The modular platform to deliver bio-orthogonal macromolecular conjugates (BMCs) for therapeutic gene editing

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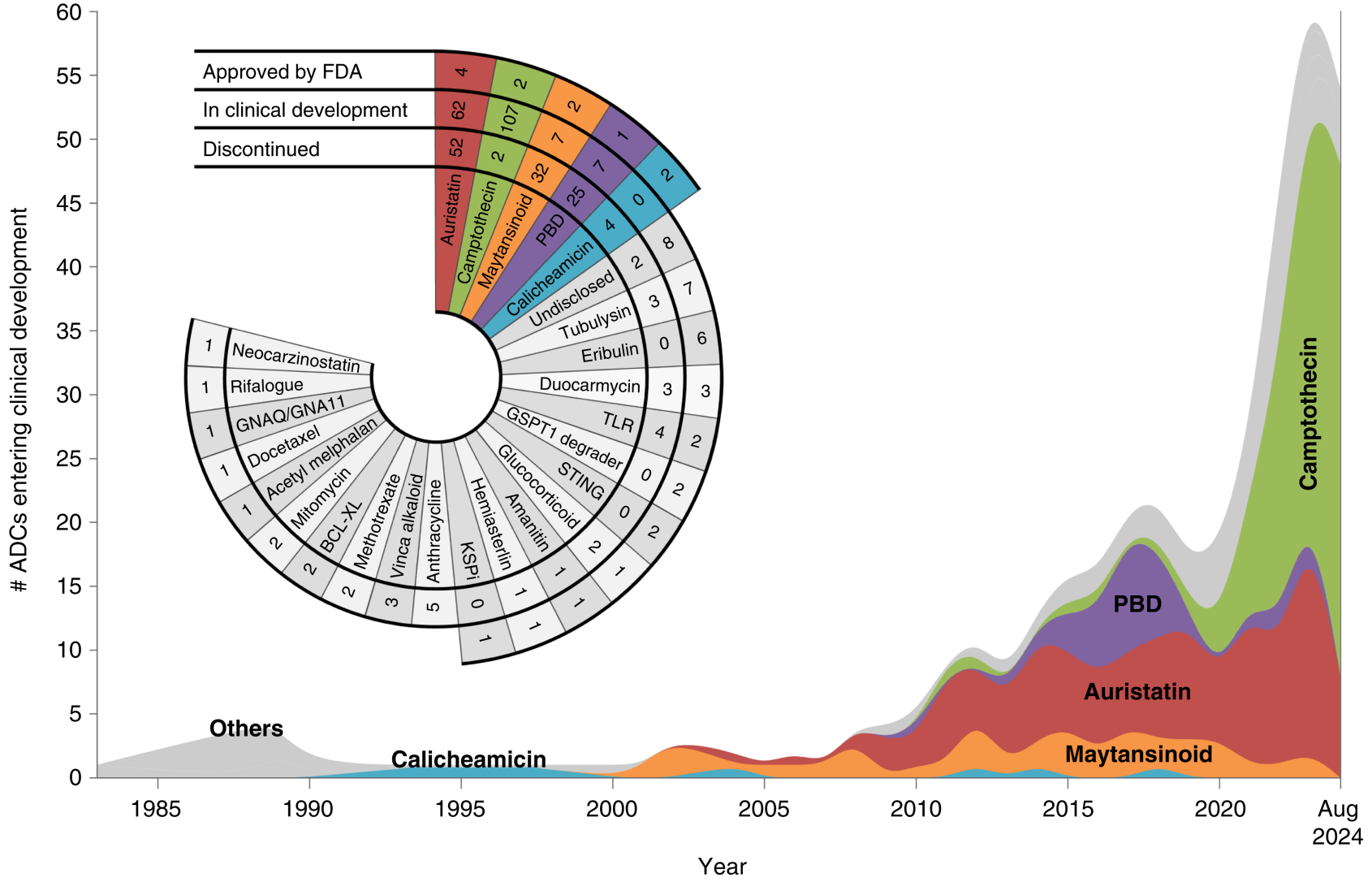
CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION DELIVERY INNOVATIONS

Small-molecule vs. Macromolecule Delivery

While small molecule delivery e.g., antibody-drug conjugates has advanced significantly, macromolecular delivery remains underdeveloped despite its potential to treat otherwise inaccessible diseases.



Cancer Discovery (2024) 14 (11): 2089–2108.

Bio-orthogonal Macromolecular Conjugates (BMCs)

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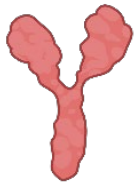

Antibody
(c-KIT, targeting HSPCs)

Plasma protein
(transferrin, albumin)

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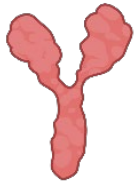
Carrier

Cargo



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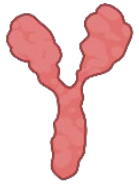
Cell penetrating peptide (CPP)



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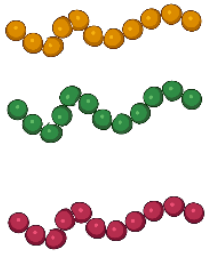

TAT
Eb
E5TAT
TAT-HA2
A5K

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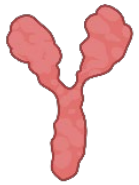

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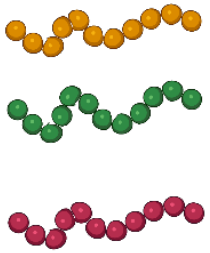

