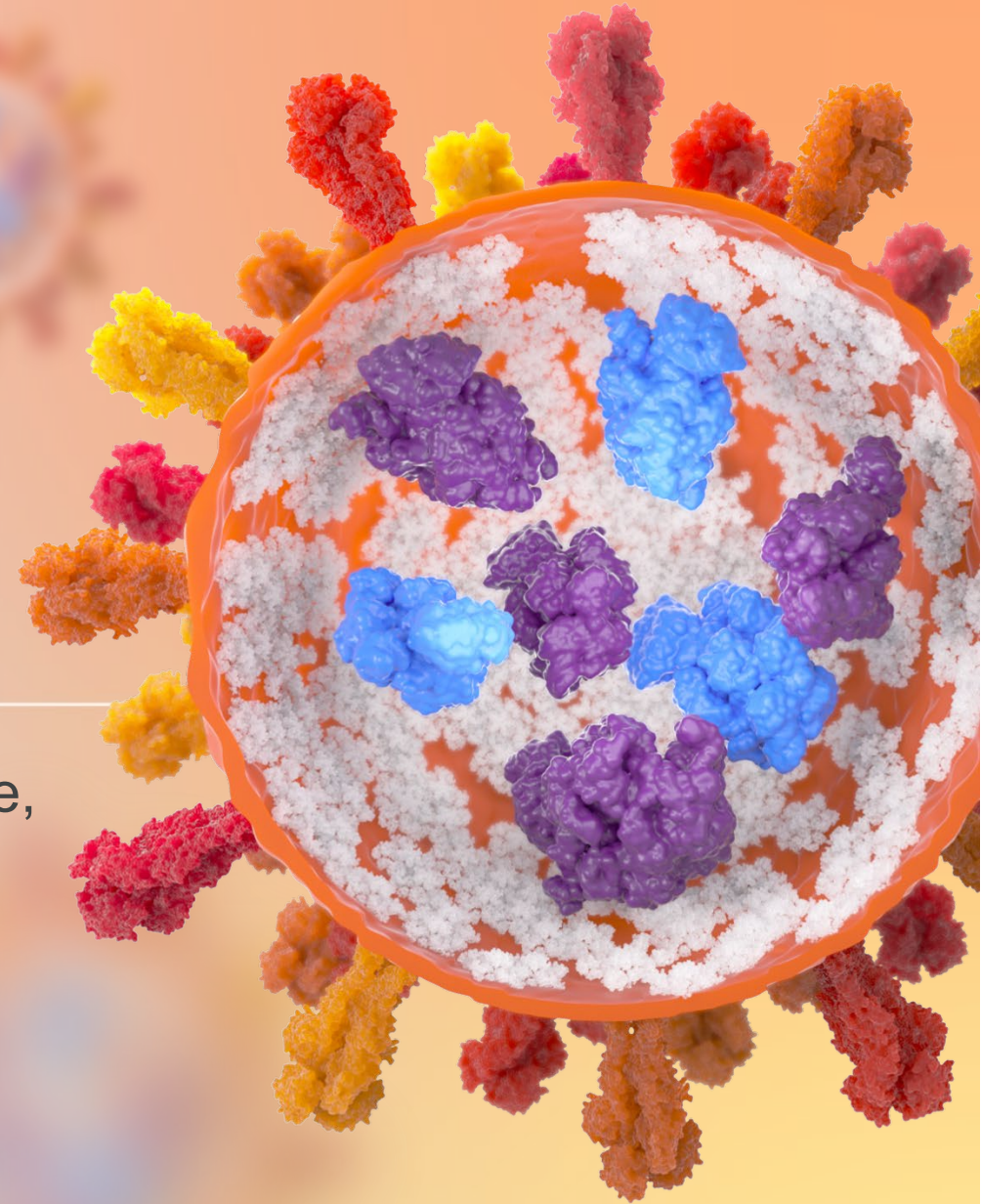




# DLVR-M: A Novel Platform for Protein Delivery

European Society for Cell & Gene Therapy, Rome,  
October 25, 2024

Peter K. Cabeceiras



AGENDA

◆ Introduction to DLVR-M Platform

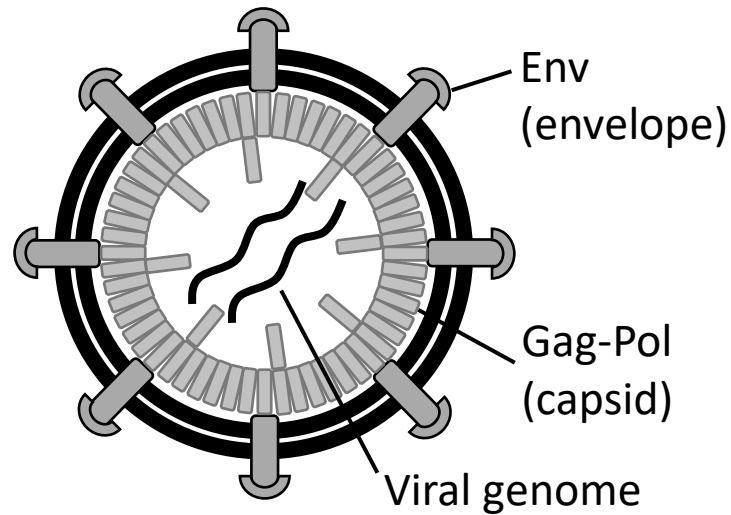
◆ DLVR-M *in vivo*

◆ Development of humanized DLVR-M particles (HuDLVR-M)

