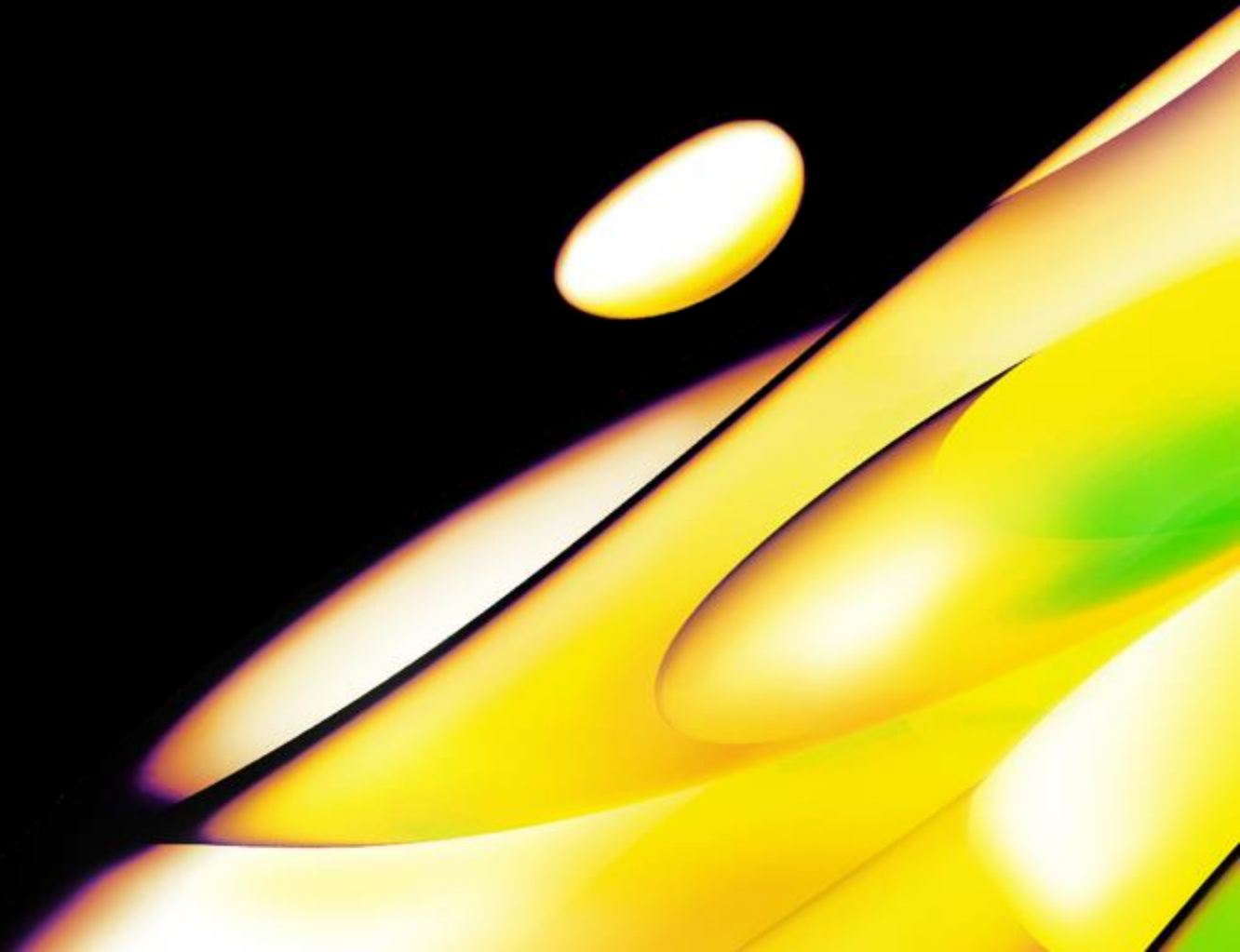


The Pin-point™ platform

A novel modular base editing system

revvity

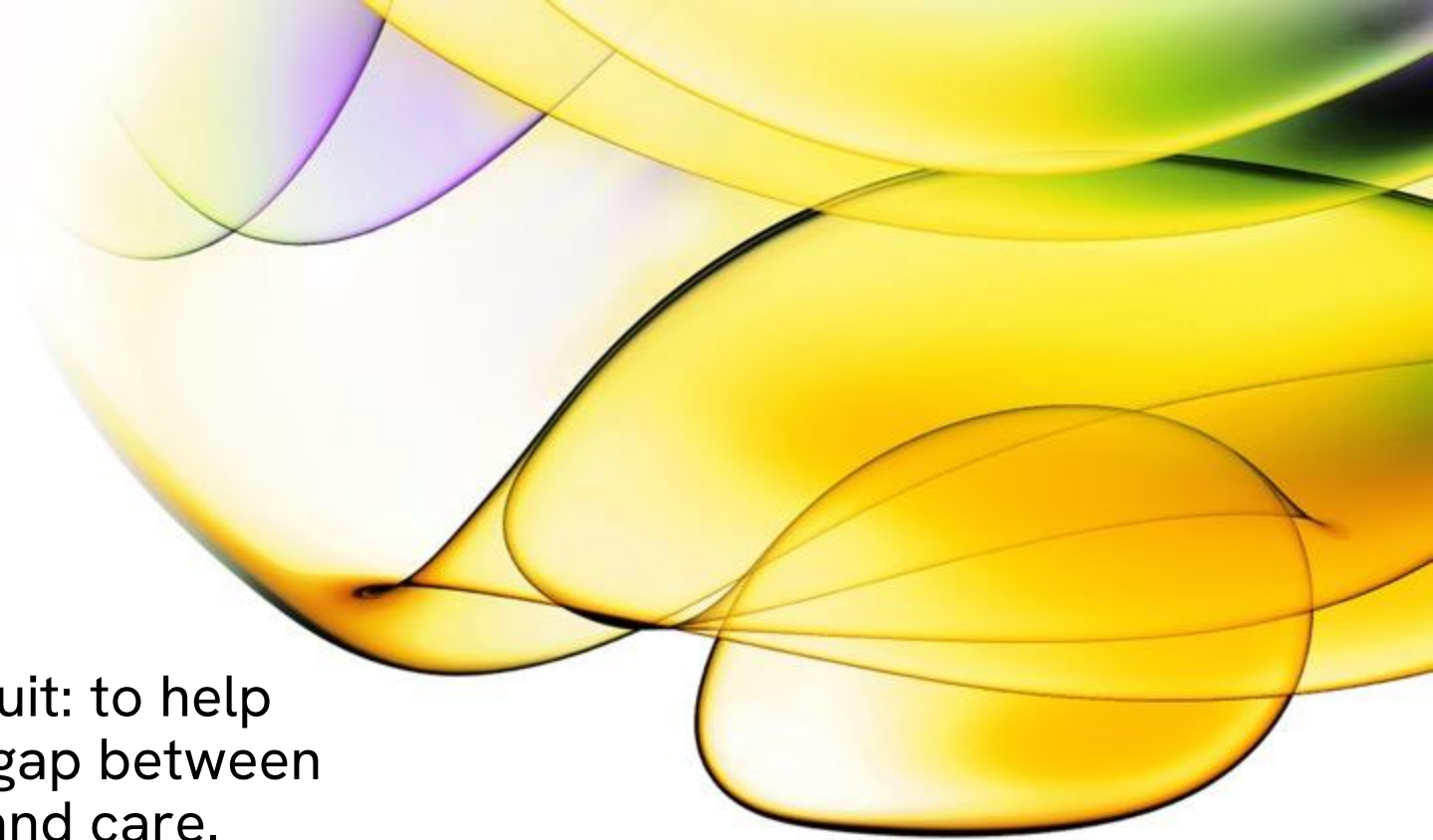
Updated 9 June 2023



revvity

Revvity is born of a single-minded pursuit: to help improve human health by bridging the gap between science and people through precision and care.

We innovate and collaborate to empower our partners to see science in unexpected ways that deliver breakthrough results.