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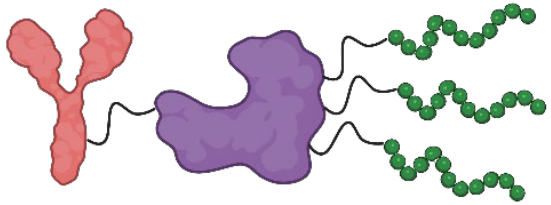
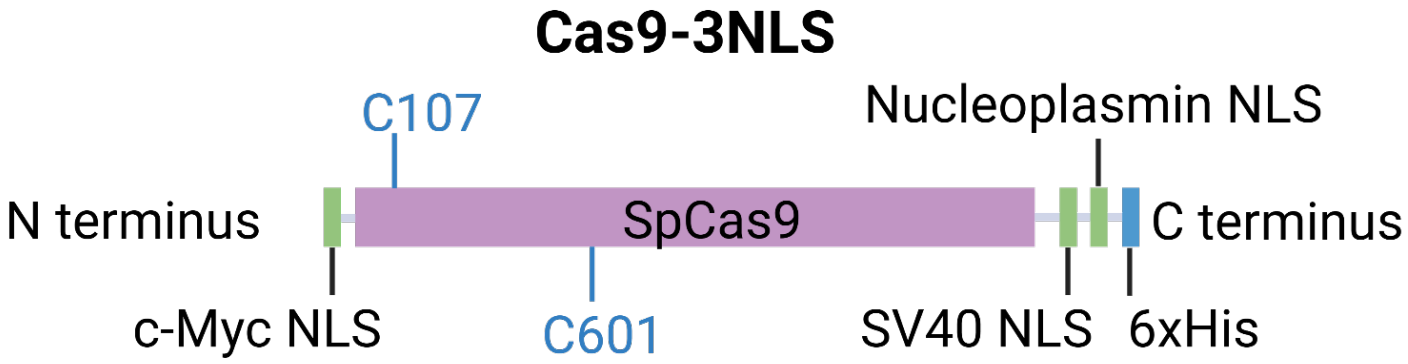
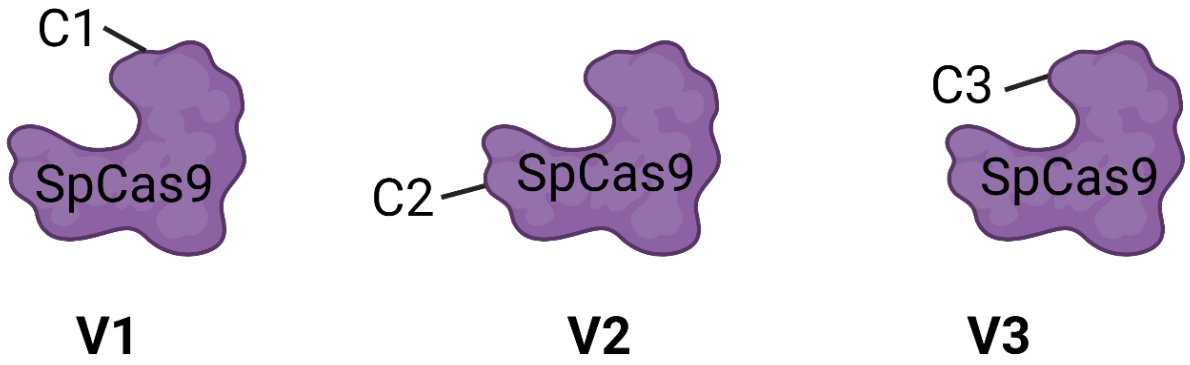


Carrier Cargo CPP

Bio-orthogonal
Macromolecular
Conjugate
(BMC)

Nuclease Delivery by Cas9 BMCs





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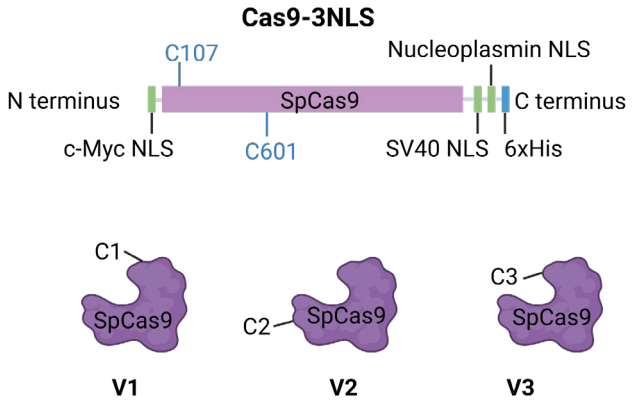