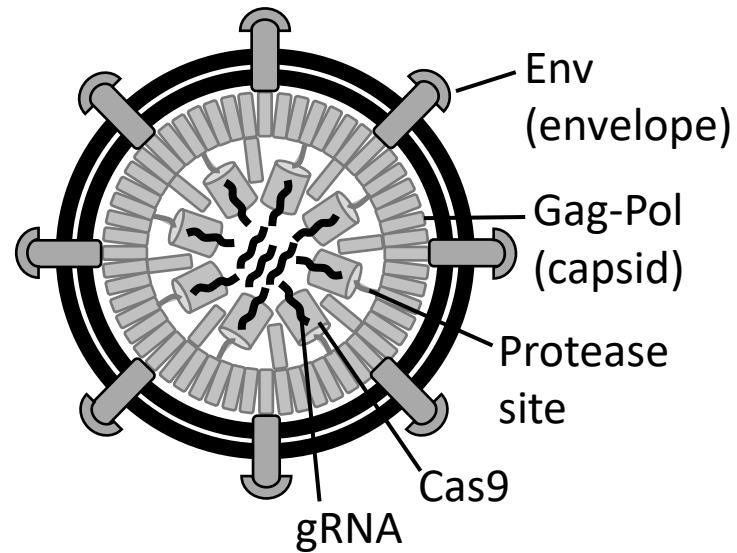
◆ Delivery Applications in HSPCs

# Virus-like Particles for in vivo delivery of gene editing cargos

*Viral Vector*

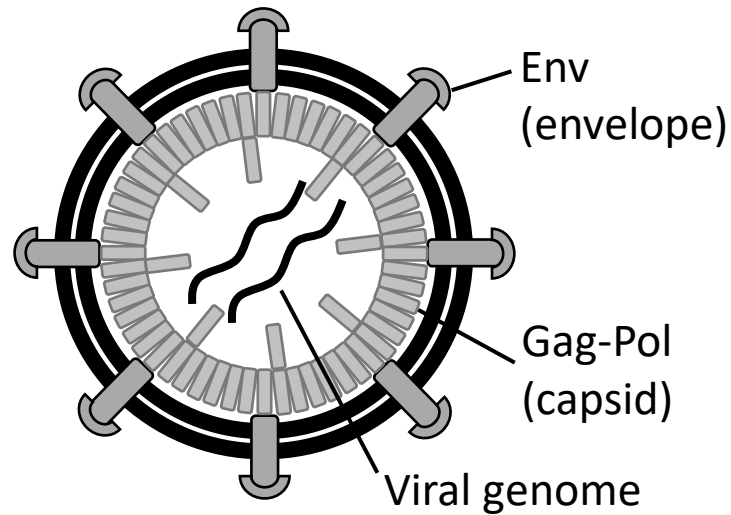


*Virus-Like Particle (VLP)*

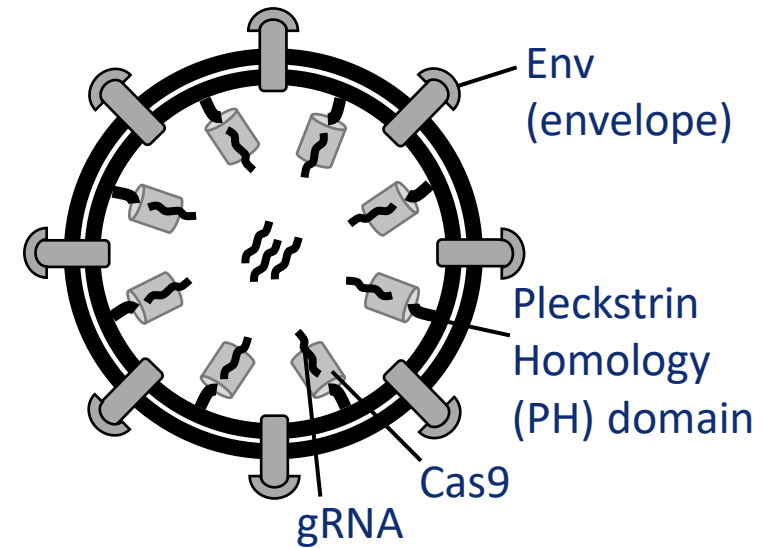
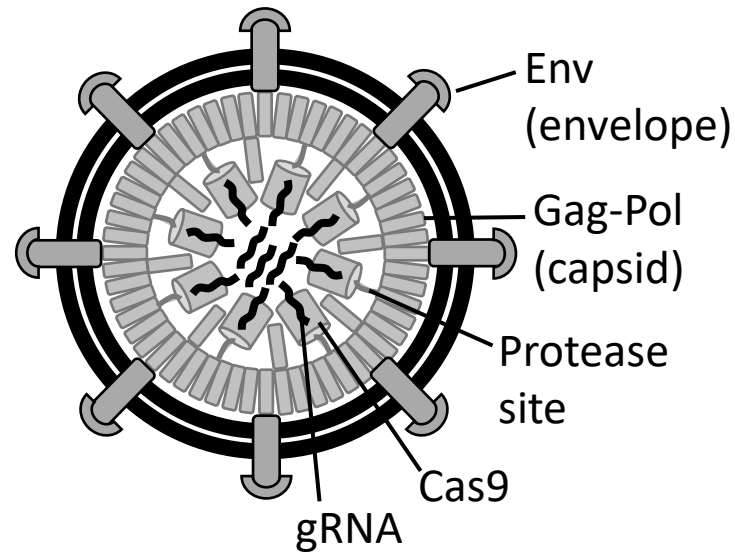


# DLVR-M is a novel type of VLP with a minimal configuration

*Viral Vector*

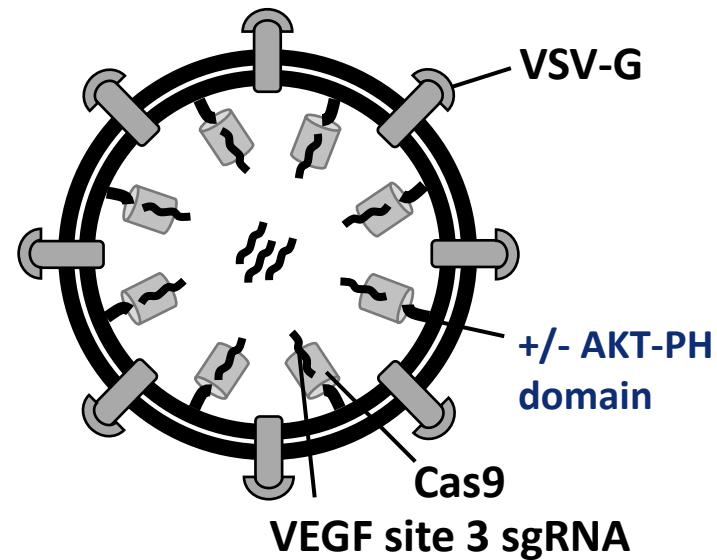


*Virus-Like Particle (VLP)*

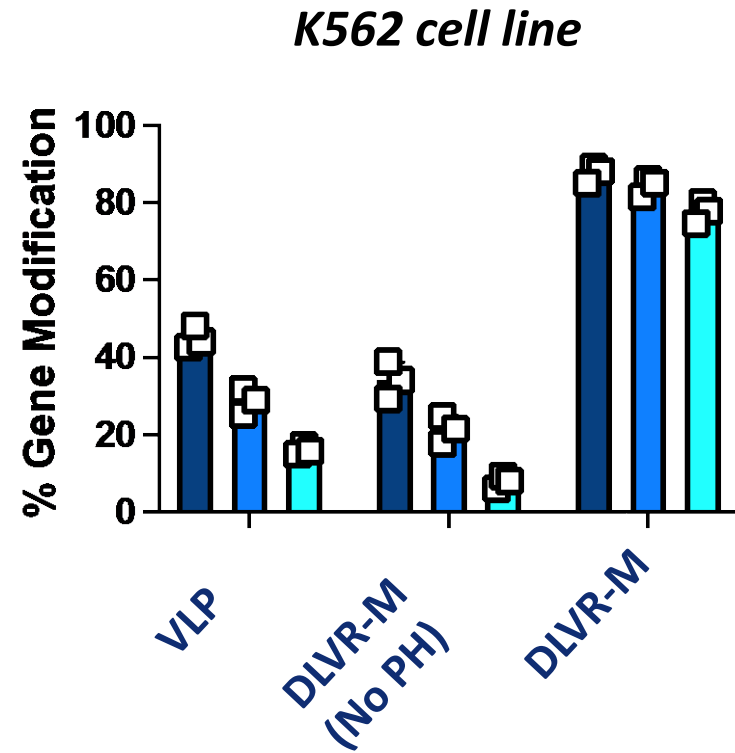
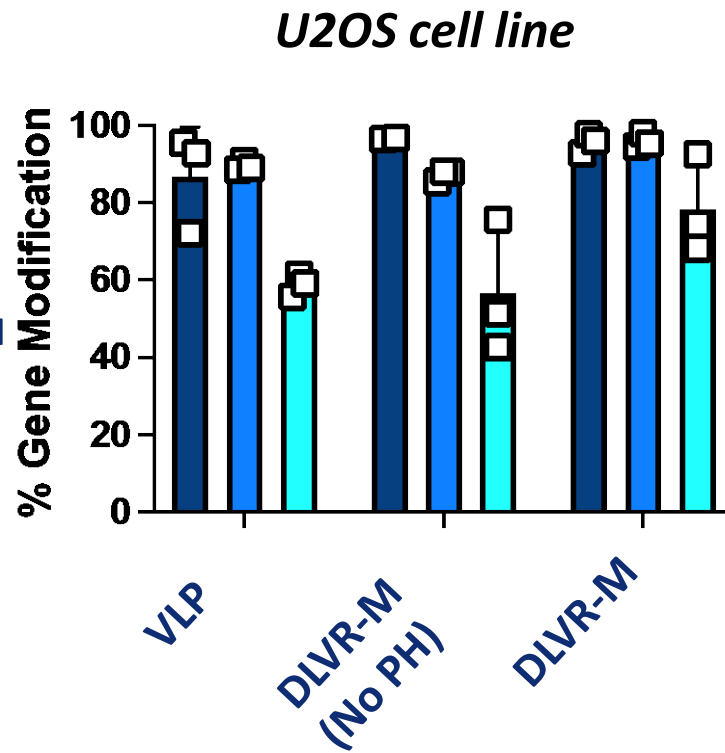
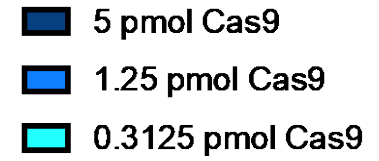