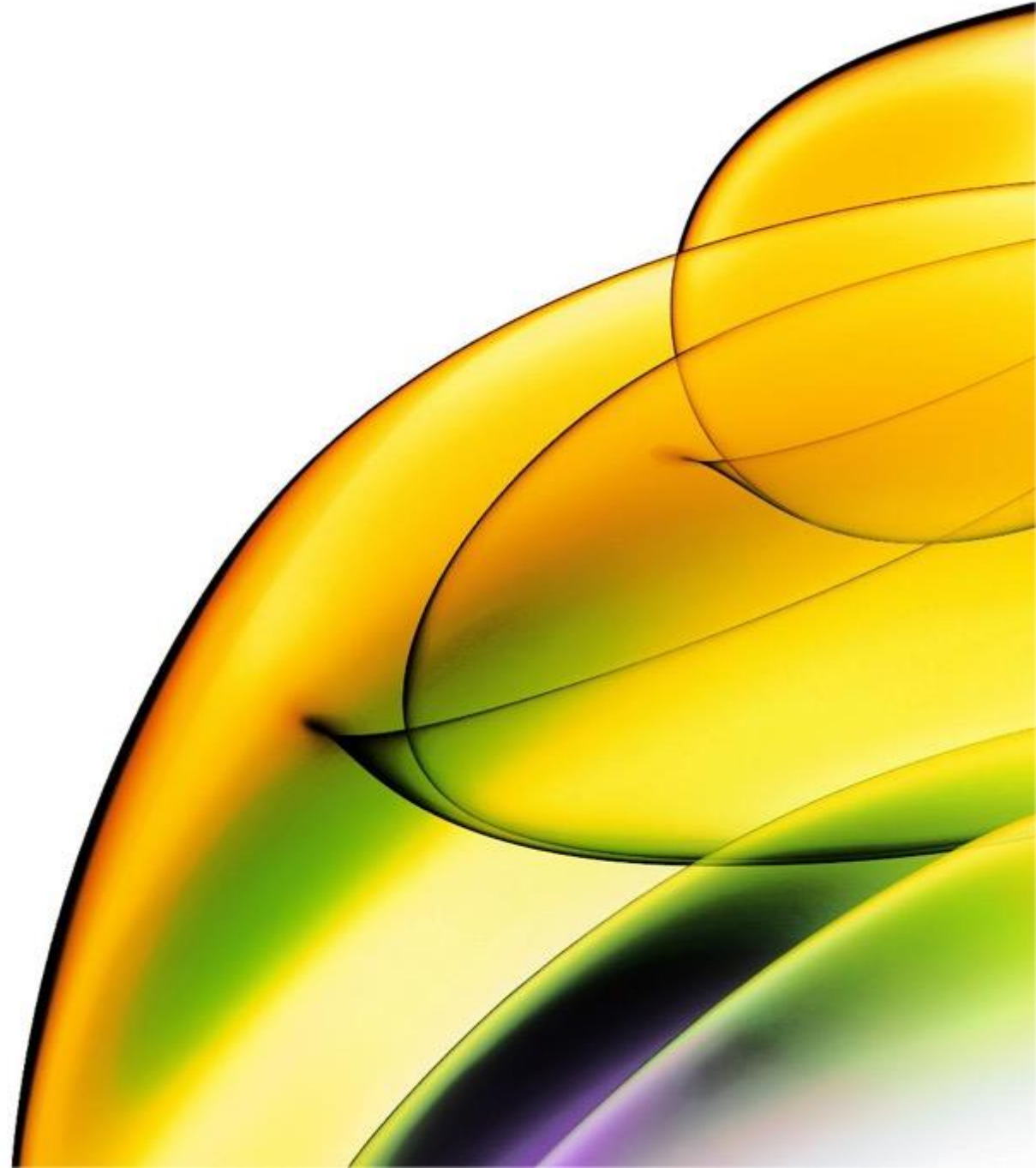
Impossible is inspiration

We are scientists who celebrate humanity. And we are here to empower scientists to improve healthcare for everyone, everywhere.

Powering innovation from discovery to cure -
- accelerating projects from inception to launch.

Increase success rates, meet customers' needs, and reduce time to market.

revvity



The Pin-point™ platform

Accelerating therapeutic development and reach into the clinic

revvity



www.ncbi.nlm.nih.gov/pmc/articles/PMC7898459/pdf/crispr.2020.0035.pdf

Why choose the Pin-point™ system?

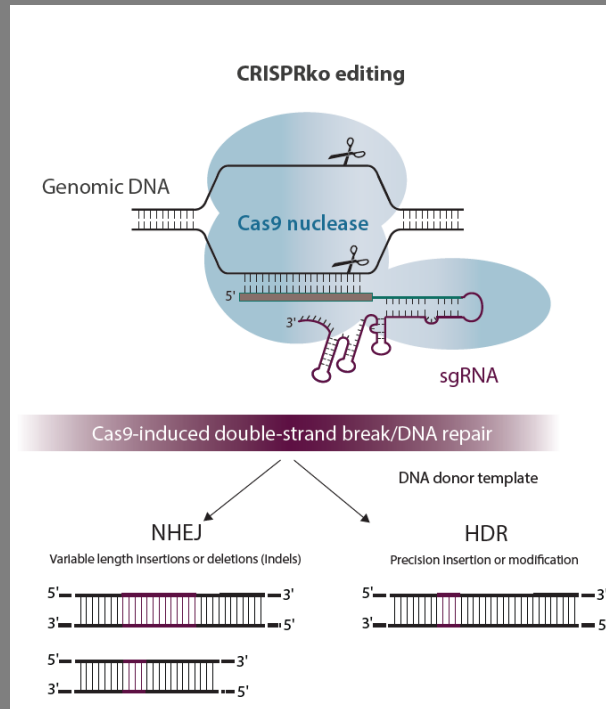


**Novel, patented aptamer-
recruited base editing
platform that can be
optimized for your research**

**Modular, tunable system
allows you to reach your
targets of interest**

**Exemplary safety profile with
no unintended impact on cell
viability or functionality**

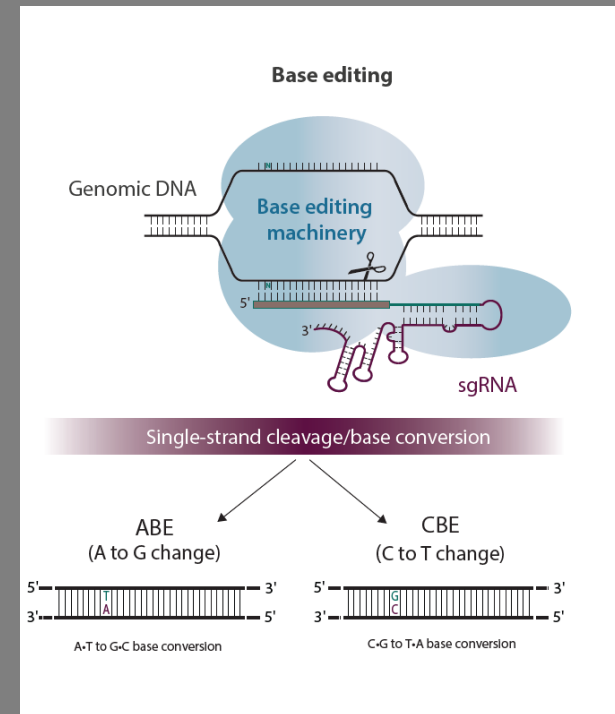
CRISPR gene editing



GENE DISRUPTION BY A DS DNA BREAK

- Indel formation to disrupt gene sequence
- complex population of indels

Base editing



GENE MODIFICATION BY POINT MUTATIONS

- Creation of stop codons or splice site disruption for knockout
- Introduction of single base conversion

The gene editing evolution is now

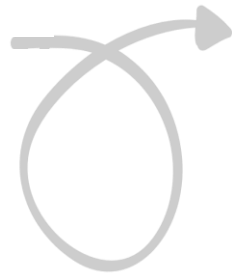
1st generation Cas enzymes

Gene disruption by a dsDNA break

2nd generation base editing

Gene modification by point mutation

- *creation of stop codons or splice site disruption for knockout*
- *not reliant on dsDNA break*
- *introduction of single base conversion*

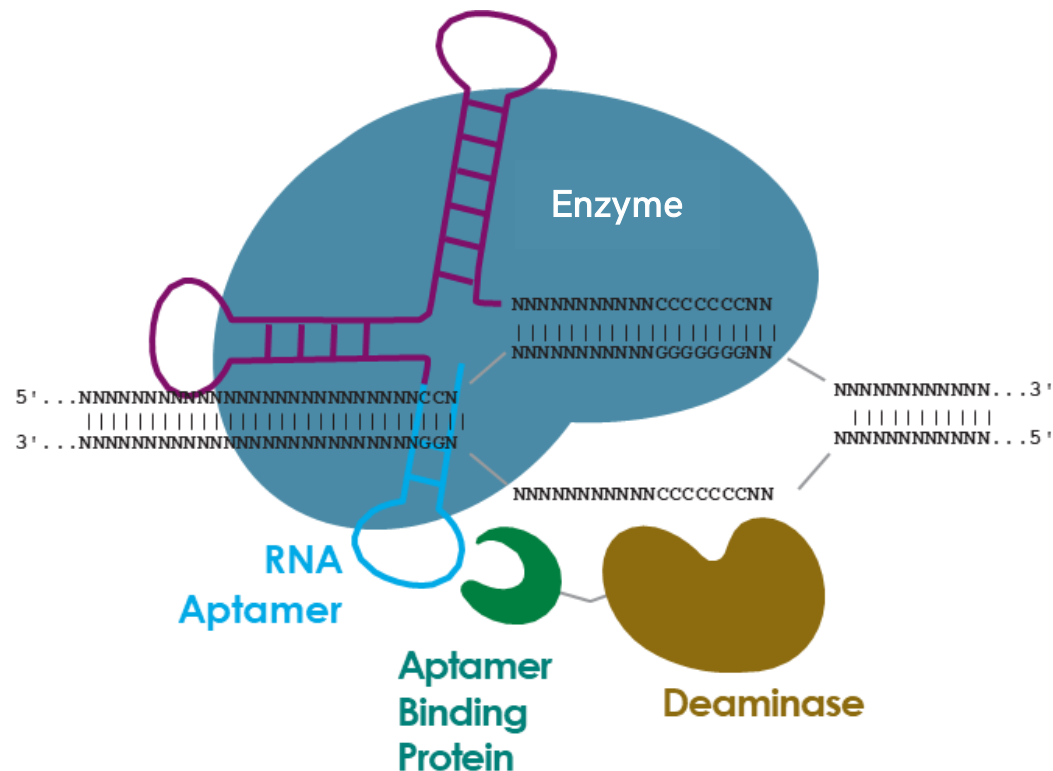


New generation Pin-point™ base editing system

- ✓ Predictable, precise and efficient single and multi-gene editing
- ✓ Simultaneous knock-in and knockout in a single reaction
- ✓ Modular control over target and editing window to specifically reach your gene of interest

What is the Pin-point™ system?

Novel | patented | aptamer-recruited
base editing platform



3 component system

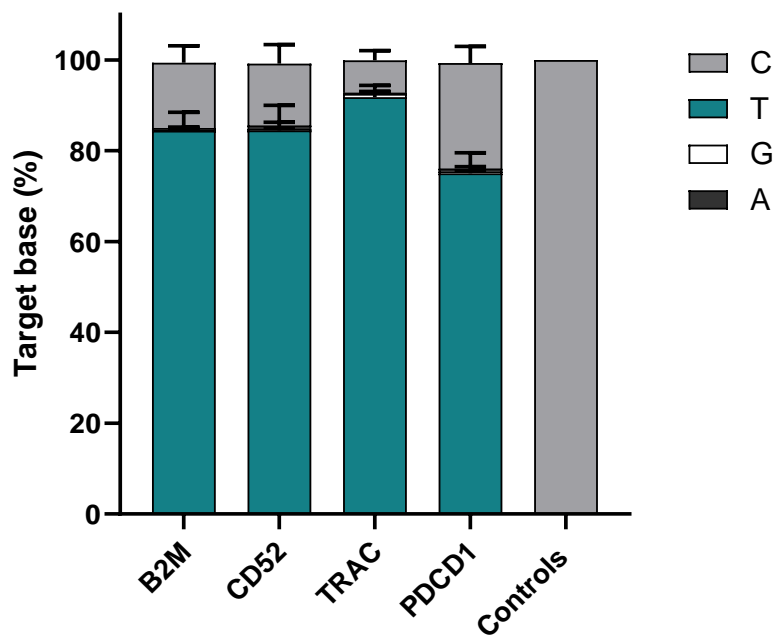
1. RNA-guided enzyme
2. Deaminase and recruitment protein
3. Guide RNA with aptamer