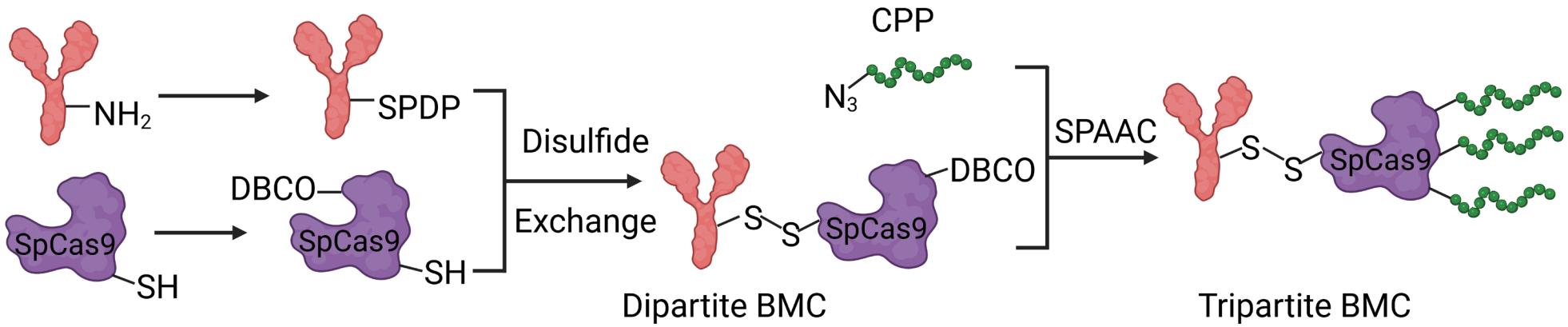

High yield, defined valency, preserved bioactivity

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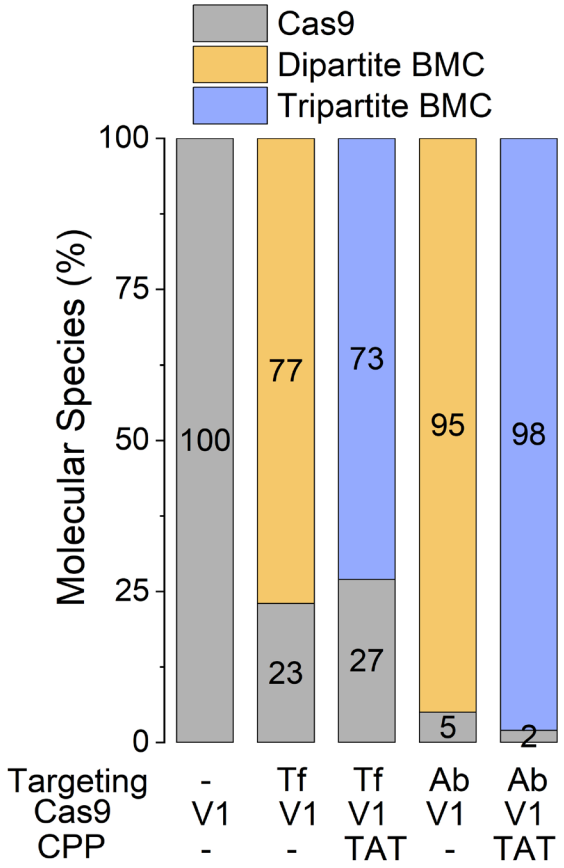
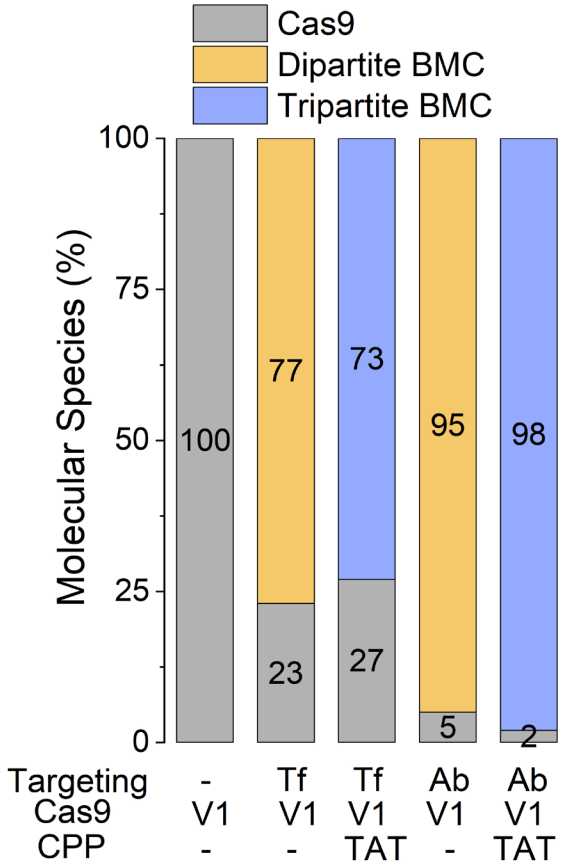


Mass Photometry

High yield, defined valency, preserved bioactivity



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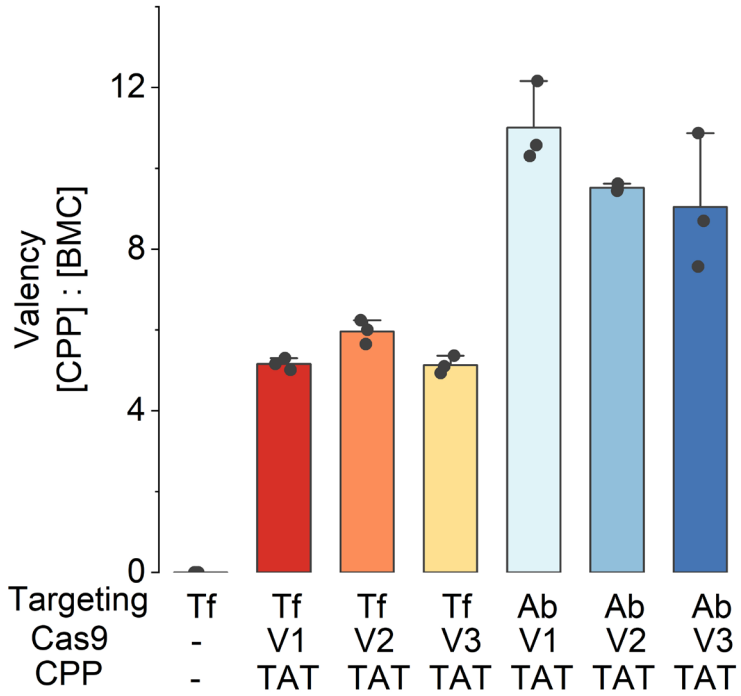
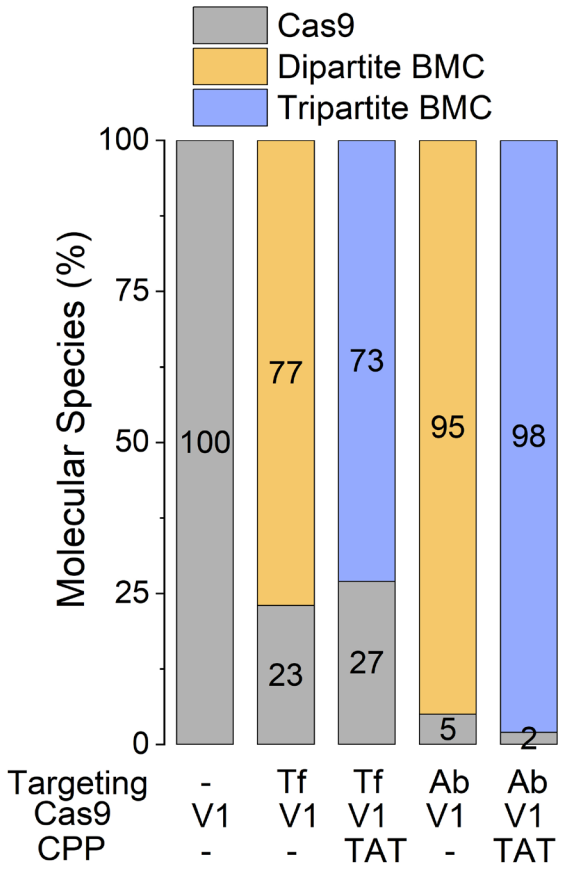


