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Gene Editing Service Offerings

OMNI™ Technology Platform

Superior Performance through AI-Driven Design

AnGes

About EmendoBio

EmendoBio has developed a nuclease discovery, engineering and AI-based computational biology platform that has produced a portfolio of high-performance OMNI™ nucleases

- Founded in U.S. in 2016 by scientists from the Weizmann Institute, Israel
- Founding investors: OrbiMed and Takeda Ventures
- AnGes became a majority shareholder in December 2020

Management

Naoya Satoh, PhD President & CEO	**Assaf Sarid** CFO	**Ella Segal** EVP, R&D, Operations

Board of Directors

Ei Yamada, PhD AnGes	**Naoya Satoh, PhD** AnGes

Key Collaborations

anocca

STANFORD UNIVERSITY

Fred Hutch Cancer Center

Maastricht University

Memorial Sloan Kettering Cancer Center

NIH National Institutes of Health

Seattle Children's HOSPITAL · RESEARCH · FOUNDATION

COLUMBIA UNIVERSITY

UNIVERSITY OF WASHINGTON 1861

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The Advantages of OMNI™ Technology

Highly Specific Nucleases

- Increased safety:
  - Low off targets
  - Reduced translocations
- Allele-specific editing

Highly Active Nucleases

- Efficient editing comparable to standard nucleases

PAM Diversity

- Increased genome coverage
- Diverse editing solutions
- Avoids IP restrictions of gRNAs

Multiple Sizes

- Compatible with common delivery modalities
  - Electroporation
  - LNP
  - LVLP
  - AAV

Novelty

- Avoids IP restrictions of nucleases

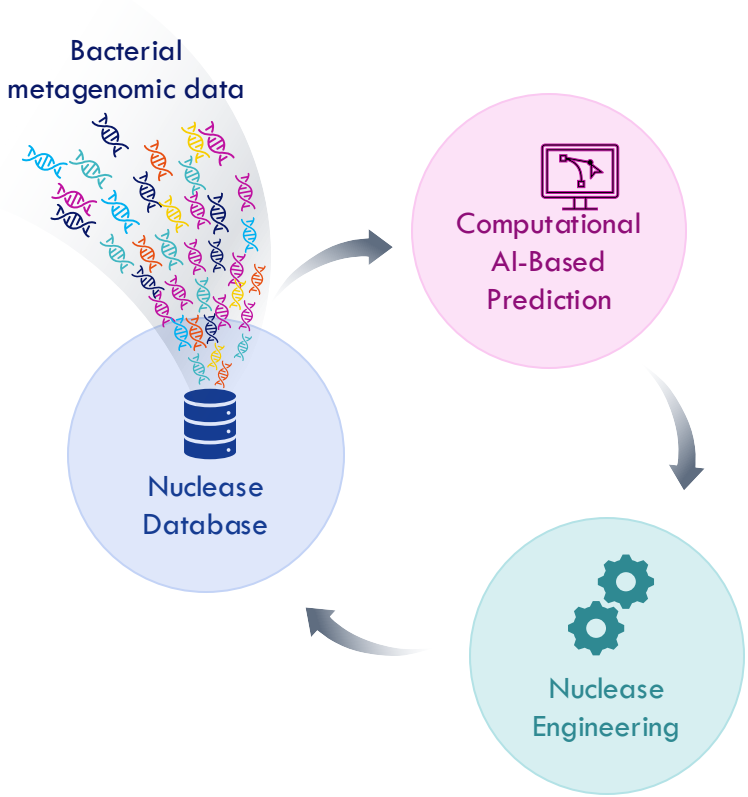
Next Generation CRISPR Tools

- HDR
- Short nucleases
- OMNI™-editors
- OMNI™-off

OMNI™ Platform Offers a Variety of Gene-Editing Solutions

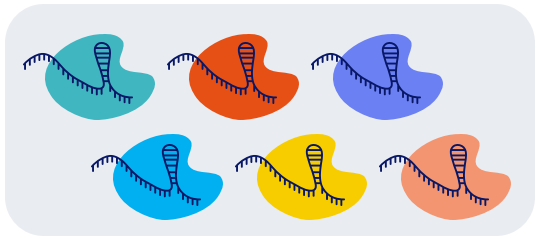
Synergistic discovery, engineering and AI-based computational technologies combine to produce a portfolio of high-performance OMNI™ nucleases