**DLVR-M**

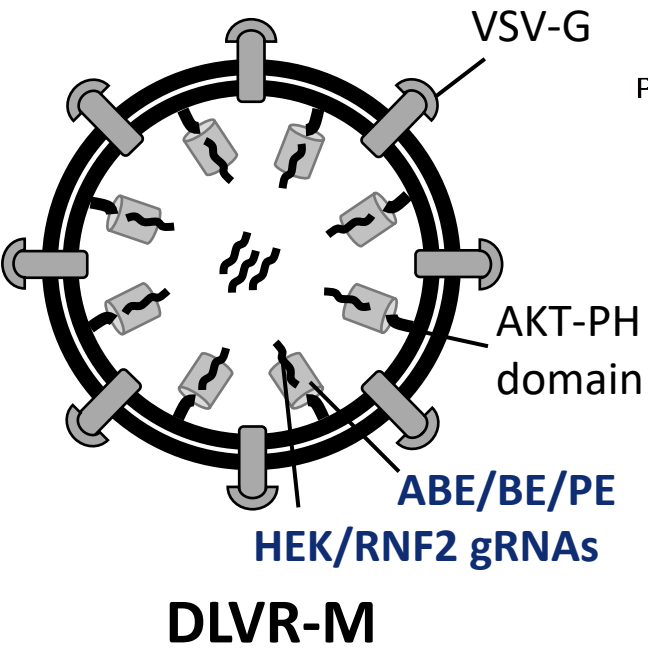
# DLVR-M show similar/superior editing efficiency compared to Conventional VLPs



**DLVR-M**

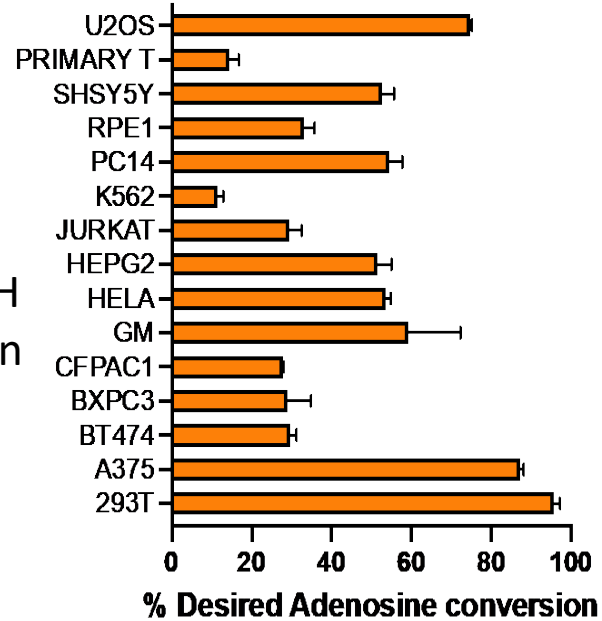


# DLVR-M can accommodate and deliver a variety of cargos



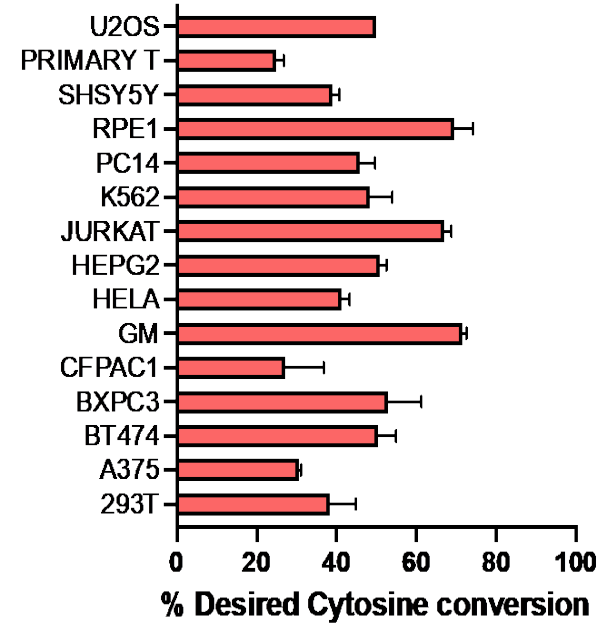
## ABE

PH-ABEMAX  
HEK gRNA



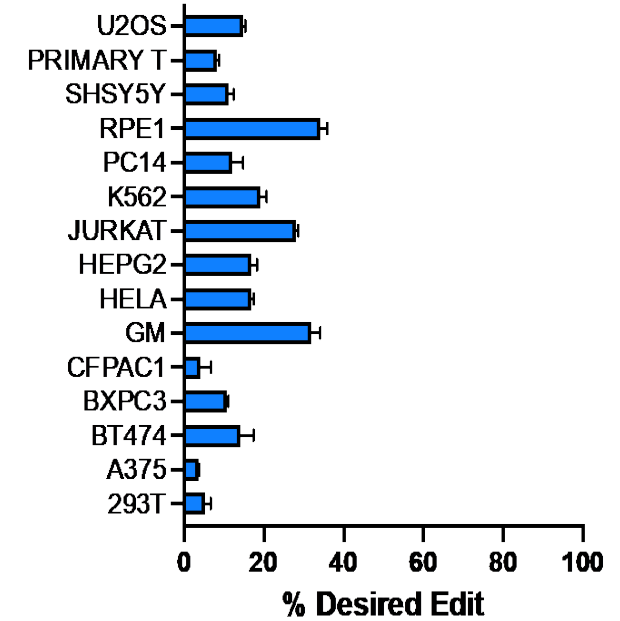
## CBE

PH-BE4MAX  
RNF2 gRNA



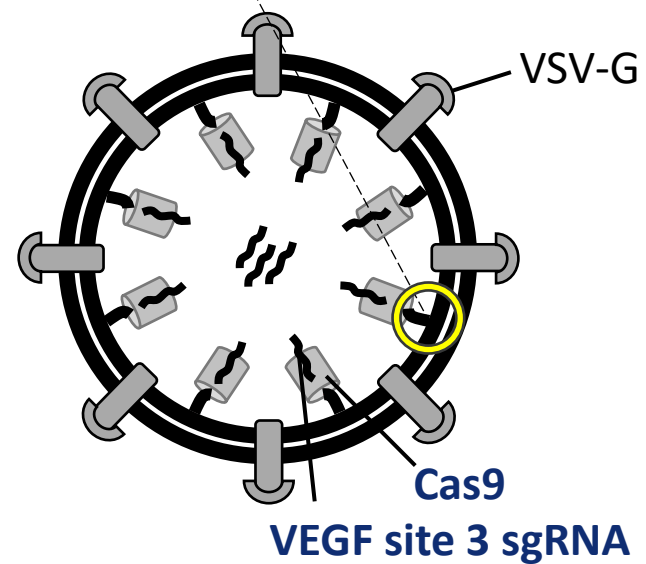
## PE

PH-PEdRH  
HEK gRNA

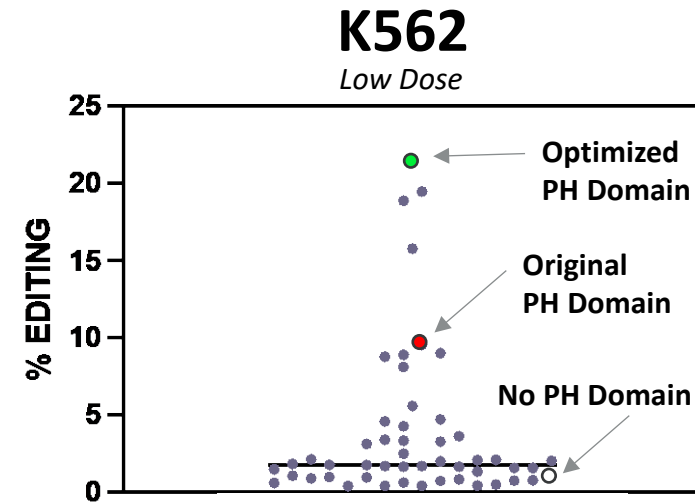
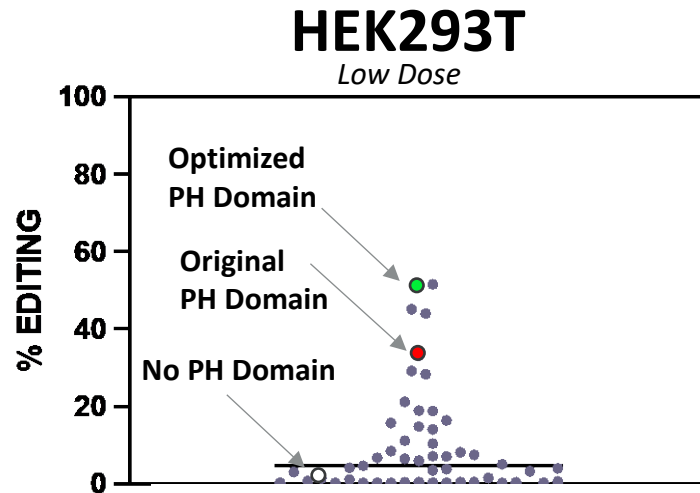