Advantages

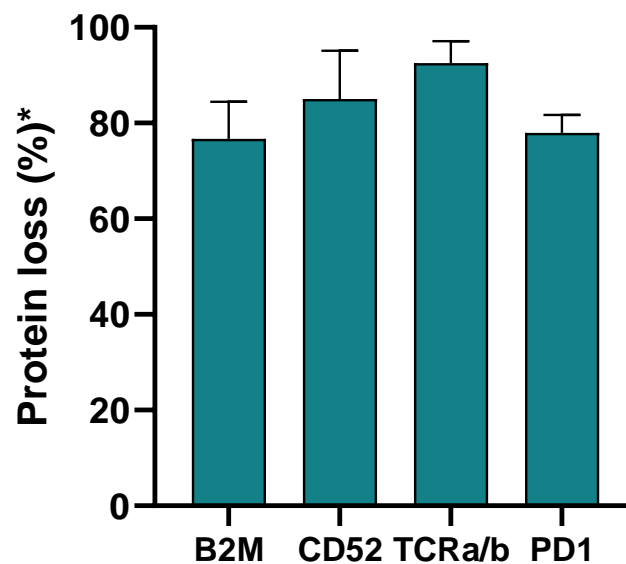
- ✓ Multiplex gene editing including knock-in and knockout with high efficiency and safety and no impact on cellular health
- ✓ Validated performance in T cells and iPSCs
- ✓ Completely mix-and-match for target specificity and efficiency

Highly efficient and precise multiplex T cell editing

>75% editing in each target base

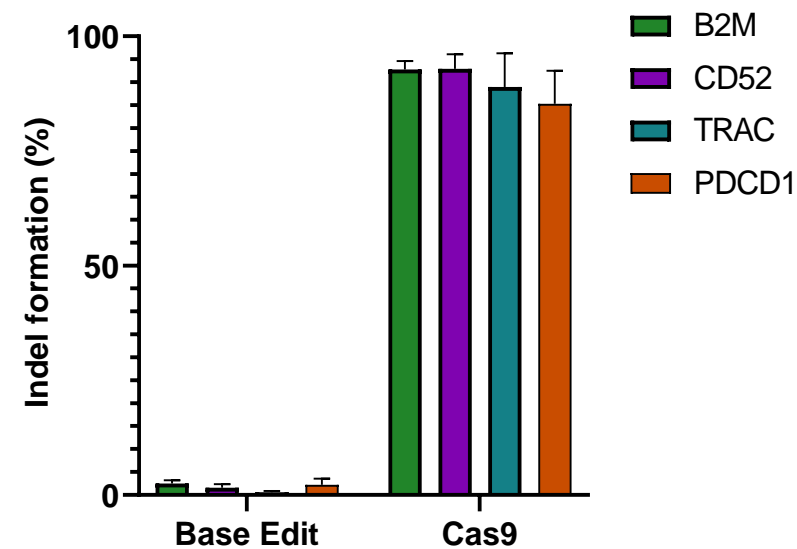


~50% of all 4 proteins knocked out



*Normalized to controls

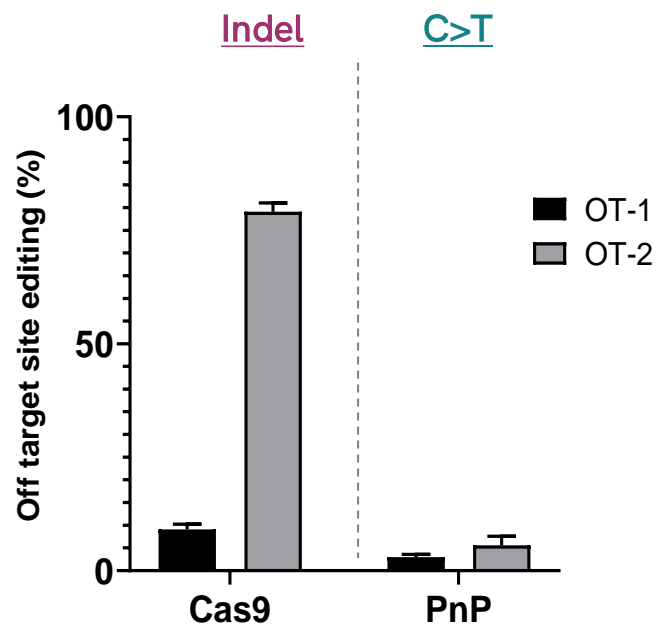
No indel formation



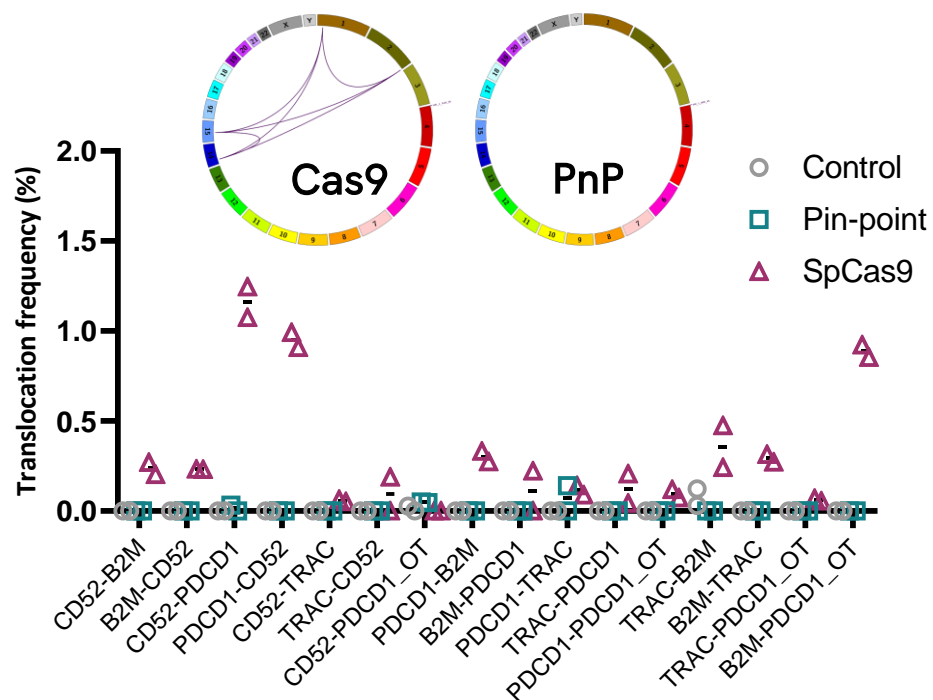
Pin-point™ base editing system is highly efficient and avoids potentially catastrophic DNA damage

Strong safety profile in T cells

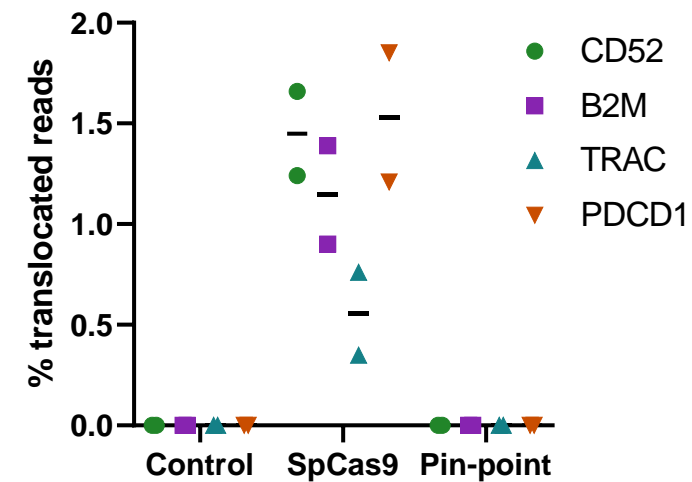
Negligible off-target edits



No detected translocations:
targets and known off-target sites



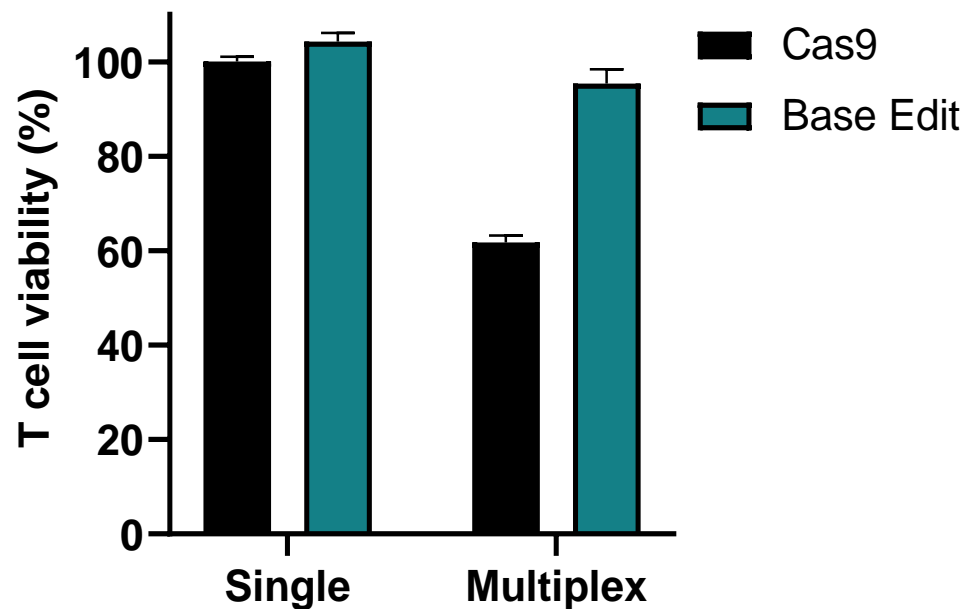
No detected translocations:
fusions



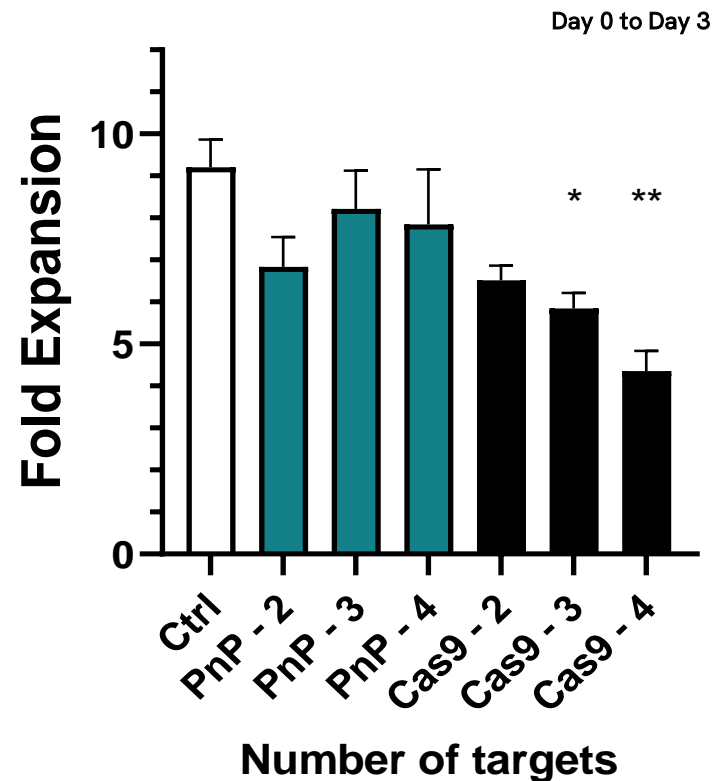
A cleaner and safer approach to multiplex gene editing in T cells

