteins" *Science Advances* 7, eabg2661 (2021).
6. BAE* et al., "PE-Designer and PE-Analyzer: Web-based design and analysis tools for CRISPR prime editing" *Nucleic Acids Research* 49, W499–W504 (2021).
7. BAE* et al., "Adenine base editors catalyze cytosine conversions in human cells" *Nature Biotechnology* 37, 1145–1148 (2019).
8. BAE* et al., "Direct observation of DNA target searching and cleavage by CRISPR-Cas12a" *Nature Communications* 9, 2777 (2018).

AI-generated small binder improves prime editing

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Abstract

The prime editing (PE) system comprises a nickase Cas9 fused to a reverse transcriptase utilizing a prime editing guide RNA to introduce desired mutations at target genomic sites. However, the PE efficiency is limited by mismatch repair. Thus, inhibiting key components of mismatch repair through transient expression of a dominant negative MLH1 (MLH1dn) increases PE efficiency, generating PE4. Herein, by utilizing RFdiffusion and AlphaFold 3, we generated a de novo MLH1 small binder (named MLH1-SB), which bind to the dimeric interface of MLH1 and PMS2. MLH1-SB's small size allowed it to be integrated into pre-existing PE architectures via the 2A system, creating a novel PE-SB platform. The PE7-SB platform demonstrates 29.4-fold improvement over PEmax and 2.4-fold increase over PE7 in HeLa cells, which is the highest PE efficiency to date. This research provides an insight that generative AI technologies will boost up the improvement of genome editing tools.