# DLVR-M PH domain optimization

- DLVR-M No PH Domain
- DLVR-M Original PH Domain (AKT PH)
- DLVR-M Optimized PH Domain
- Other PH Domains

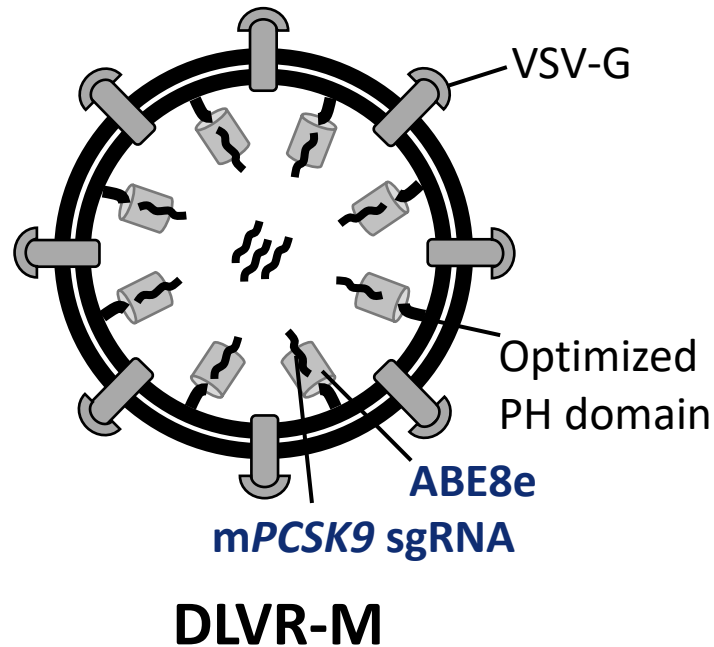


**DLVR-M**

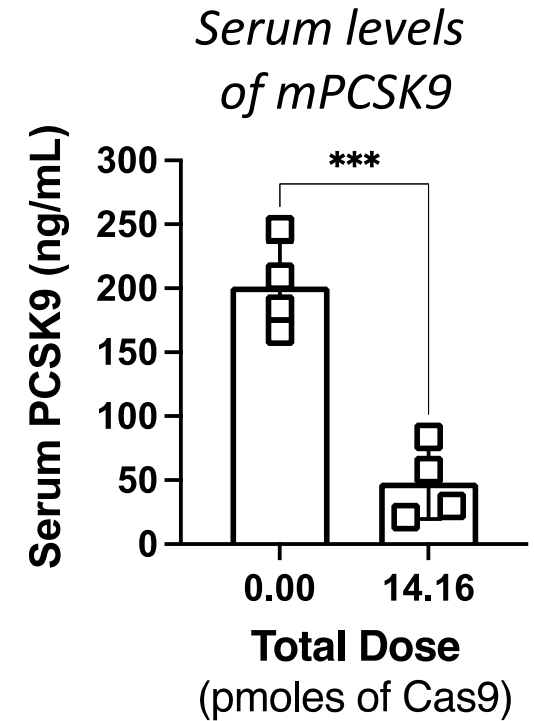
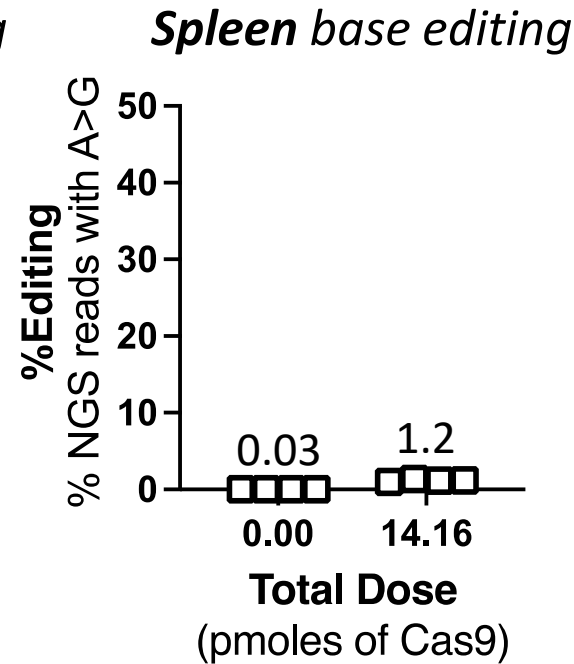
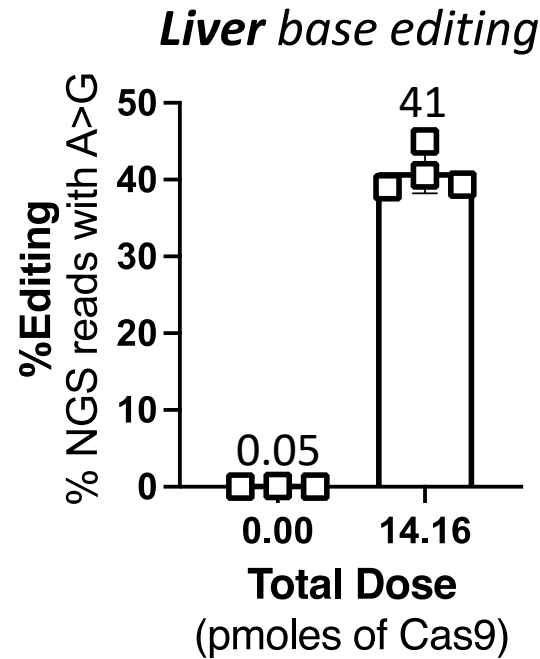


# 1st generation DLVR-M particles show high efficiency *in vivo*

Systemic delivery  
(tail vein)