EmendoBio's Platform



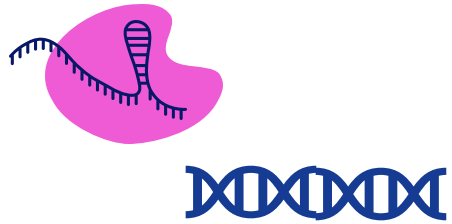
Panel of Engineered OMNI™ Nucleases

- Novel
- Highly active
- Highly specific



Optimal Therapeutic Compositions per Target

- High safety profile
- Expanded range of applications
- Freedom to operate



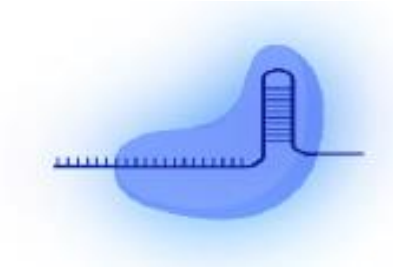
Nuclease Engineering Platform

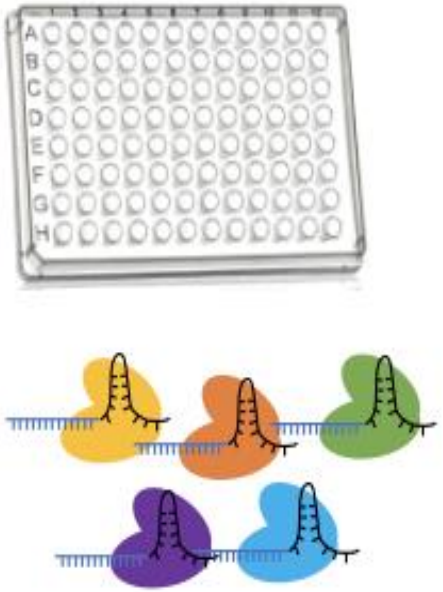
OMNI™ nuclease (from panel)