CPP Valency

High yield, defined valency, preserved bioactivity



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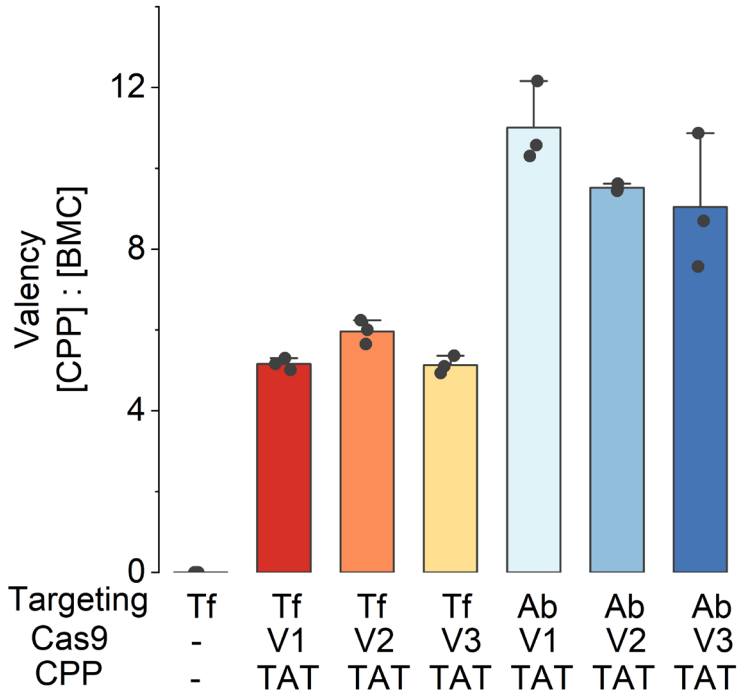

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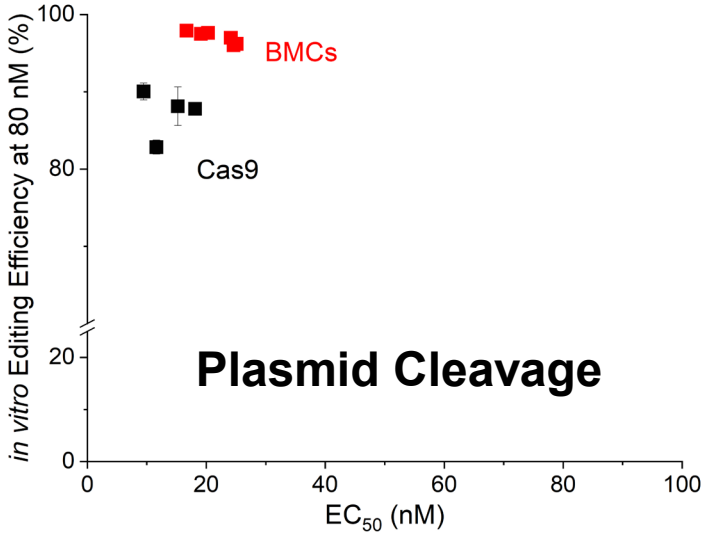
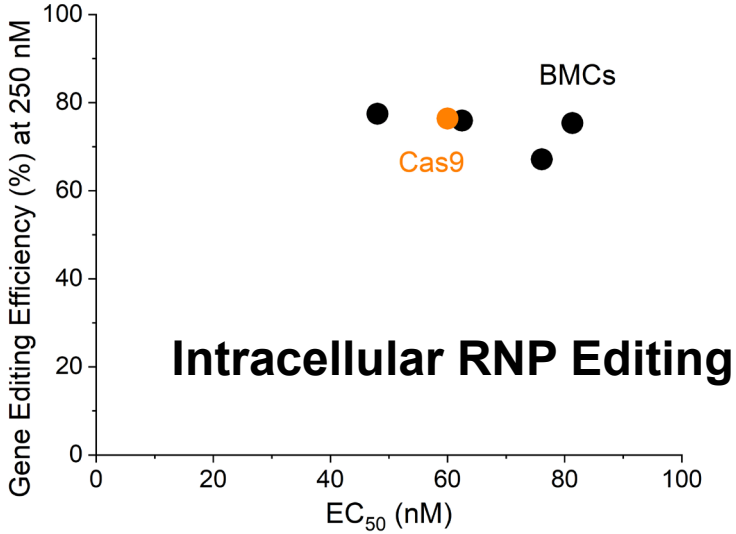
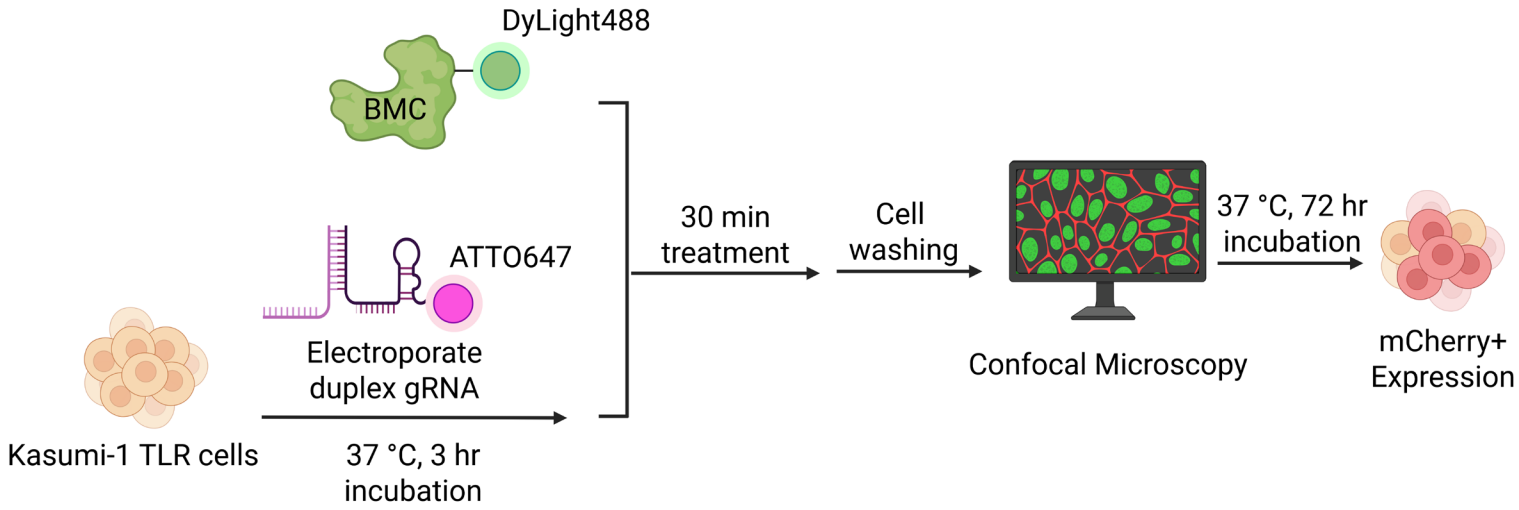