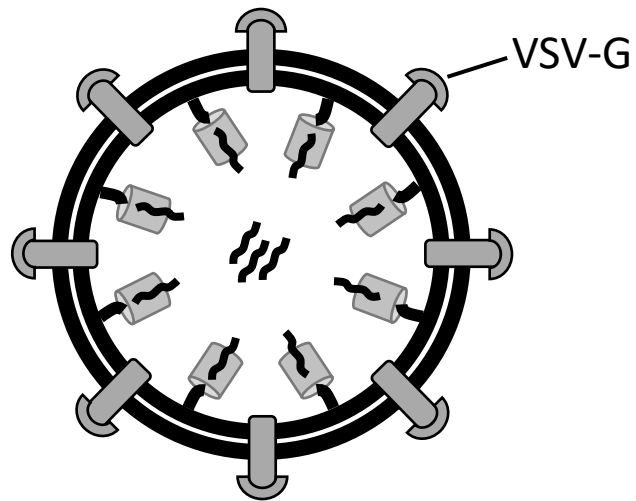


Analysis conducted 7 days after delivery

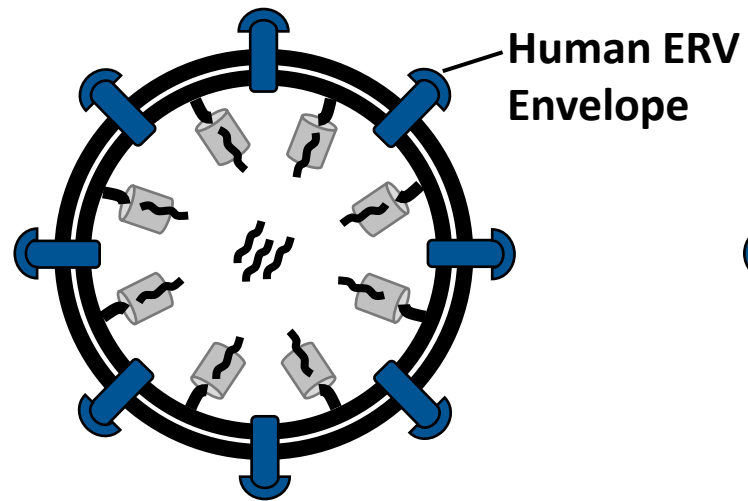




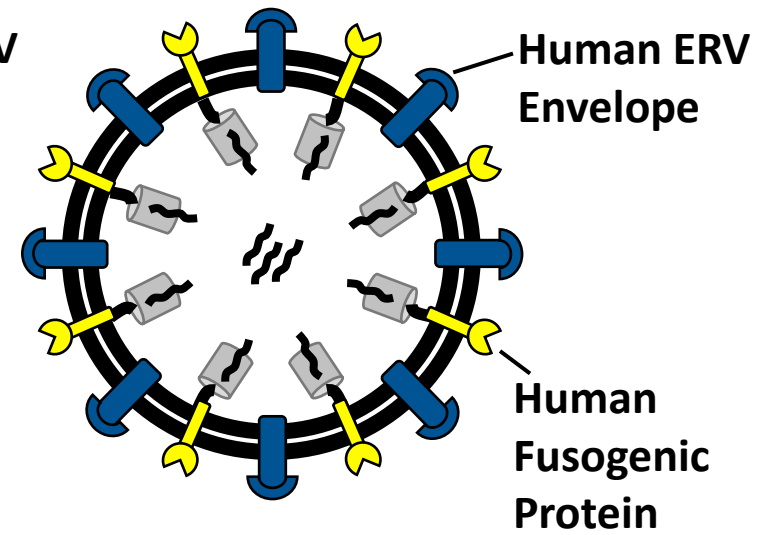
# Development of Humanized DLVR-M Particles (HuDLVR-M)