AI based engineering for variant library generation

Libraries of nuclease variants

Screening in mammalian cell line





Highly Active and Specific
Optimized OMNI™ Variants

OMNI™ Panel Genome Accessibility

Nuclease Portfolio

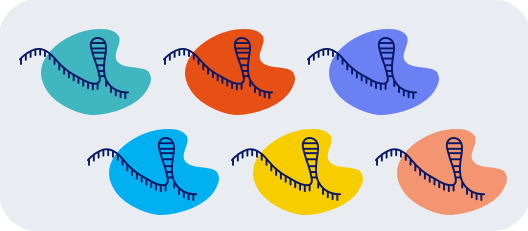
10,000 discovered nucleases

300 validated in vitro

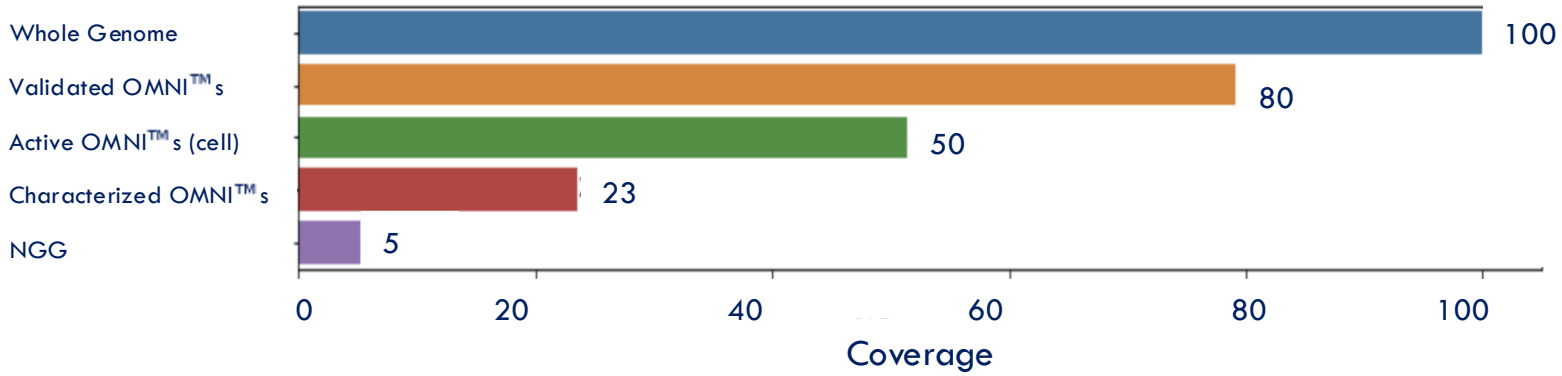
80 shown active in cells

12 characterized

3 engineered



OMNI™ Genomic PAM Coverage

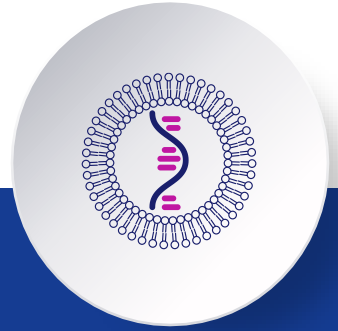


The diversity of PAM sites of the OMNI™ nucleases overcomes PAM constraints and significantly widens genome accessibility, making **any gene targetable**

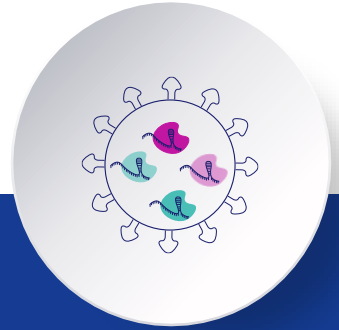
OMNI™-Generated Nucleases

Compatible with all commonly used delivery platforms

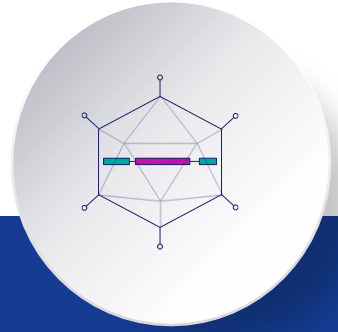
Ribonucleoprotein (RNPs)



Lipid Nano Particles (LNPs)



Lenti Virus Like Particles (LVLPs)



Adeno Associated Virus (AAV)

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Extensive Intellectual Property Portfolio

- Strong IP position – ~200 patents/applications worldwide
- Coverage extending to 2040s
- Gene editing techniques