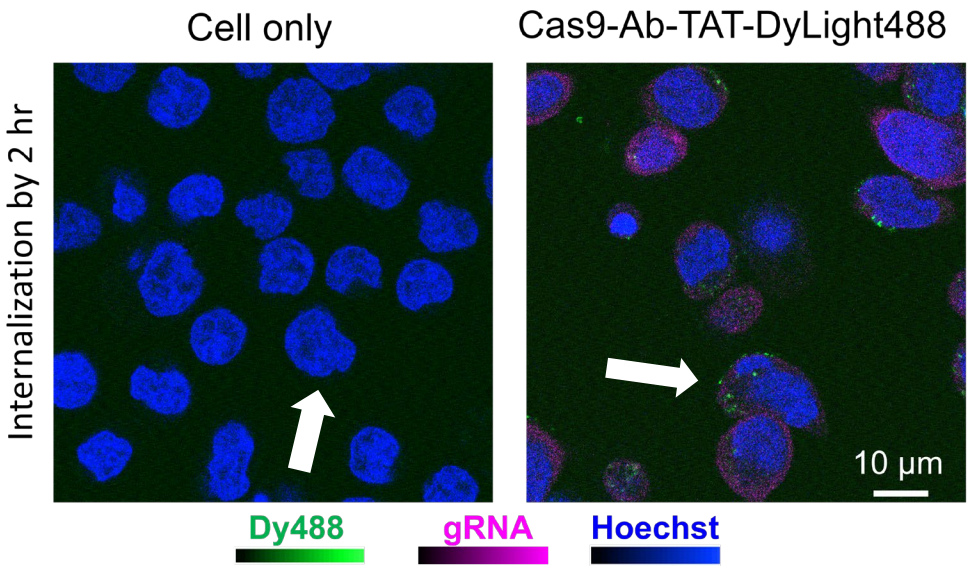
Plasmid Cleavage

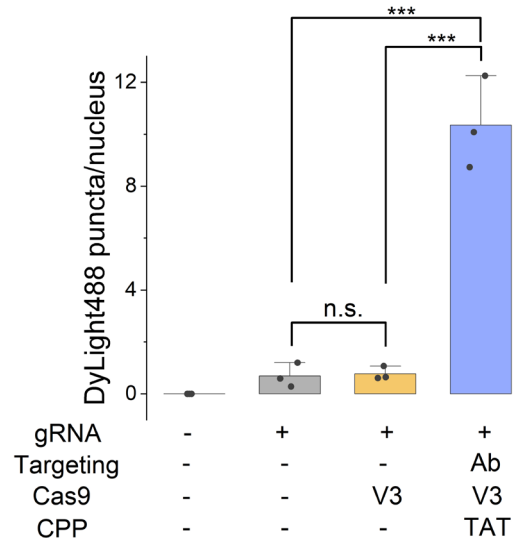


Intracellular RNP Editing

Rapid intracellular delivery and efficient gene editing







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