No impact on T cell health

Cell viability maintained



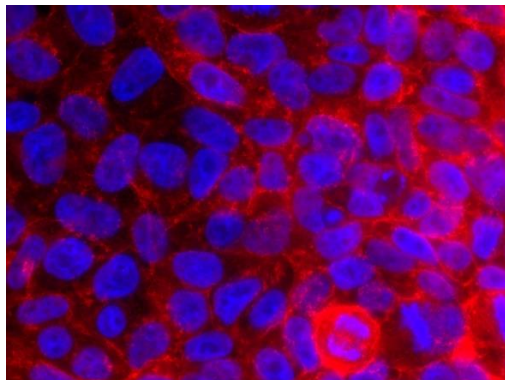
Rate of cell expansion unaffected



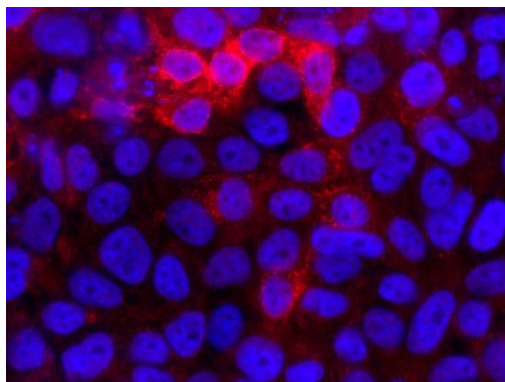
High multiplexing does not compromise cellular health or yield

Base editing with a Pin-point™ system in iPSCs

Mock

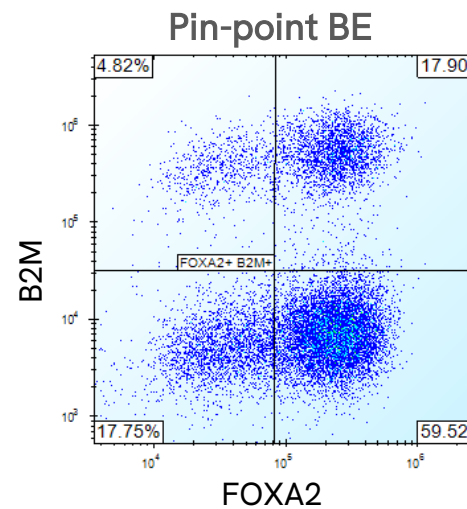
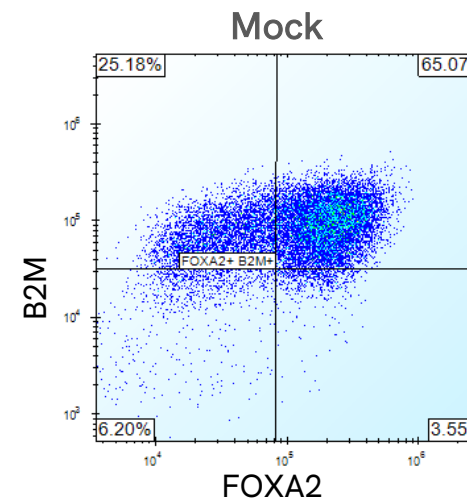
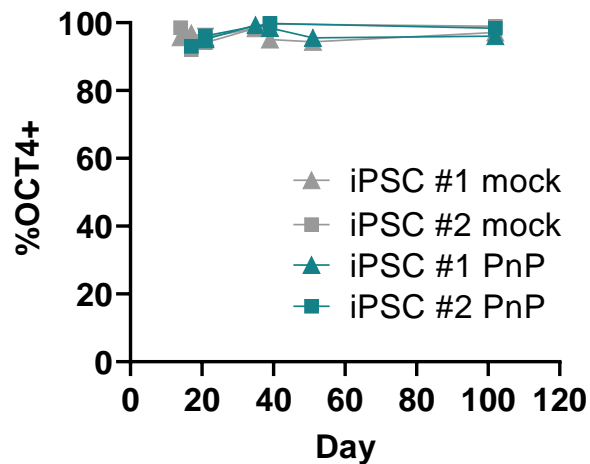
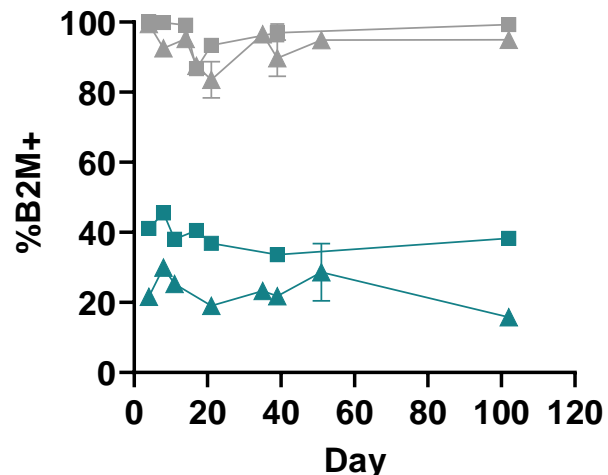


Pin-point BE



DAPI (nucleus)

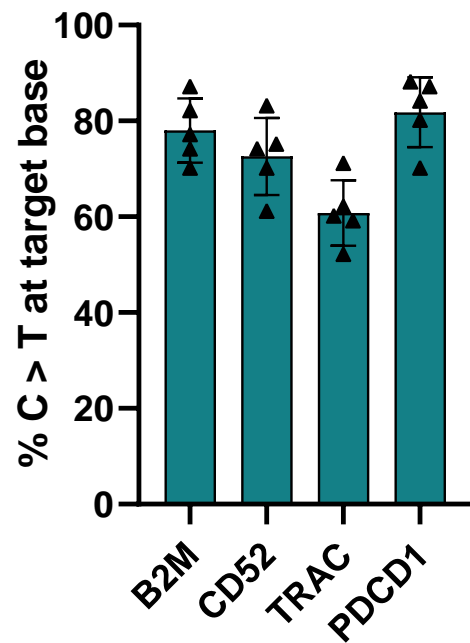
B2M



Edited iPSCs are stable with no growth defects when cultured up to 100 days and retain differentiation potential

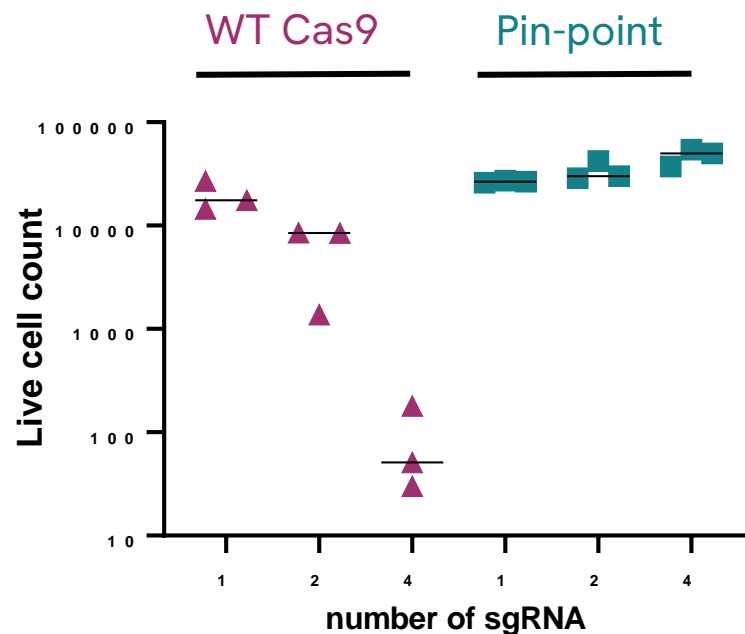
Multi-gene editing in iPSCs

Effective multiplex base editing



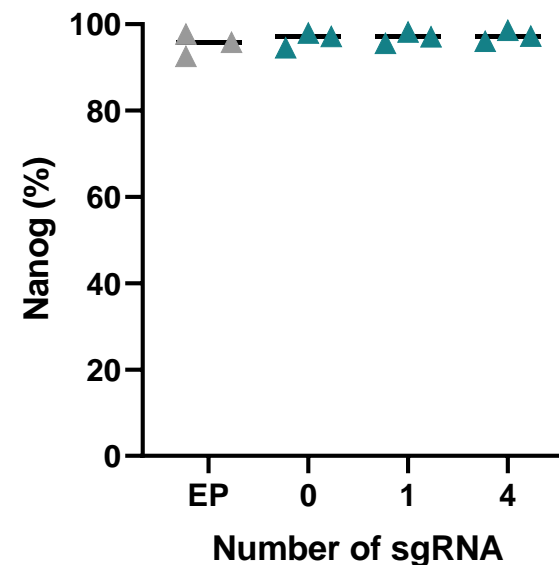
High base editing efficiency at target loci in a multiplex setting