DLVR-M

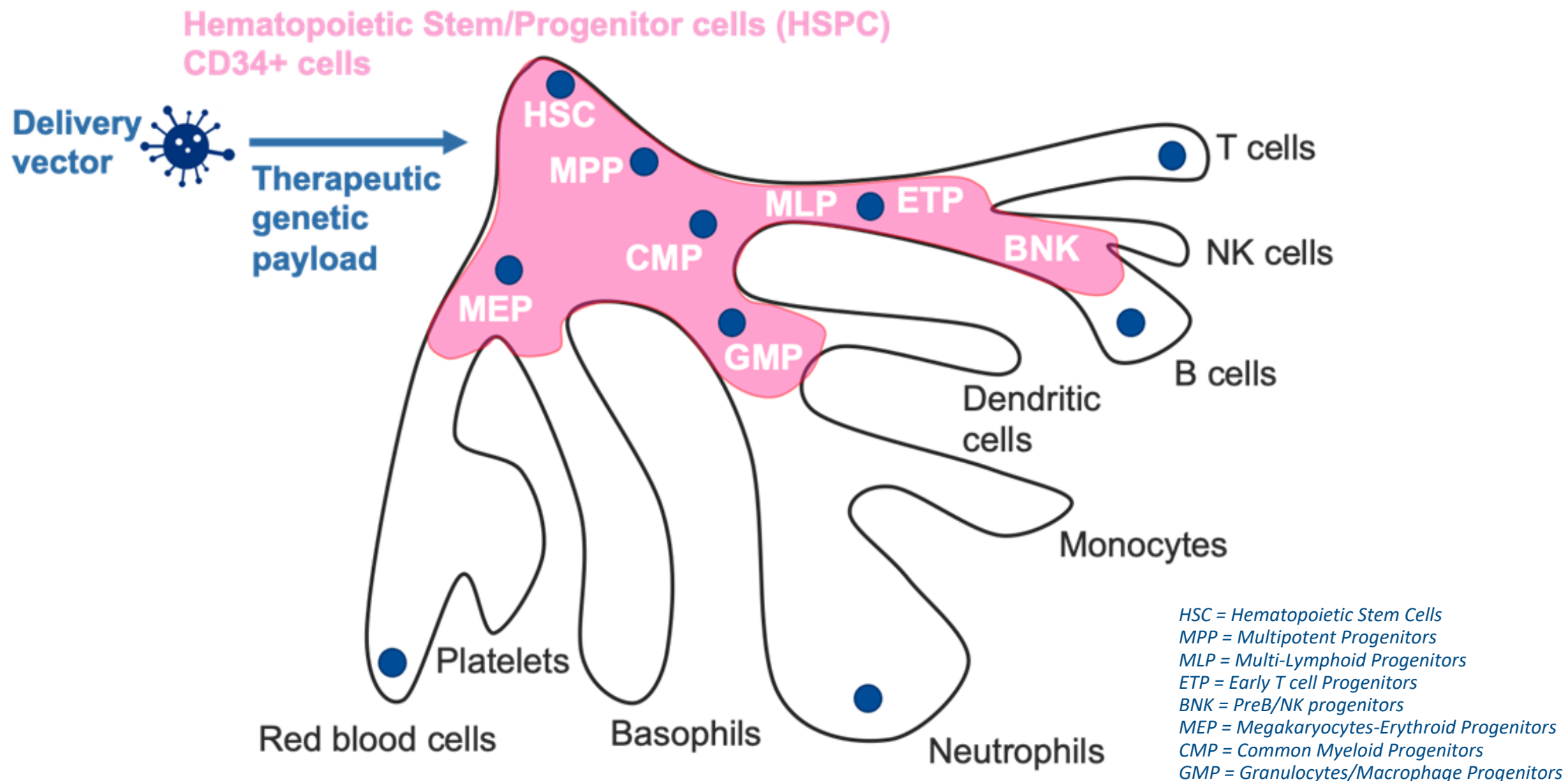


HuDLVR-M\_v1.0

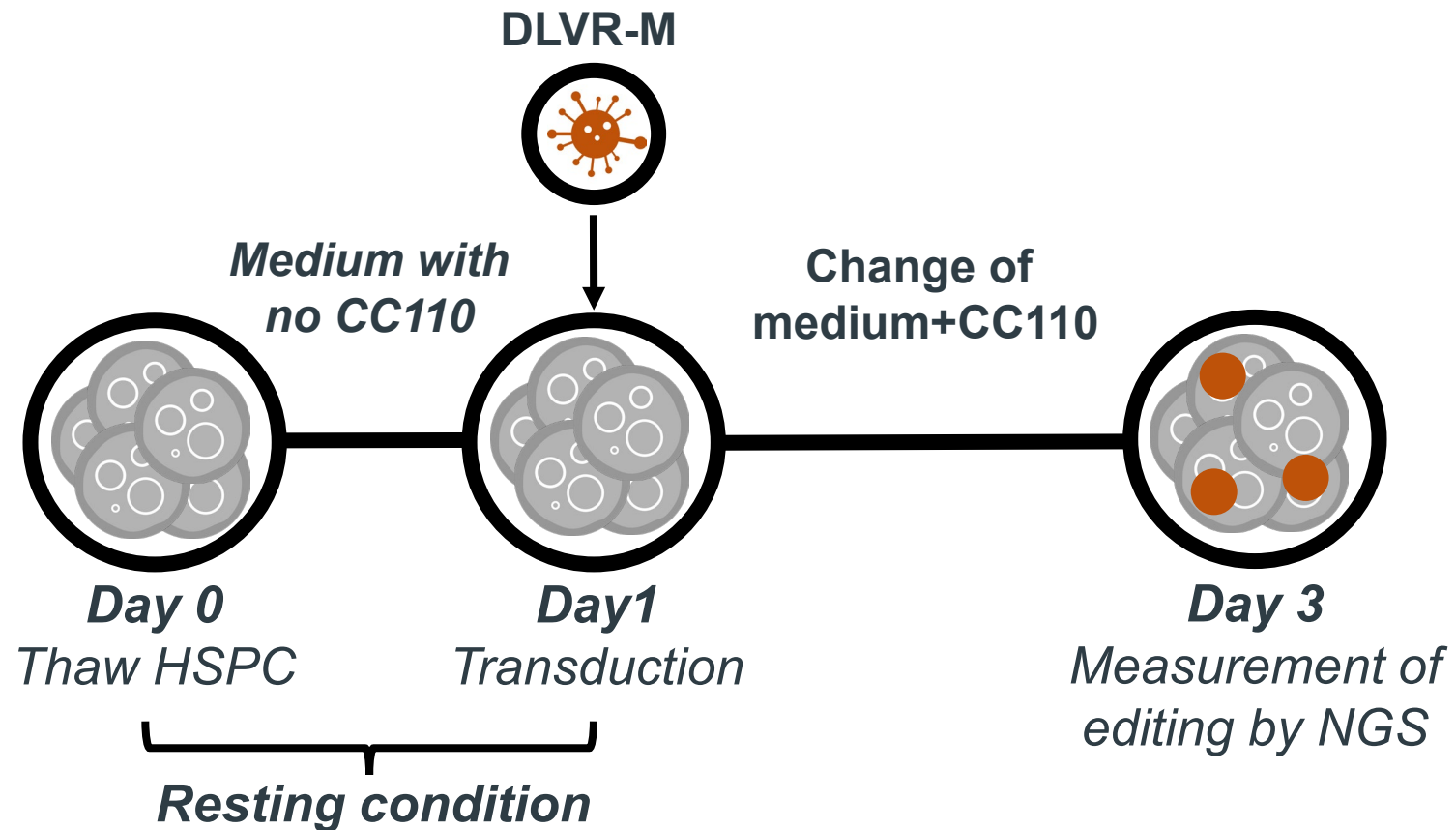


HuDLVR-M\_v2.0

# Testing huDLVR-M for delivering therapeutic cargos for HSPC GT

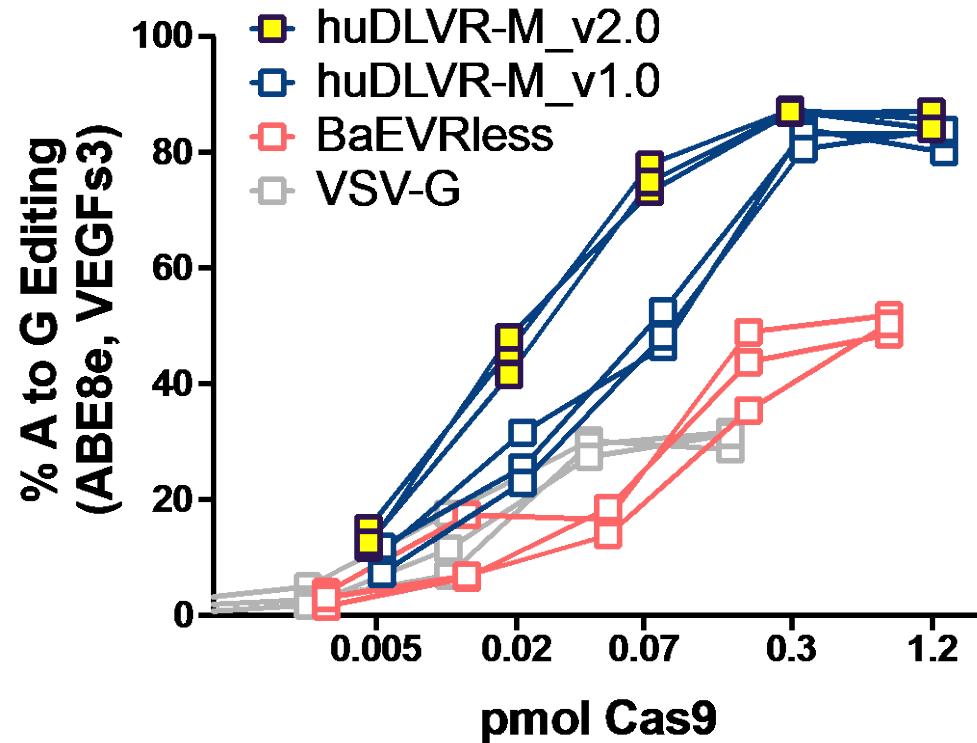


# Testing huDLVR-M on human HSPC in vitro in resting conditions

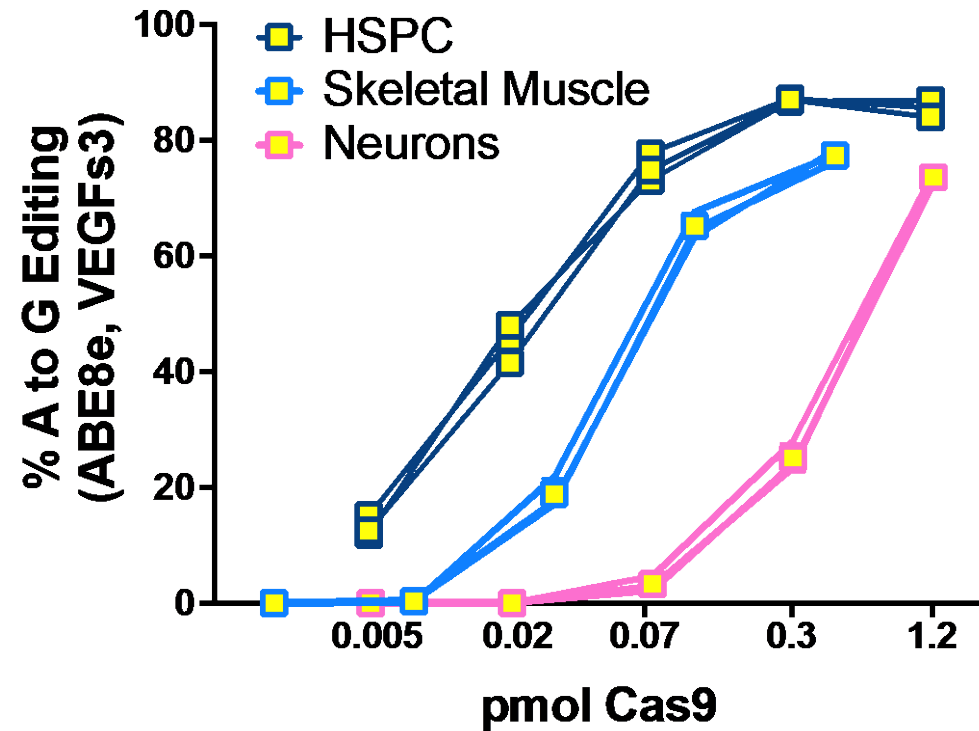


# HuDLVR-M can transduce human HSPC with high efficiency

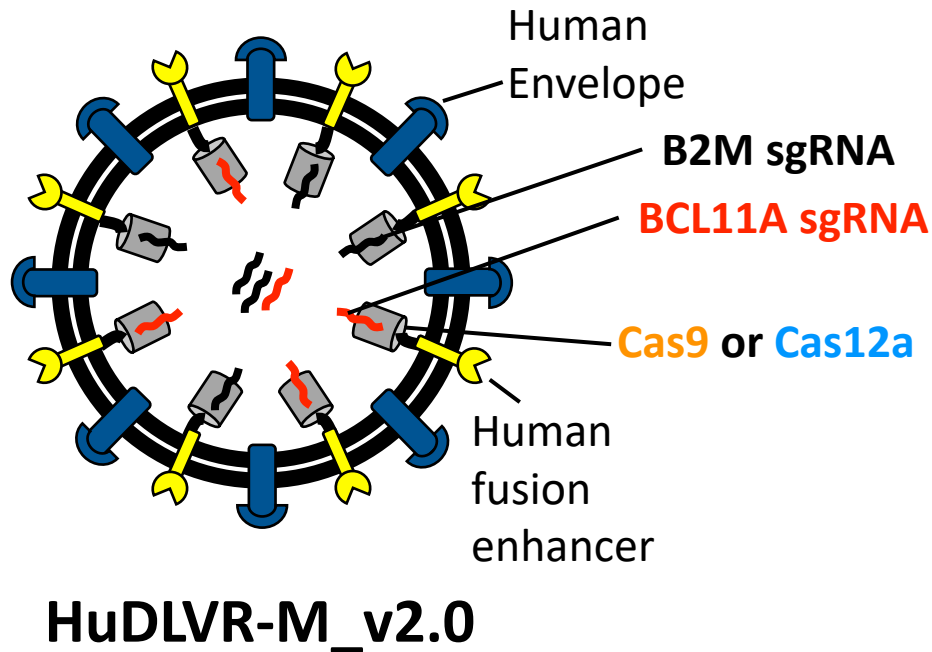
## HuDLVR-M Outperforms BaEVR-Less in resting human HSPCs