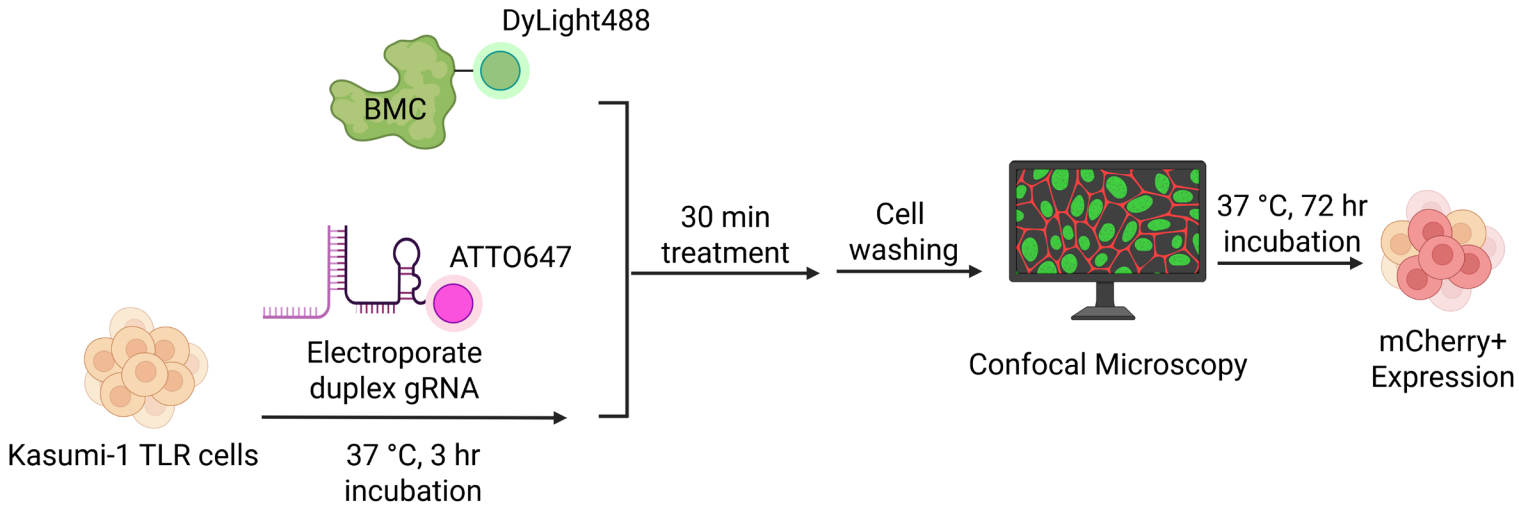
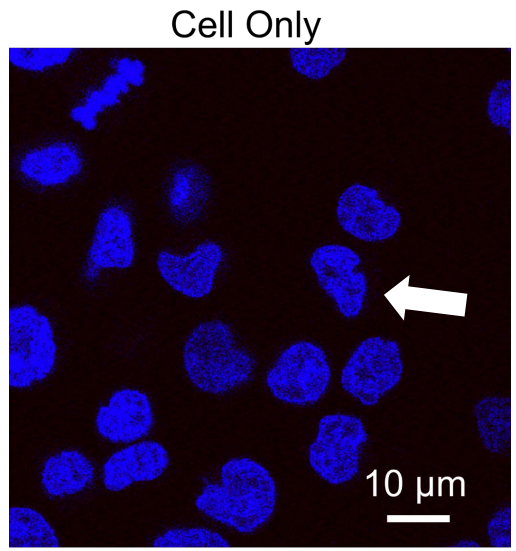
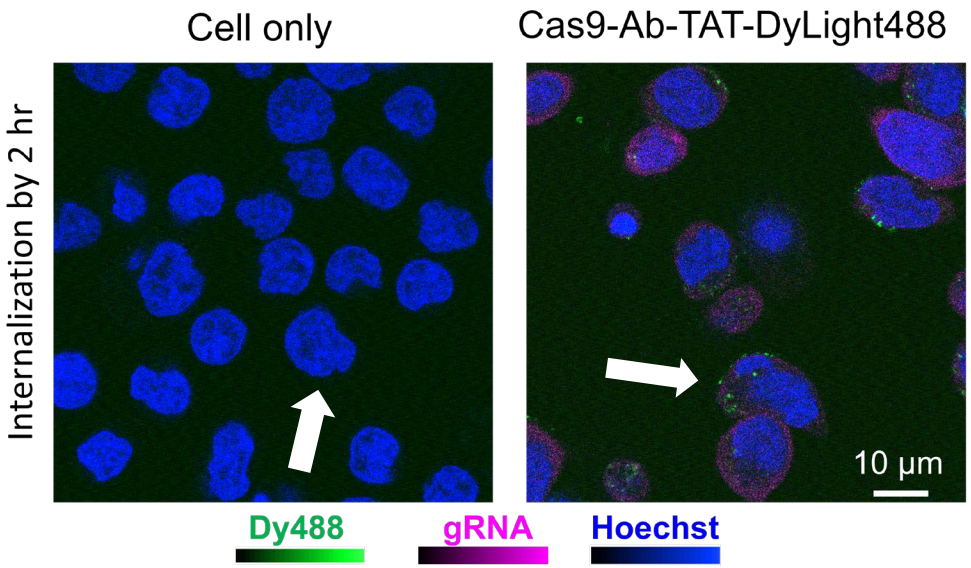
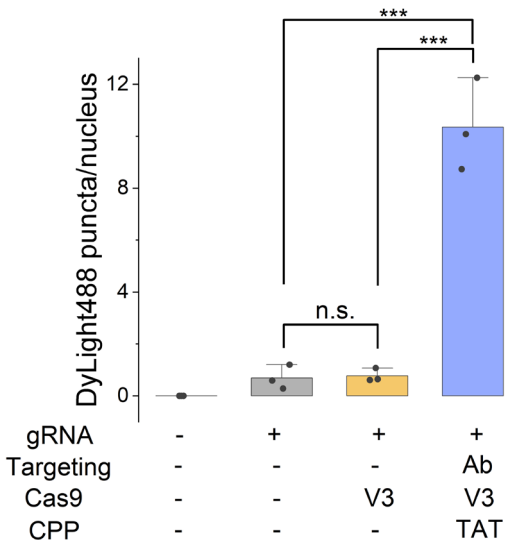
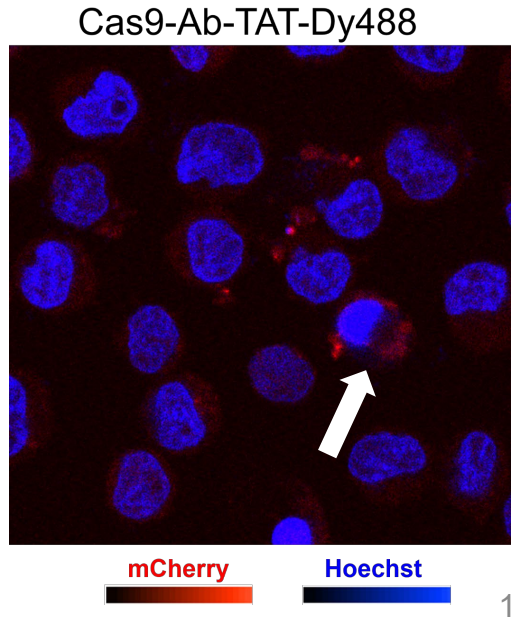