- Compositions for gene editing
  - Knock-out and knock-in compositions
  - Allele-specific compositions
  - Numerous target genes & indications
- Novel CRISPR nucleases
  - OMNI™ panel nucleases
  - High-fidelity variants
  - Variants with increased activity, specificity

A Portfolio of "Off-the-Shelf" Editing Solutions

SAFE HARBOR

#	Target Gene	Computational	Cell Line	Target Cells
1	AAVS1	•	•	
2	ROSA26	•	•	
3	C3	•	•	
4	APLP2	•	•	•

HEMATOPOETIC STEM CELLS

#	Target Gene	Disease	Computational	Cell Line	Target Cells
5	ELANE	Severe Congenital Neutropenia	•	•	•
6	SAMD9L	Myeloid malignancies	•	•	
7	GATA2	Myeloid malignancies	•	•	
8	SAMD9	Myeloid malignancies	•	•	
9	RPS19	Diamond Blackfan Anemia	•	•	

IMMUNO-ONCOLOGY

#	Target Gene	Computational	Cell Line	Target Cells
10	PDCD1	•	•	•
11	TRAC	•	•	•
12	TRBC1	•	•	•
13	TRBC2	•	•	•
14	B2M	•	•	•
15	CTLA4	•	•	•
16	TET2	•	•	•
17	CD3E	•	•	•
18	LAG3	•	•	•
19	FAS	•	•	•
20	HAVCR2 (TIM3)	•	•	•
21	HLAE	•	•	•
22	CIITA	•	•	•
23	FASLG	•	•	•
24	IL15	•	•	•
25	TIGIT	•	•	•
26	CISH	•	•	•

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A Portfolio of "Off-the-Shelf" Editing Solutions