Edited cells are viable



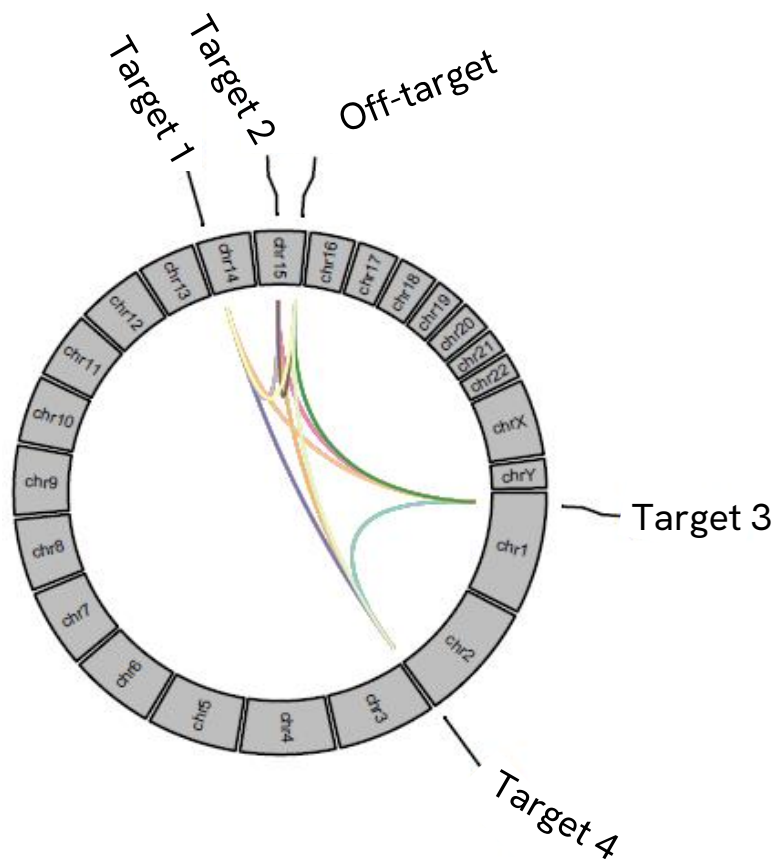
High survival of multi-edited iPSCs with a Pin-point system

Edited cells retain their pluripotency



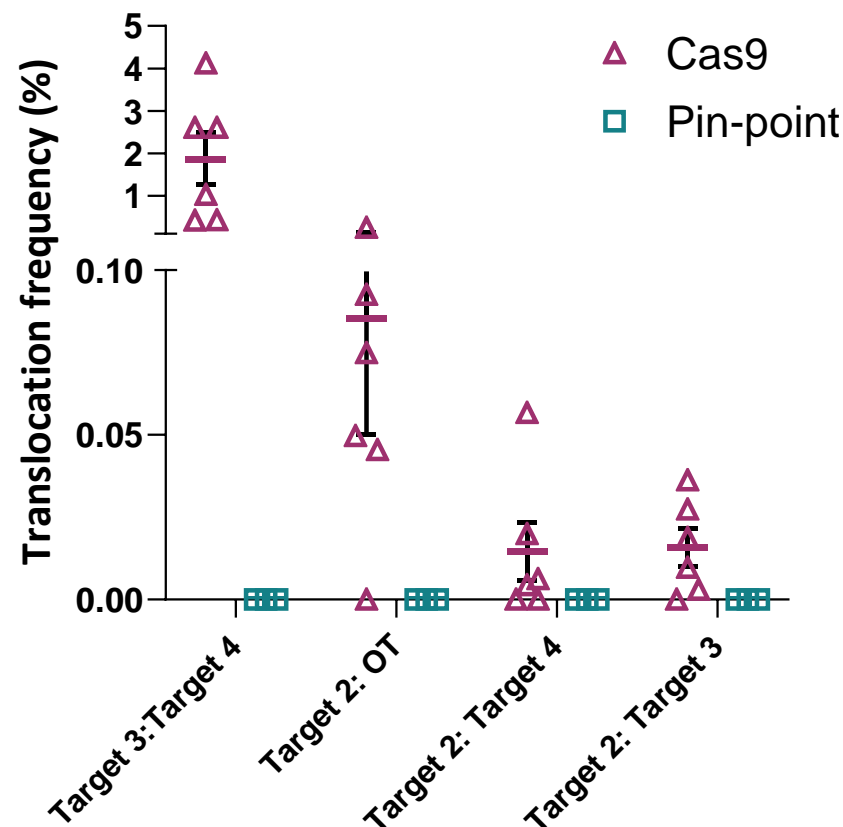
Pluripotency is retained in iPSCs edited with a Pin-point system

Strong safety profile in iPSCs



in-silico predicted translocations
previously validated in T cells

Undetectable translocations after multiplex base editing with a Pin-point system



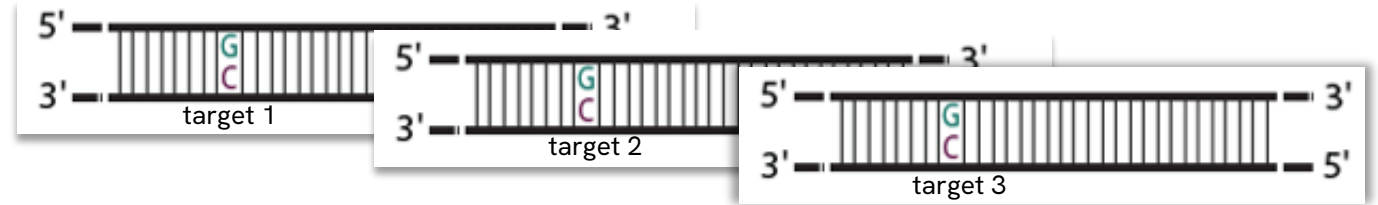
A cleaner and safer approach to multiplex gene editing in iPSCs

A solution for complex engineering

One-step simultaneous knock-in and multiple knockout in T cells

Base Editing with aptamer gRNAs

Knockout B2M, CD52, PDCD1

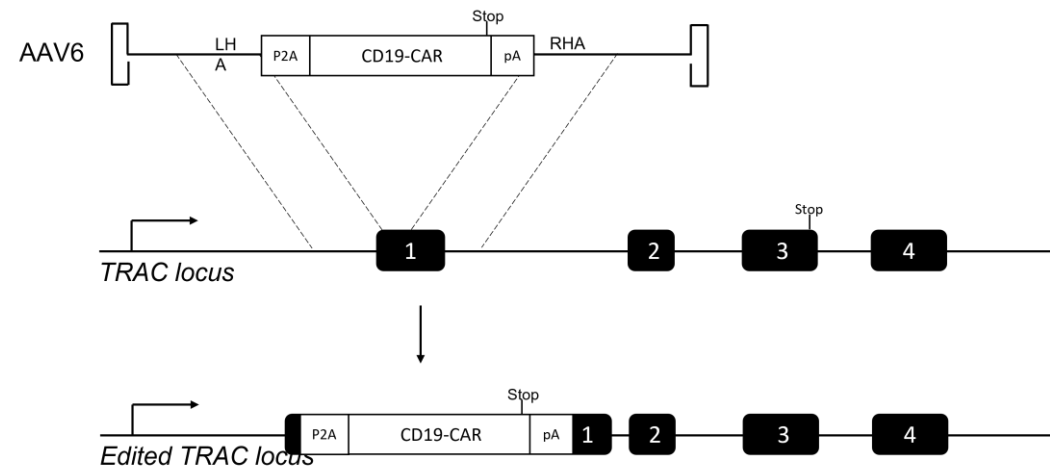


One transfection

- Pin-point deaminase
- Pin-point aptamer gRNA (3)
- Nickase Cas
- Nicking gRNAs (2)
- Donor insert template

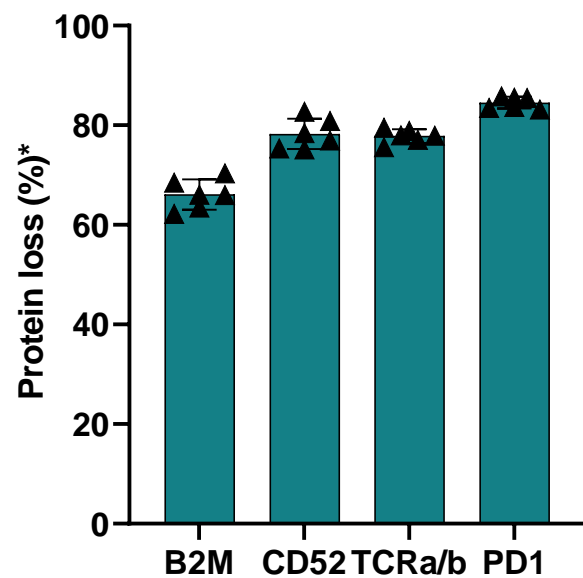
Insertion of a transgene by non-aptamer nicking gRNAs