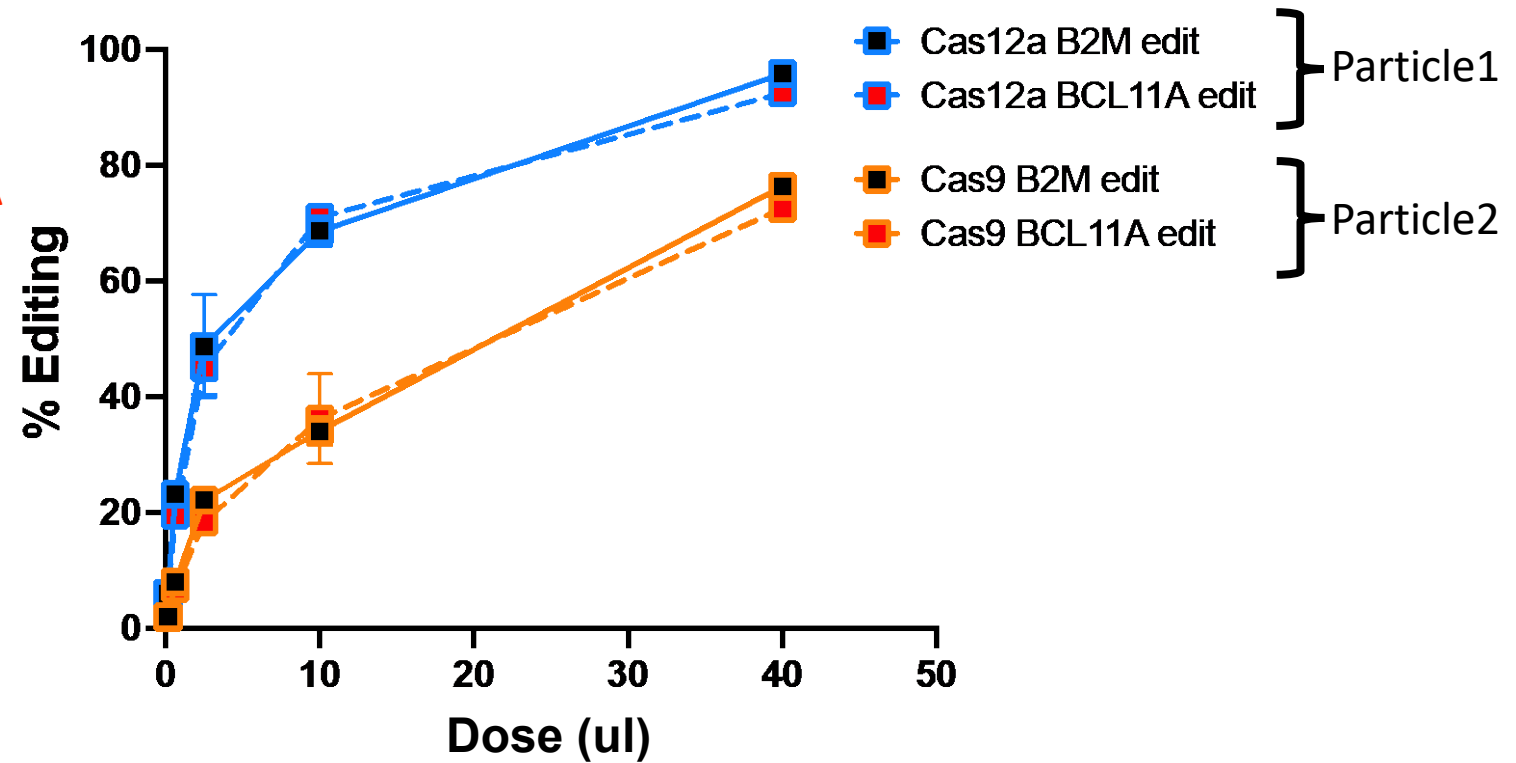
## HuDLVR-M v2.0 displays selective high potency in resting human HSPC in vitro



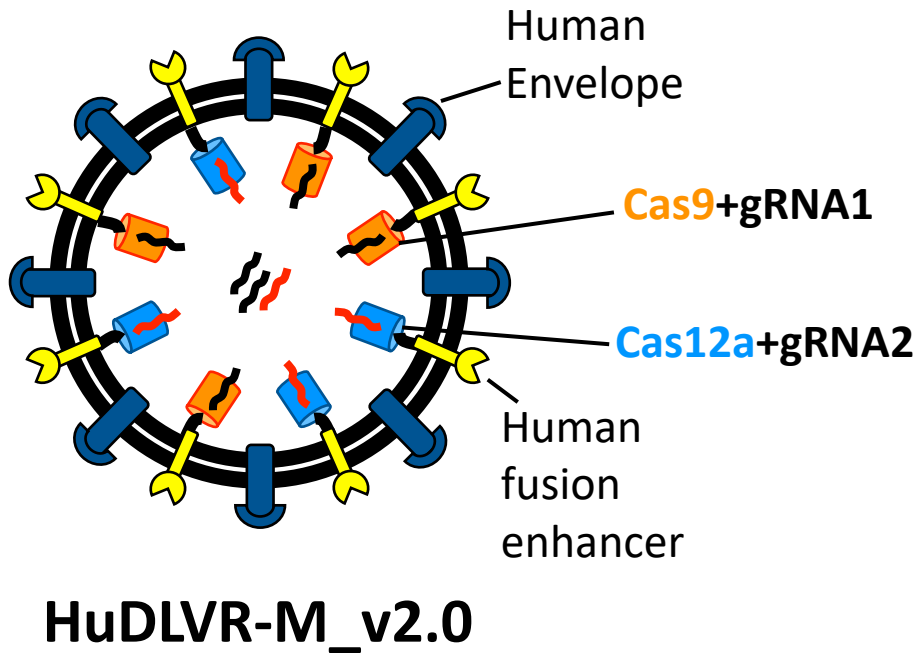
# Achieving multiplex editing with a single editor and multiple gRNAs