LIVER

#	Target Gene	Disease	Computational	Cell Line	Target Cells
27	SERPINA1	A1AD	•	•	•
28	ANGPTL3	Dyslipidemia including homozygous familial hypercholesterolemia	•	•	•
29	LDLR	Atherosclerotic cardiovascular disease	•	•	•
30	HBV	Hepatitis	•	•	

CNS

#	Target Gene	Disease	Computational	Cell Line	Target Cells
31	LRRK2	Parkinson's disease	•	•	

OPHTHALMOLOGY

#	Target Gene	Disease	Computational	Cell Line	Target Cells
32	TCF4	Fuchs Endothelial Corneal Dystrophy	•	•	
33	TGFBi	Corneal Dystrophies	•	•	
34	SARM1	Neuronal and macular degeneration	•	•	
35	RPE65	Retinitis Pigmentosa	•	•	
36	RHO	Retinitis Pigmentosa	•	•	
37	FLG	Ichthyosis vulgaris	•	•	
38	BEST1	Autosomal dominant vitreoretinochoroidopathy	•	•	
39	PRPH2	Retinitis Pigmentosa	•	•	

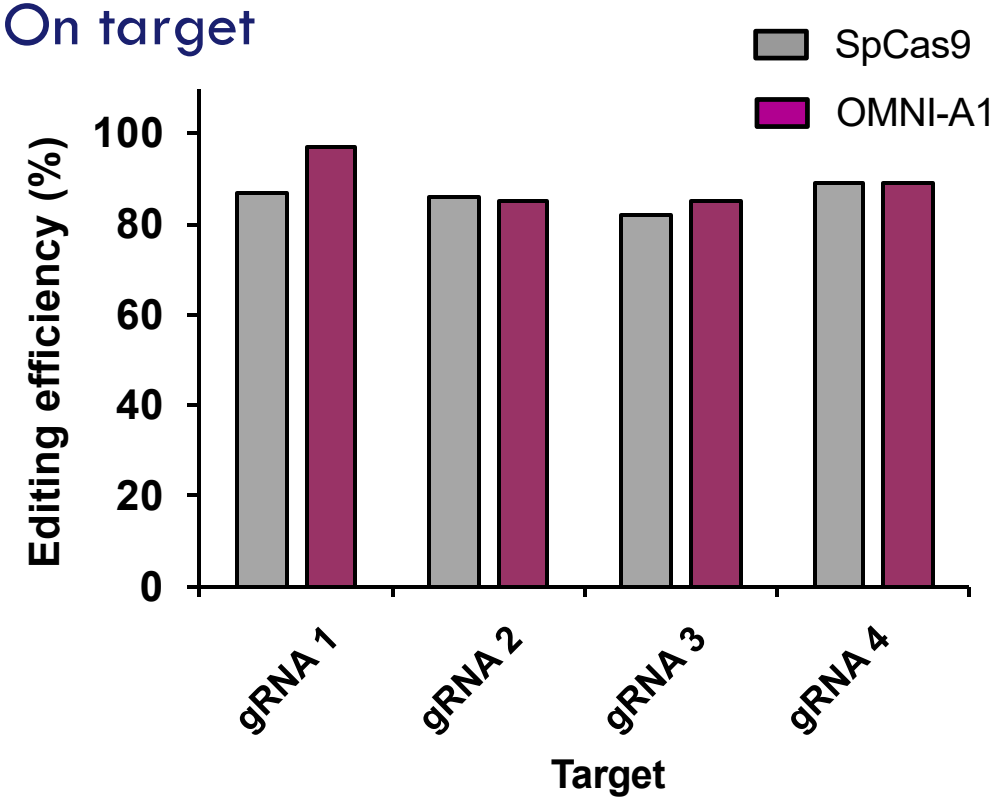
CASE STUDIES

SELECTED OMNI™ DATA

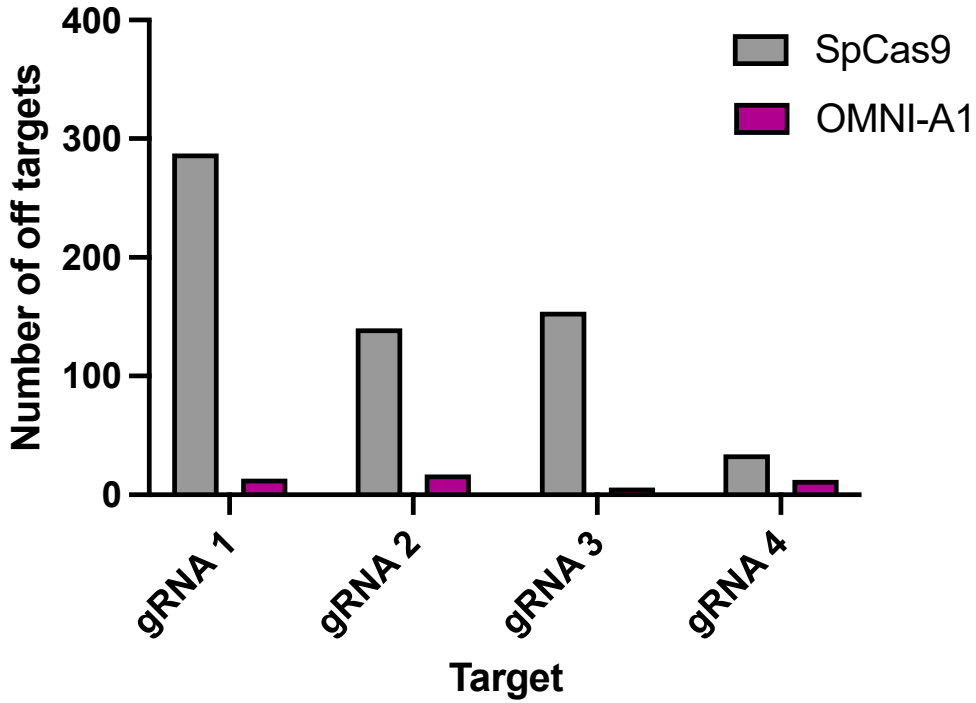
Activity and Specificity of OMNI-A1™

OMNI-A1™ vs SpCas9

On target



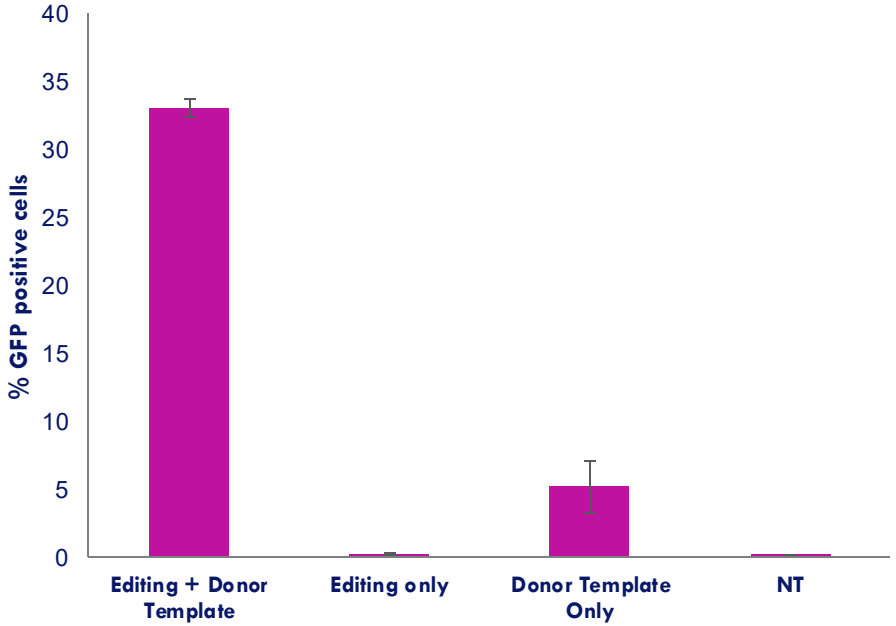
Off target



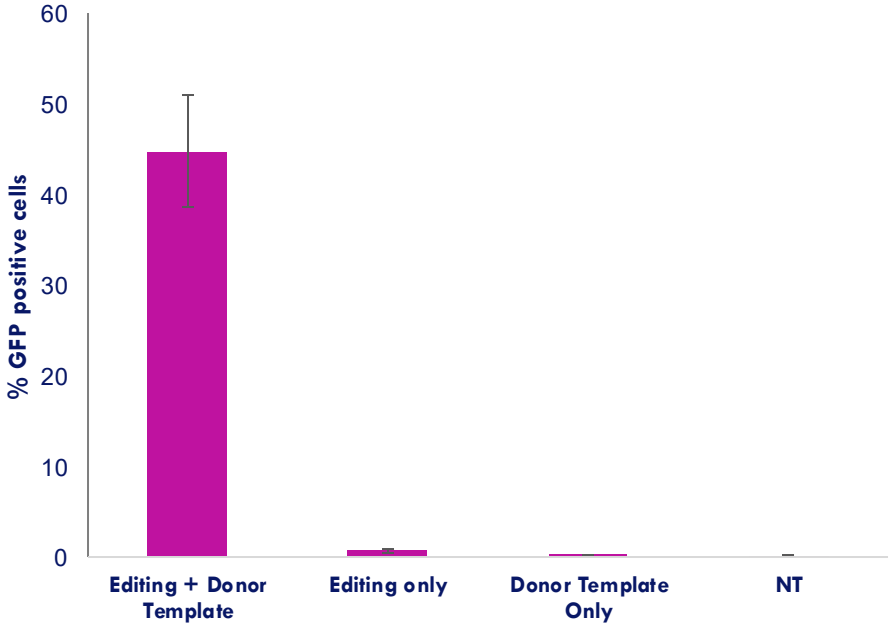
OMNI-A1™ has higher specificity compared to SpCas9

HDR Efficiency of OMNI-A1 ™

- OMNI-A1 ™ RNP complex delivered by electroporation
- GFP expression cassette template delivered by AAV
- Efficiency measured as percetage of GFP-expressing cells