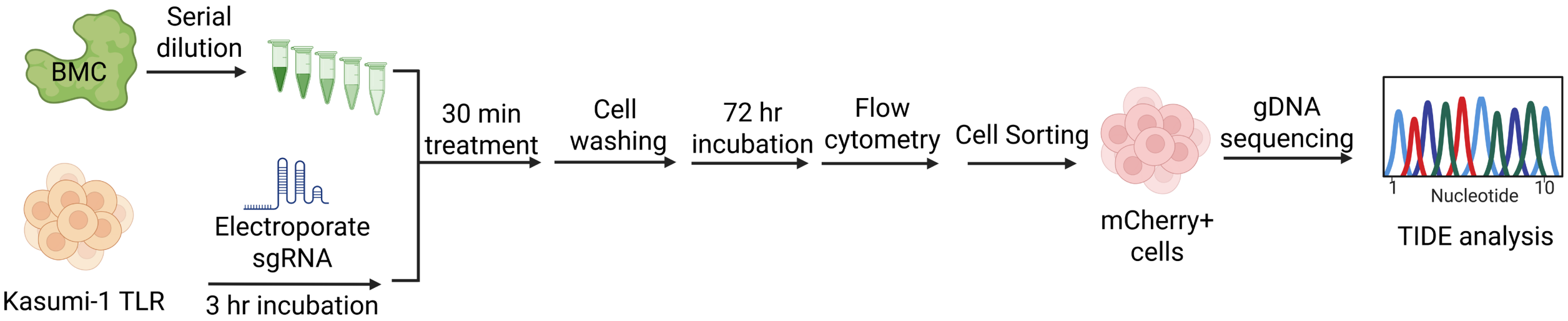








Cell type-specific human gene editing



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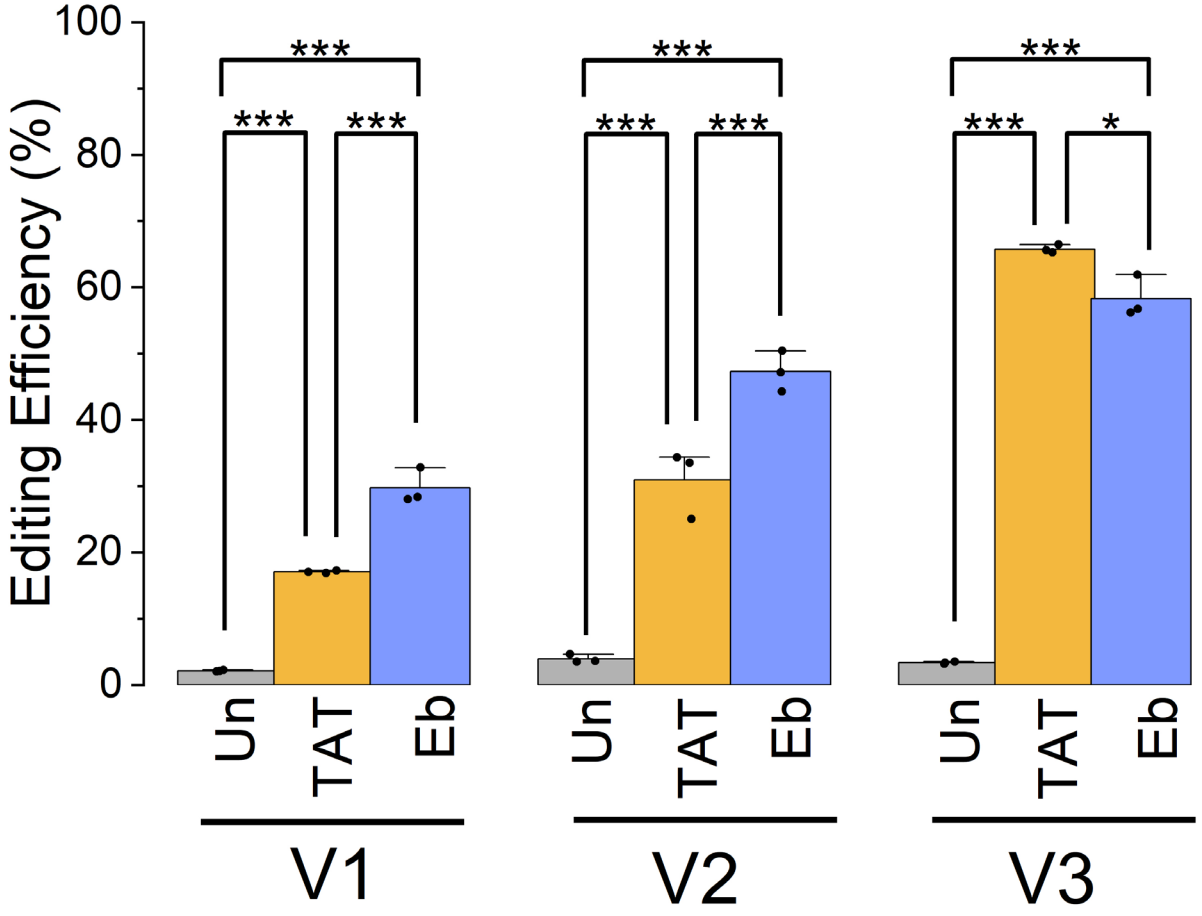

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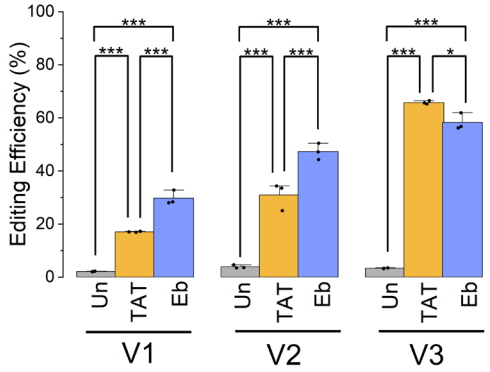