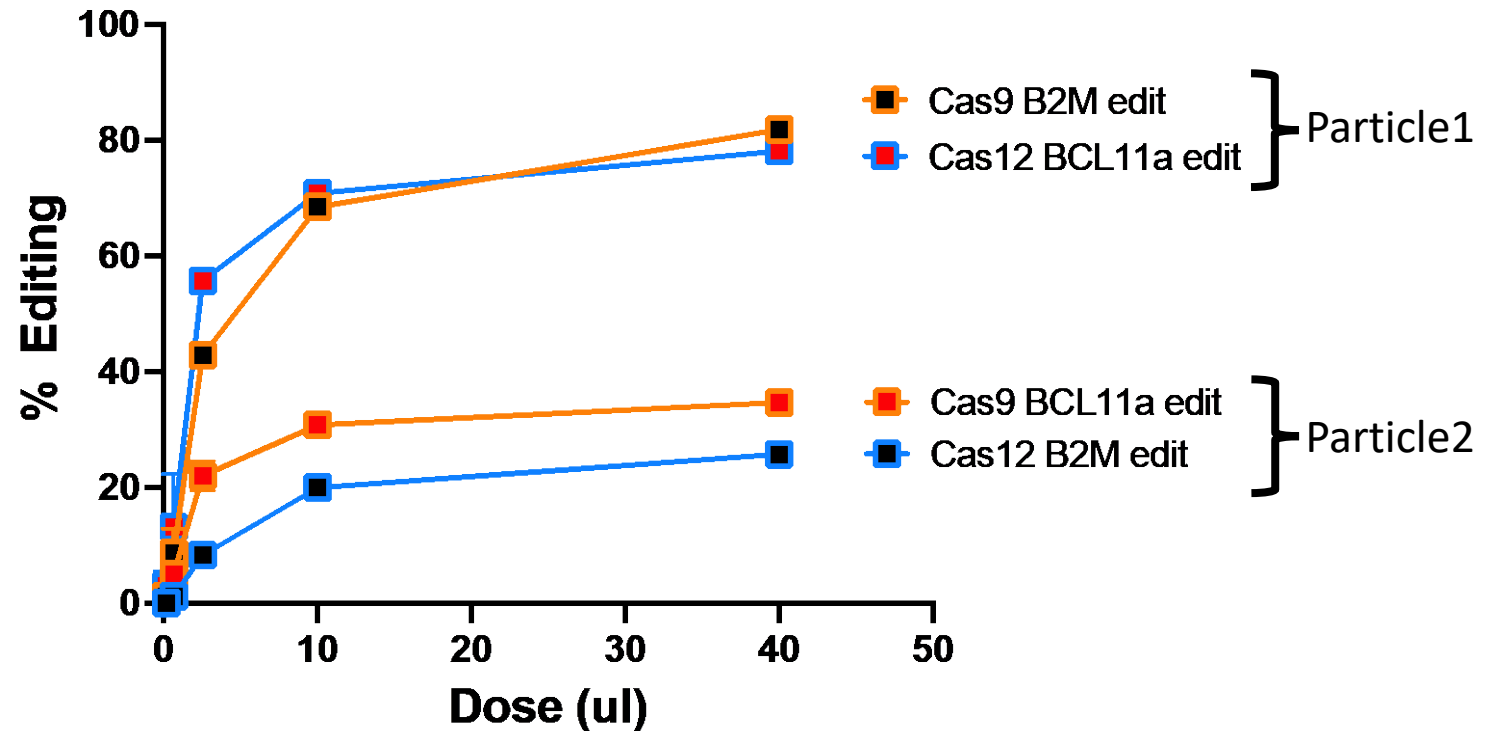
Multiplex editing in resting human HSPC in vitro



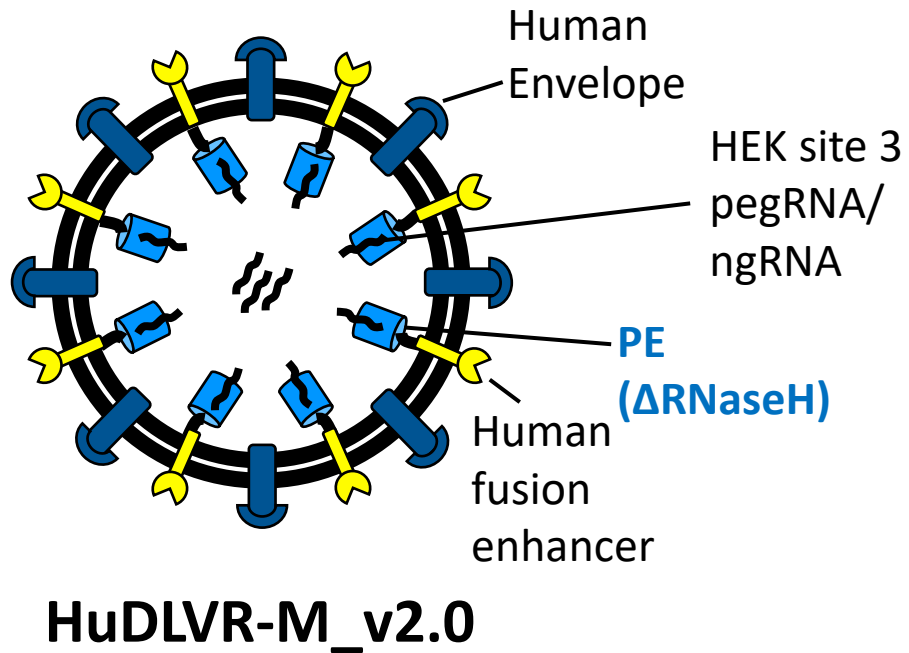
# Combining editing cargos in huDLVR-M to achieve multiplex editing



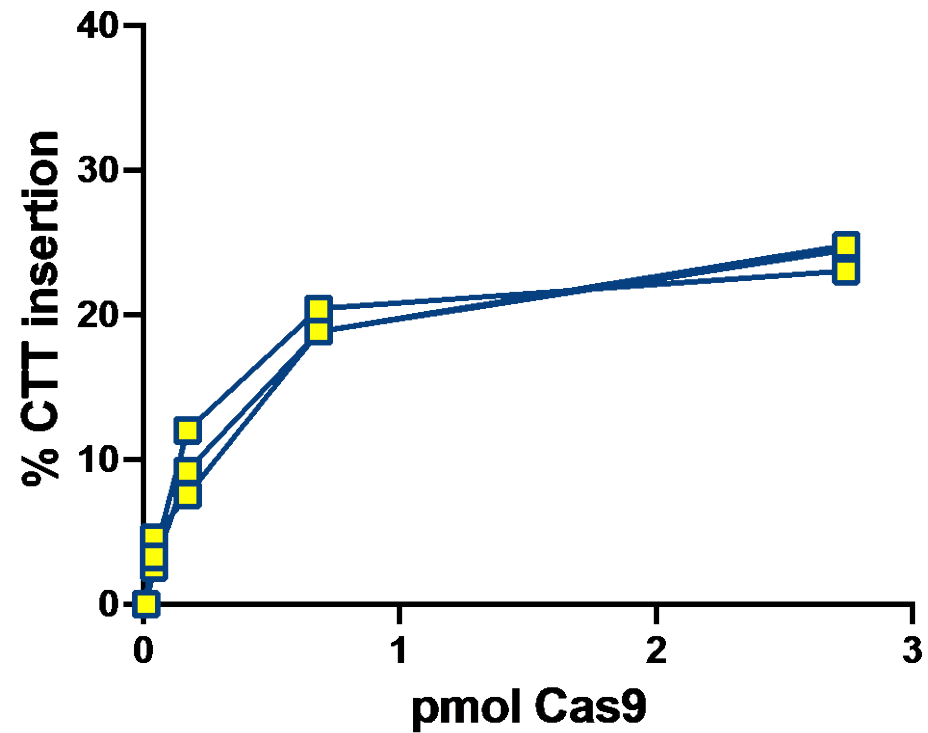
## Multiplex editing in resting human HSPC in vitro



# Achieving prime editing in resting HSPC with huDLVR-M



## Prime editing in resting human HSPC in vitro



# Key Conclusions

## DLVR-M Platform Validation Data Summary



### High Editing Efficiency

- ✓ Efficient editing *in vivo* with low dose of ABE8e
- ✓ >80-90% *in vitro* editing (Cas9, Cas12 & BE) in unstimulated HSPCs (without transduction enhancers or electroporation)



### Large & Diverse Cargo

- ✓ Delivery of CRISPR nucleases and base/prime editors
- ✓ >80-90% multiplex editing in HSPCs with multiple editors/guides in single particle



### Programmable Specificity

- ✓ Validated interchangeability of particle components
- ✓ Human-derived envelopes deliver to HSPCs, neurons and skeletal muscle



### Particle Humanization

- ✓ Developed huDLVR-M which lacks virus derived components (e.g., protease, Gag/Pol, etc.)



# Acknowledgments

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