CAR in TRAC

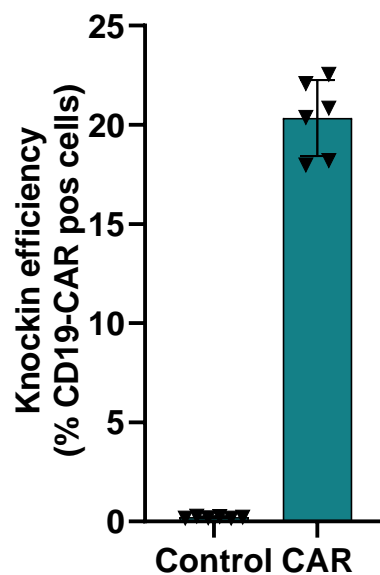


Streamlined creation of CAR-T cells is enabled with the Pin-point™ platform

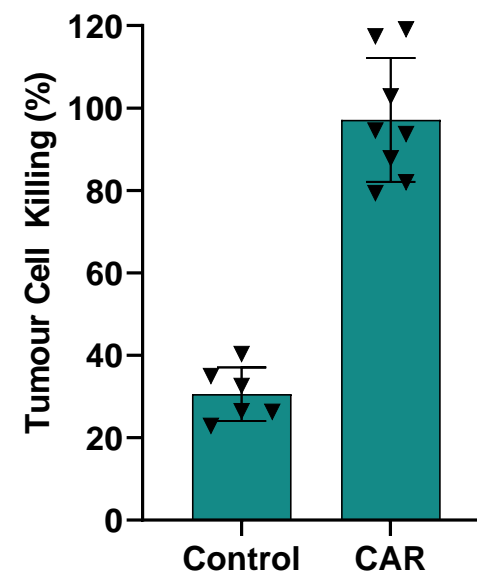
Multiple proteins are knocked out



... while enabling protein knock-in



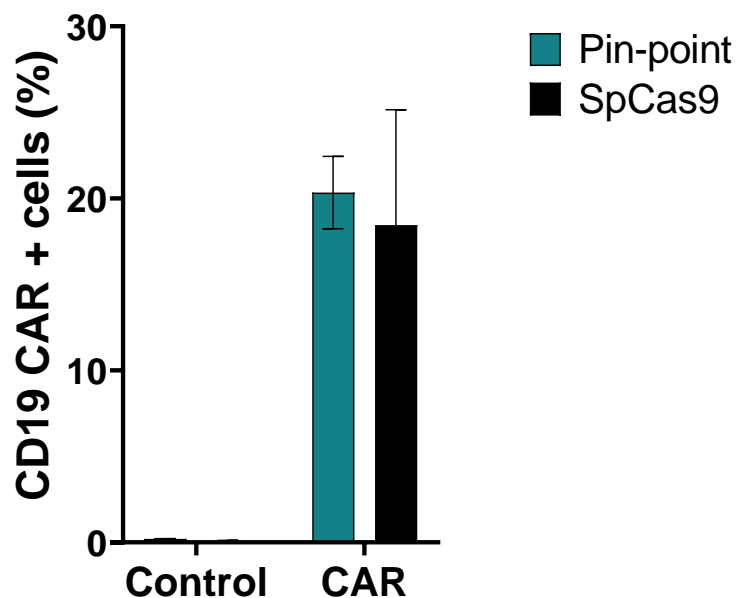
... and weaponizing T cells against cancer cells



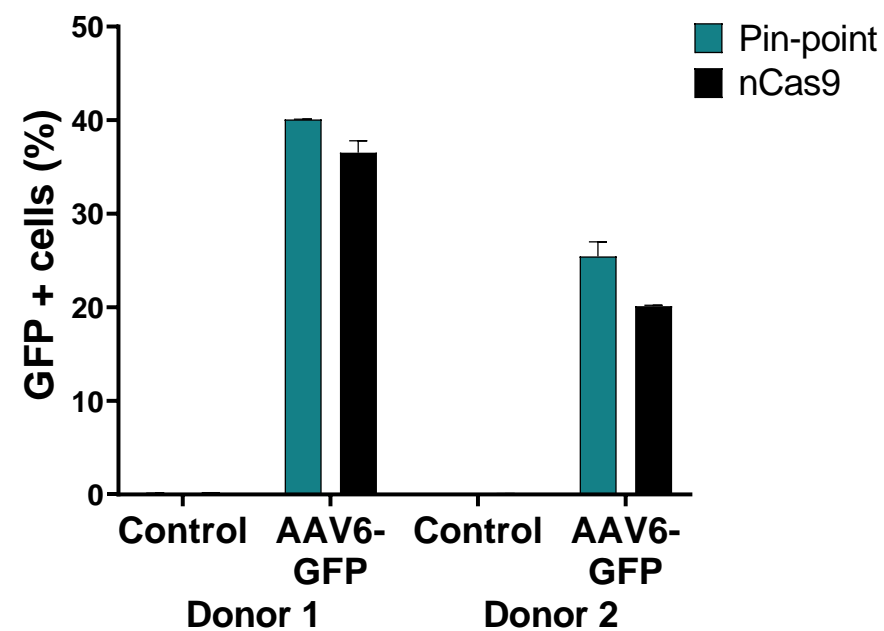
The Pin-point platform is efficient and accurate for concurrent transgene insertion and multiplex base editing

No loss of efficiency in payload deliveries

Equivalent to dsDNA knock-in



Presence of modular deaminase has no impact on knock-in



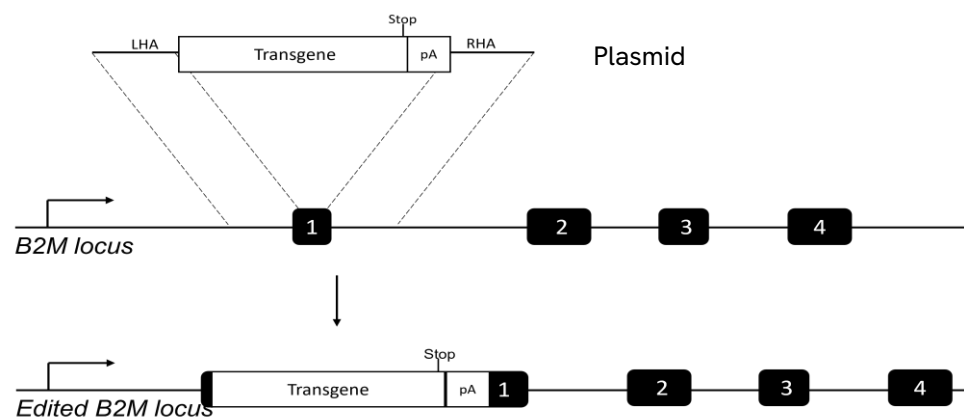
The Pin-point platform can deliver payloads equivalently to standard Cas9 or nCas9 knock-in strategies

Demonstrated simultaneous knock-in and multiple knockout in iPSCs

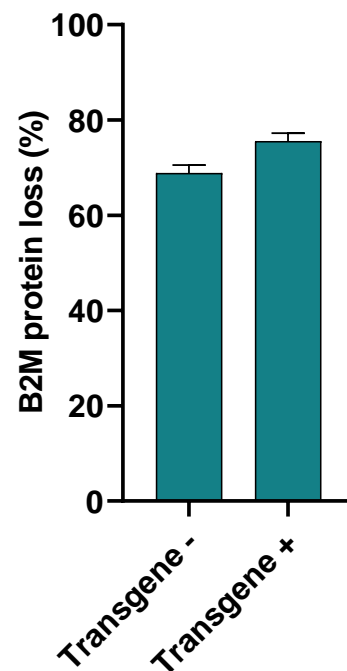
Base editing
Knockout CIITA

&

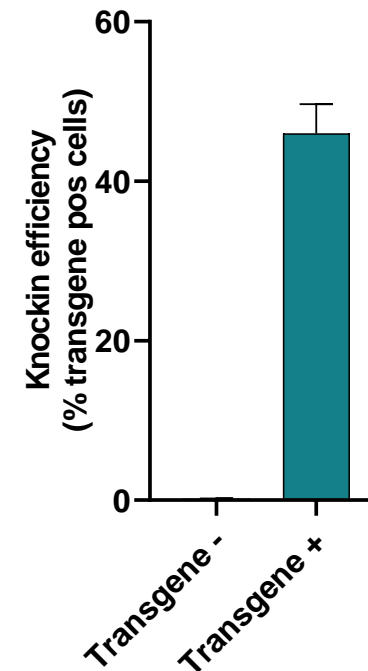
Insertion of a transgene
in B2M (promoter-less GFP)