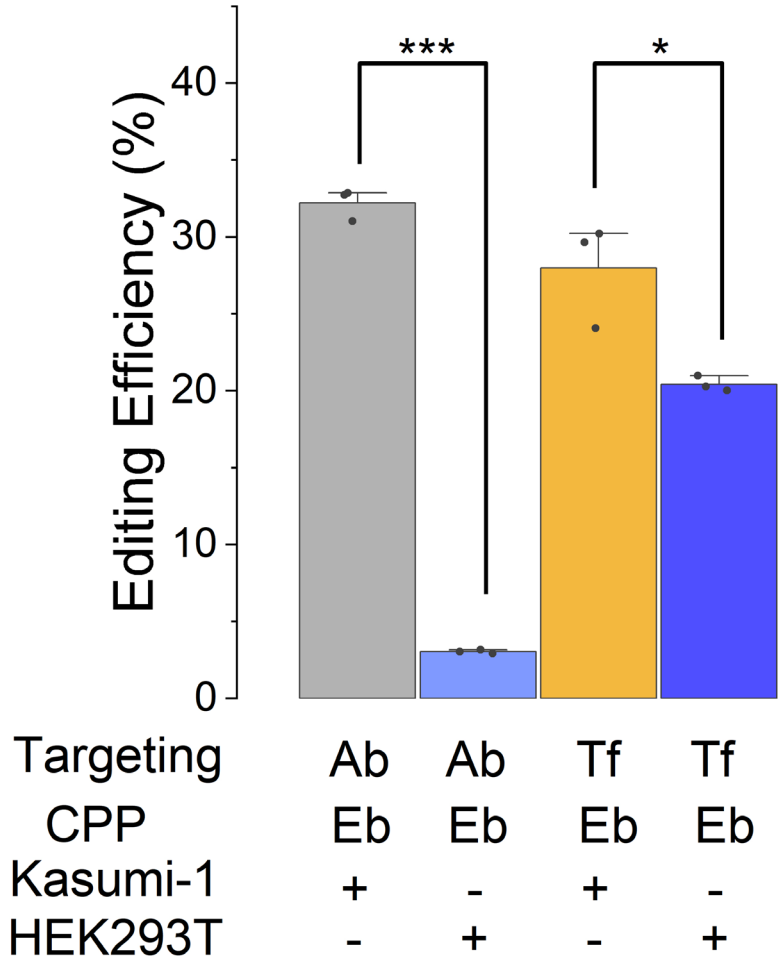

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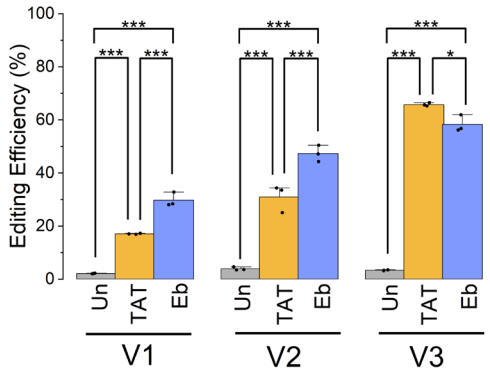

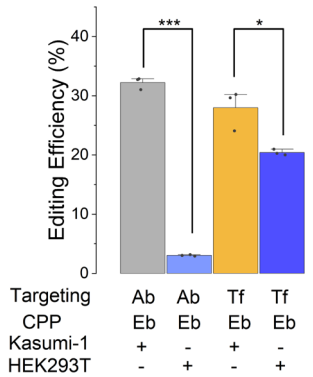

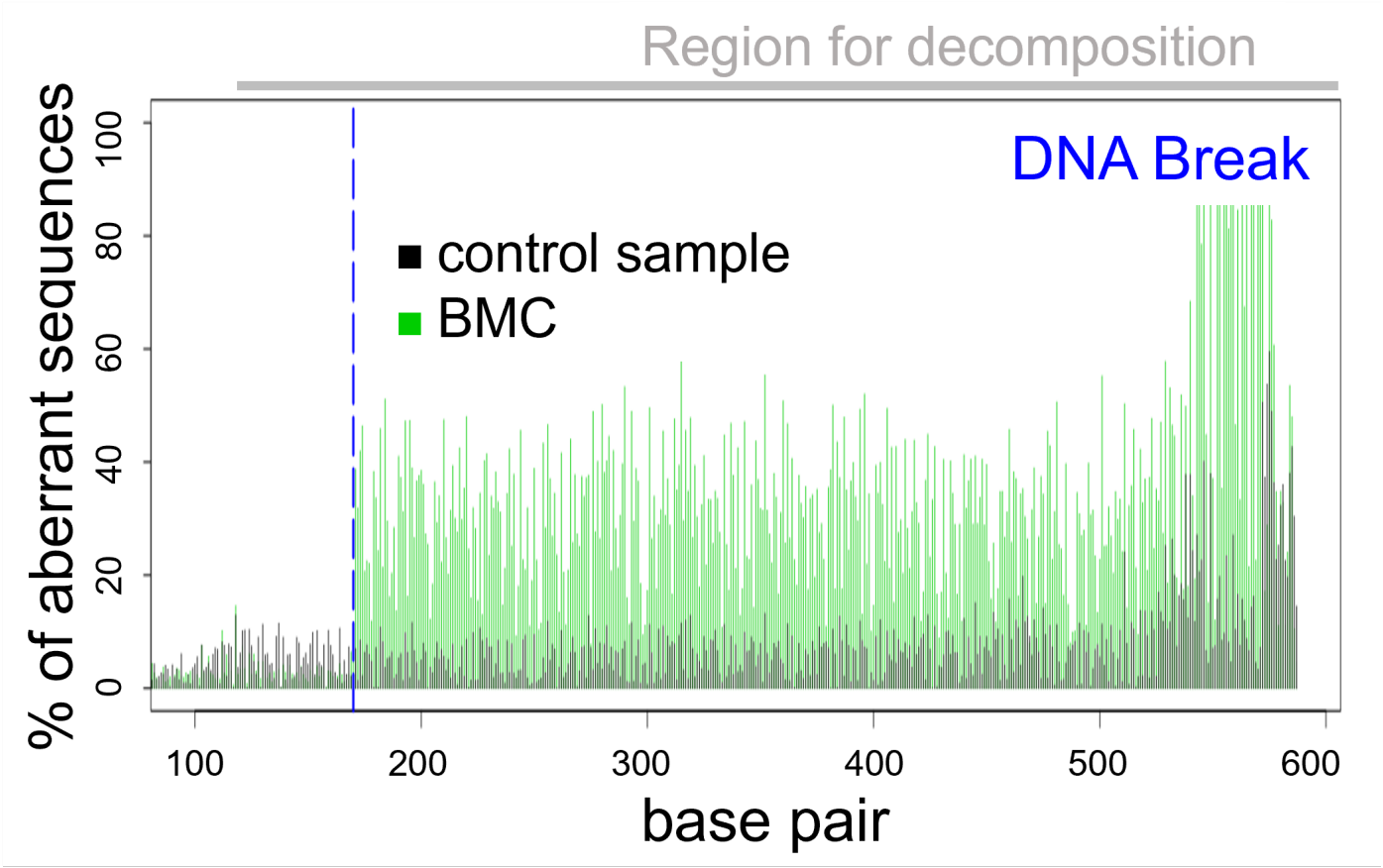

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- This modular BMC platform offers a generalizable strategy for targeted delivery of diverse macromolecular drugs, with promising applications in gene therapy, oncology, metabolic disorders, and beyond

Co-authors

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- Masahiro Uni
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- Anna Zychlinsky-Scharff

Funding Sources

- Doris Duke Charitable Foundation
- Center for Experimental Therapeutics

Memorial Sloan Kettering
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