Safe harbor site - locus 1
HepG2 cells

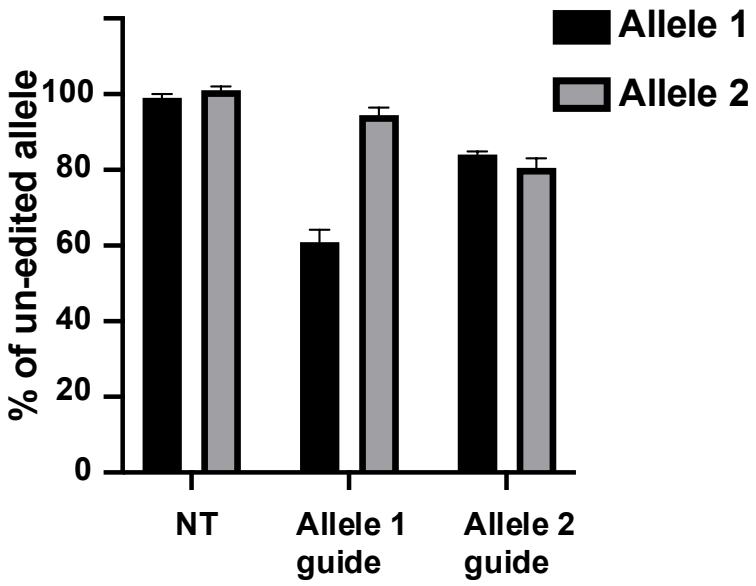


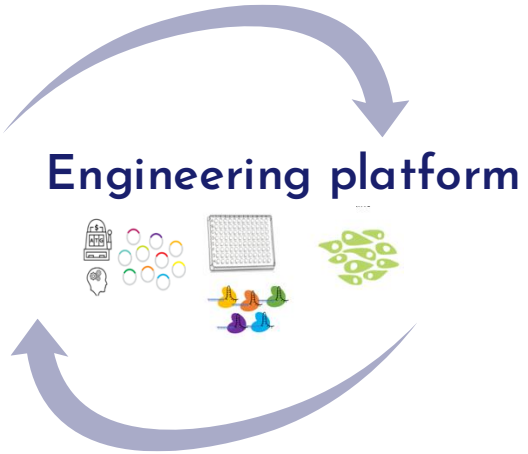
Safe harbor site - locus 2
Primary HSCs

Increased Specificity

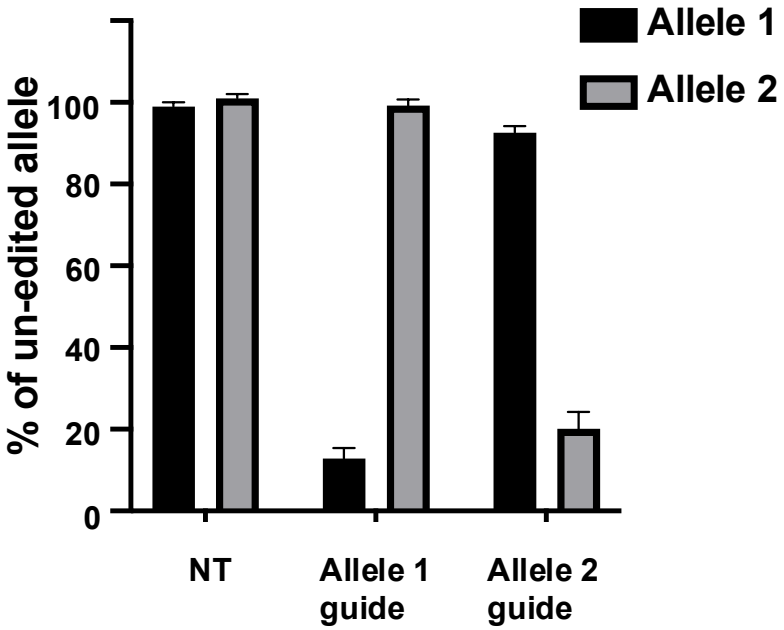
OMNI-A1 ™ – powerful engineering platform

OMNI-A1™





OMNI-A1 V10™



Non-Compromised Nuclease Safety

Engineering platform achieves systematic elimination of off-targets

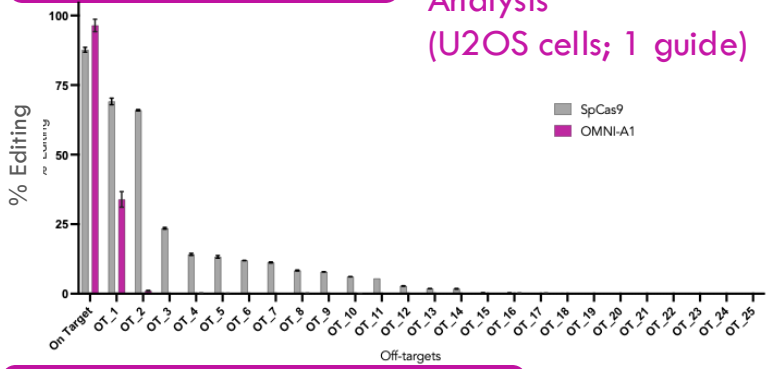
Optimized to be highly active and specific

Engineering further eliminates off-targets

Limits potential for off-target mediated translocations (OMTs)