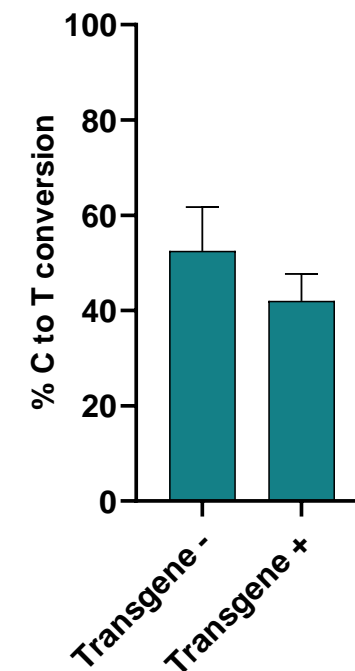
High level
of B2M
knockout



High level of
transgene
knock-in



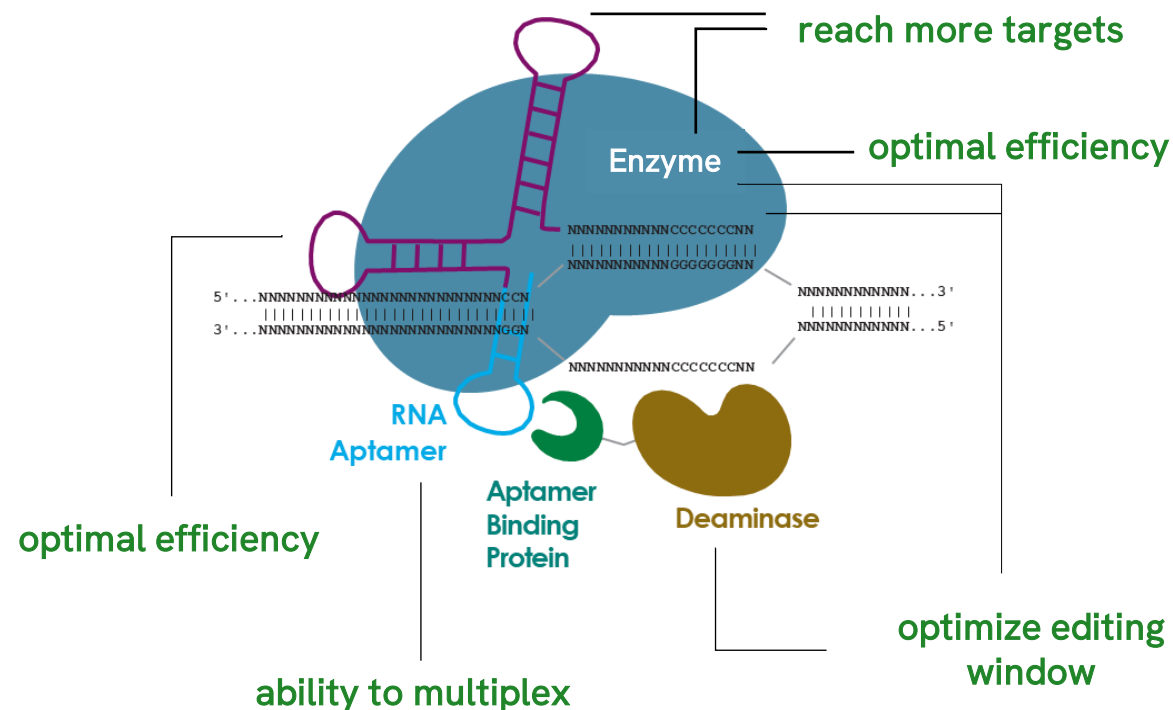
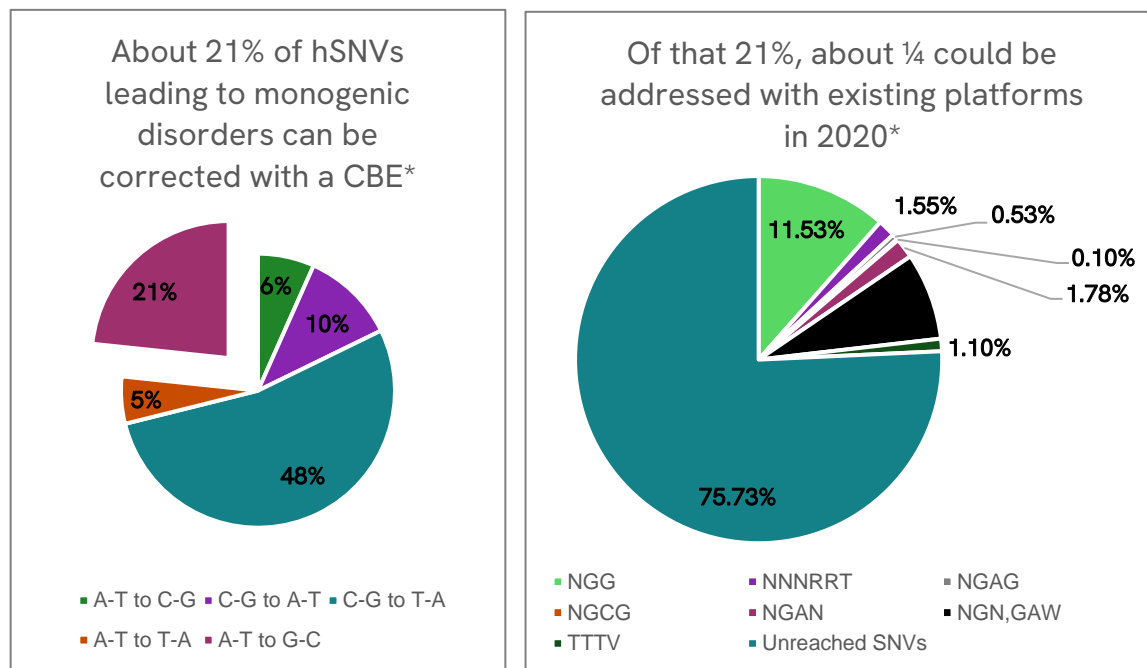
... and base
editing
(CIITA KO)



The Pin-point platform enables one-step simultaneous knock-in and multiple knockout in iPSCs

Choose components for locus-specific optimization

Most pathogenic SNVs with potential CBE correction are not reachable with published systems*



The modular Pin-point platform can be customized to combine optimal components for a wide range of base editing applications

A benefit of modularity of the Pin-point™ platform

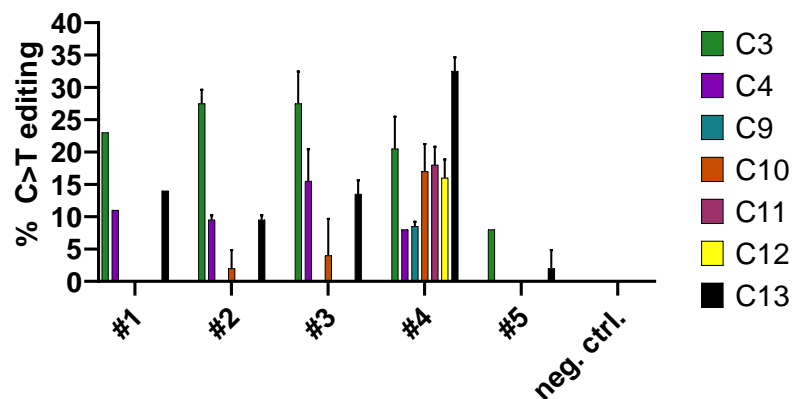
Demonstrated compatibility with numerous nucleases

	Type II			Type V							
	A	B	C	D	E	F	G	H	I	J	
Enzyme activity	nickase	nickase	nickase	deactivated	deactivated	deactivated	deactivated	deactivated	deactivated	deactivated	
Demonstrated activity in mammalian cells	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Demonstrated with the Pin-point system	✓	✓	In progress	✓	In progress	✓	In progress	✓	✓	In progress	
sgRNA optimized	✓	In progress		In progress		✓		✓	✓		
Enzyme optimized	✓					✓					
Confirmed at multiple targets (2+)	✓	In progress				✓		✓	✓		
Demonstrated in multiple cell types (2+)	✓	In progress				✓		✓			
Demonstrated with multiple deaminases (2+)	✓							✓	✓		

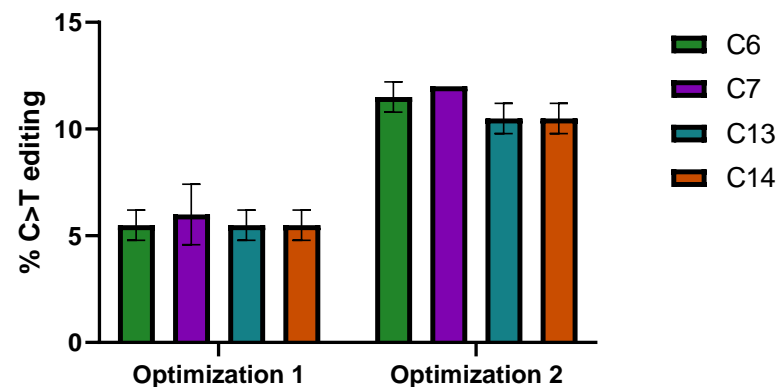
The Pin-point platform enables utilization of a variety of RNA-guided nucleases, which can be further optimized for editing efficiency

Optimization using the modularity of the Pin-point platform

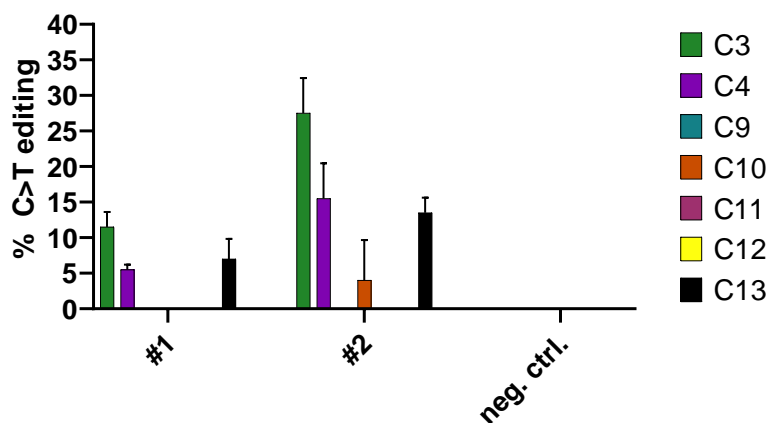
...for sgRNA design



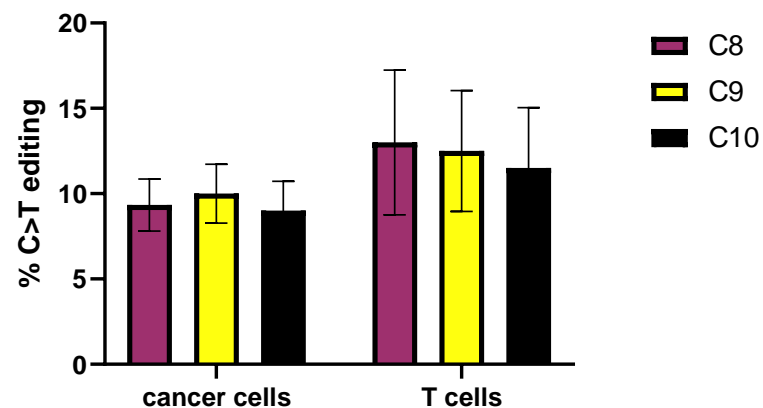
...for enzyme function



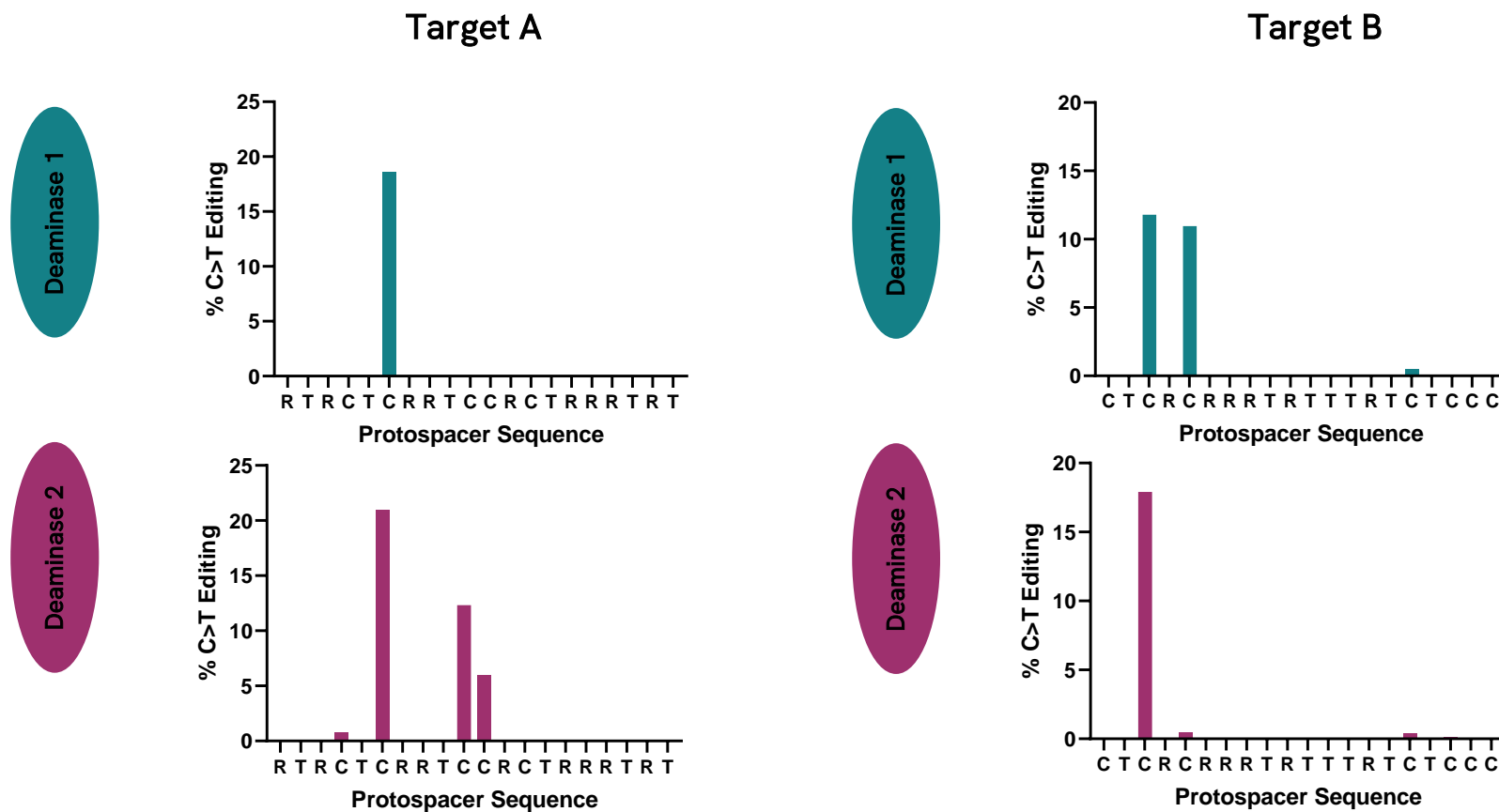
...with multiple deaminases



...in multiple cell types



Optimize synthetic guide RNAs and deaminase pairings



The Pin-point platform enables optimization of the editing window by selecting the best guide RNA and deaminase pairings

The Pin-point™ system is a transformational next-generation gene editing technology



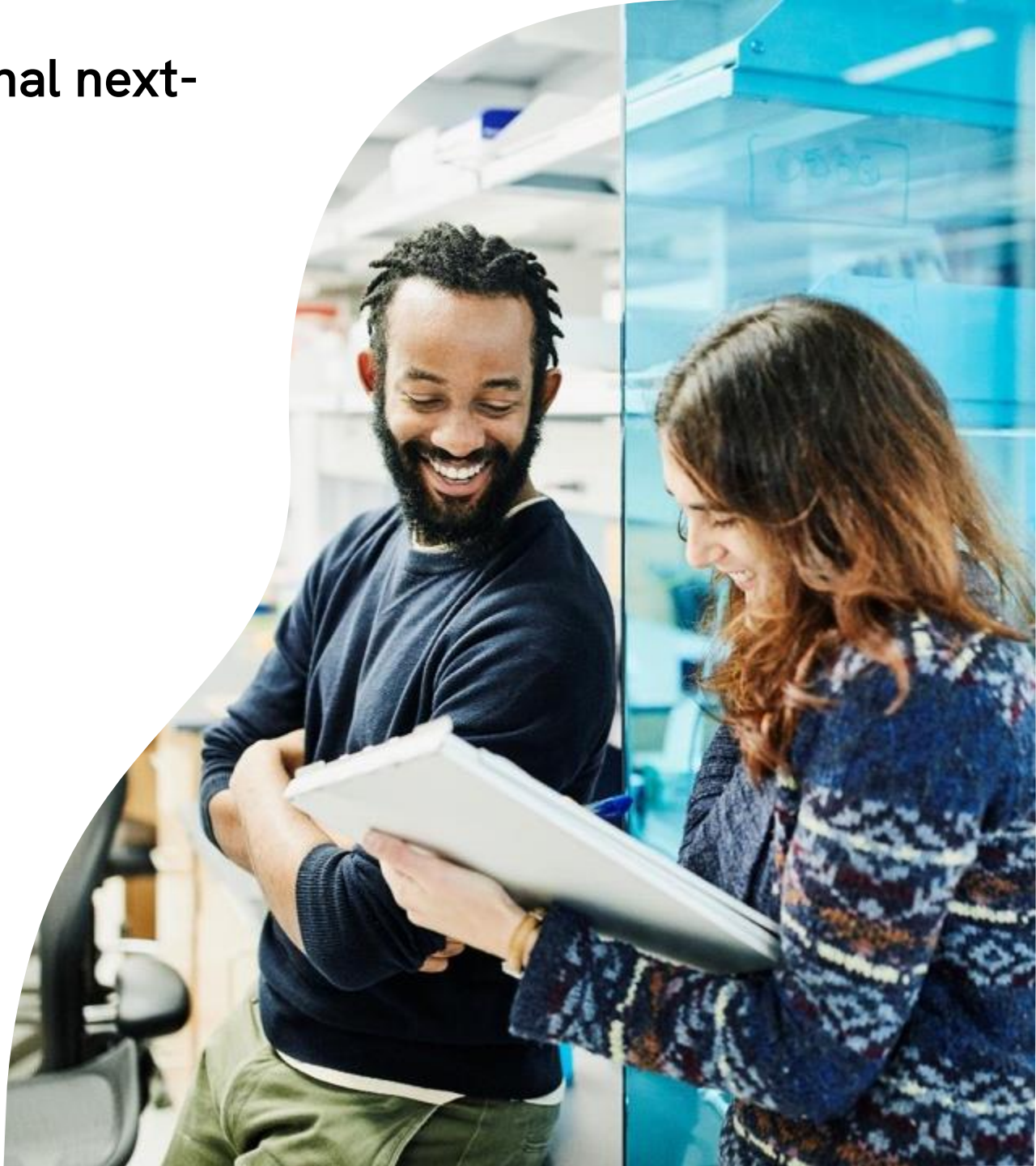
Highly effective editing platform, even for complex edits



Versatile technology modular and capable of generating locus-specific effects for novel therapies



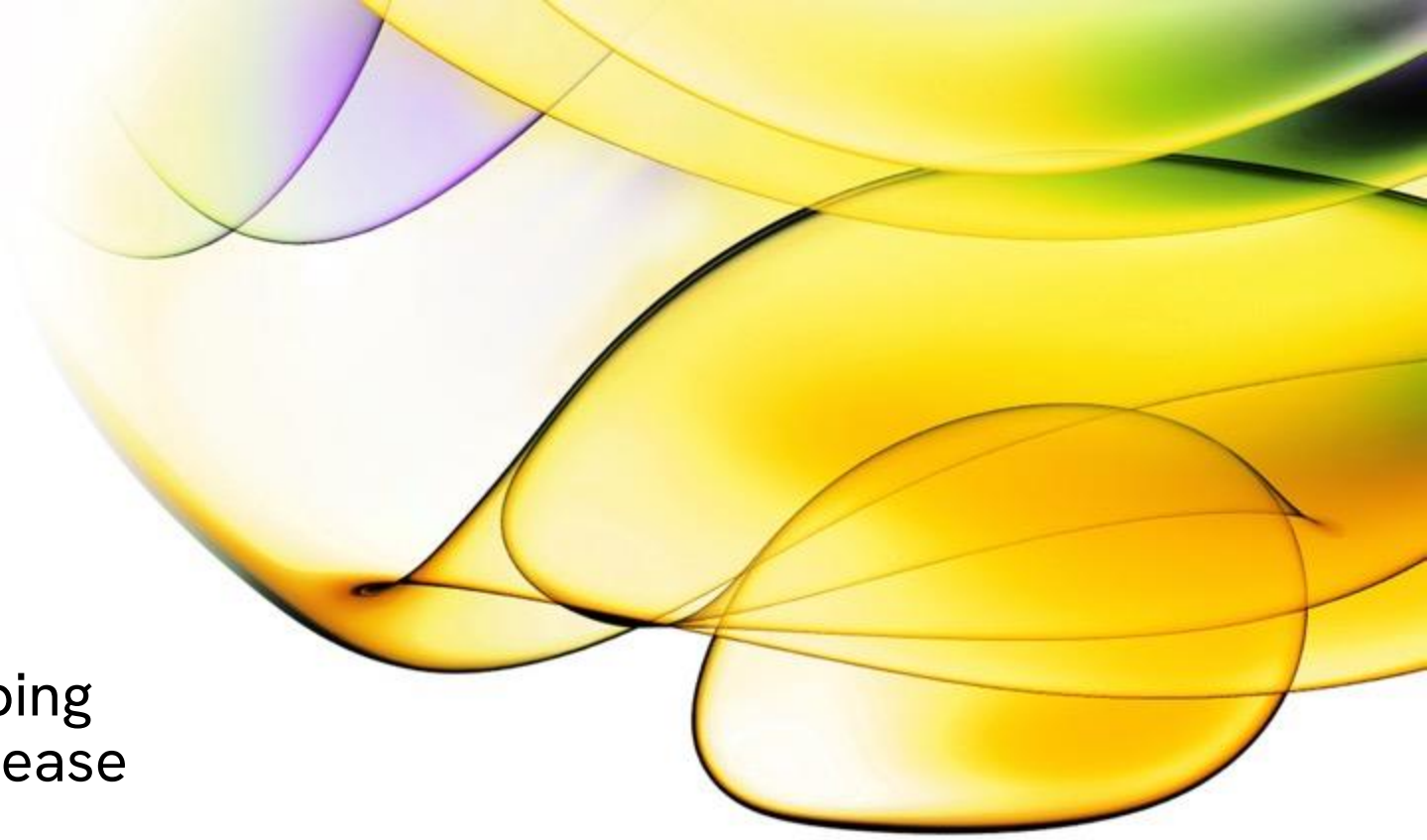
Improved safety compared to standard CRISPR-Cas9 systems

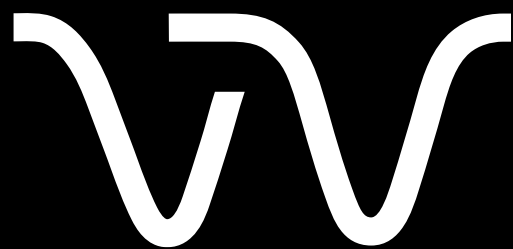


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We are a visionary partner in developing technologies and solutions across disease pathways.

Here for a healthier humankind.





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