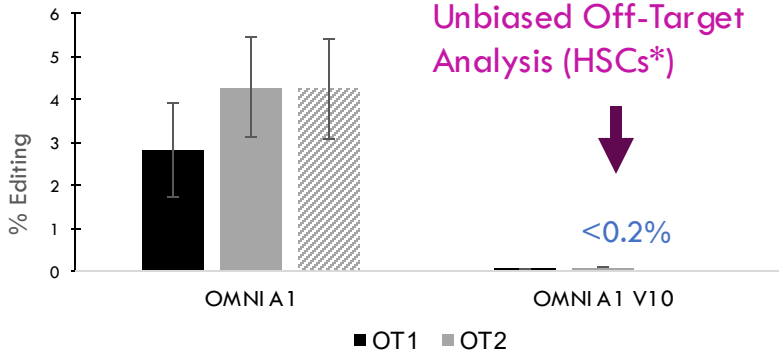
OMNI-A1™ vs SpCas9

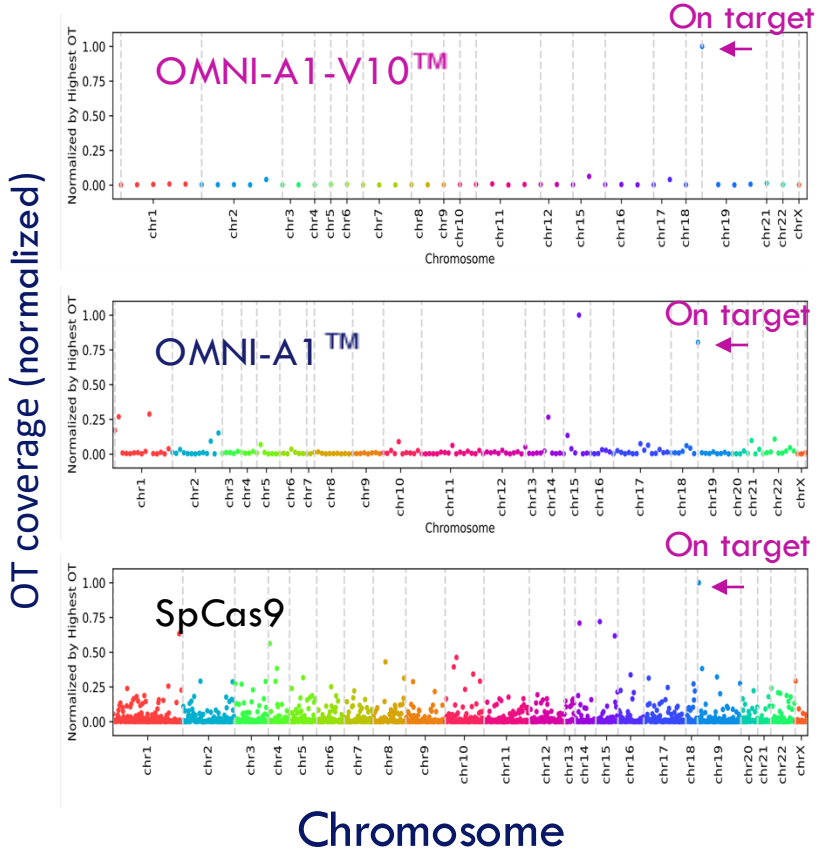
Unbiased Off-Target Analysis (U2OS cells; 1 guide)

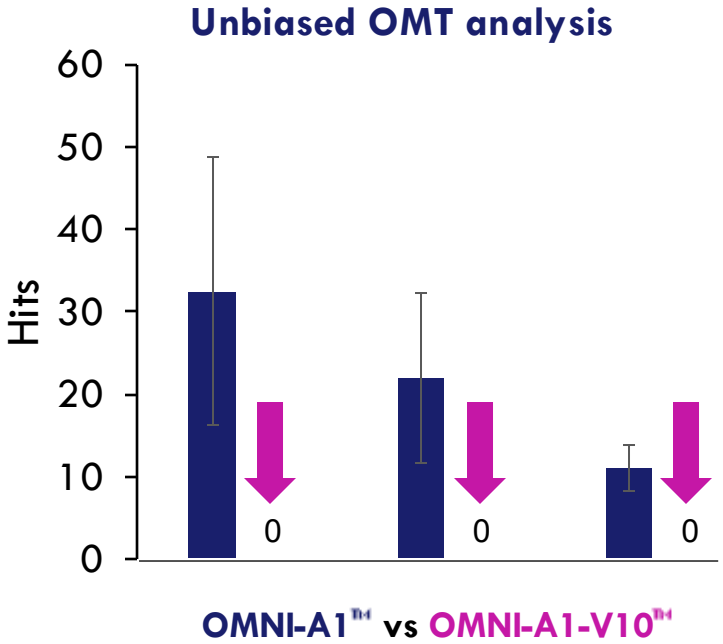


OMNI-A1™ vs OMNI-A1-V10™

Unbiased Off-Target Analysis (HSCs*)





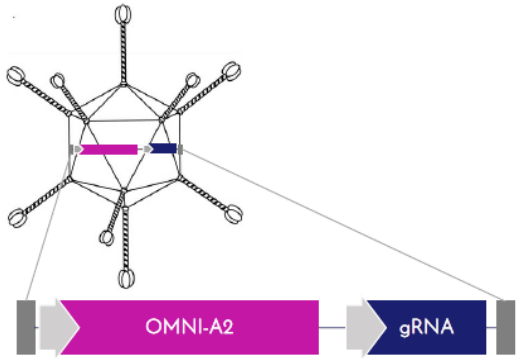


HSCs - hematopoietic stem cells

OMNI-A2™, Short AAV-Deliverable Nuclease

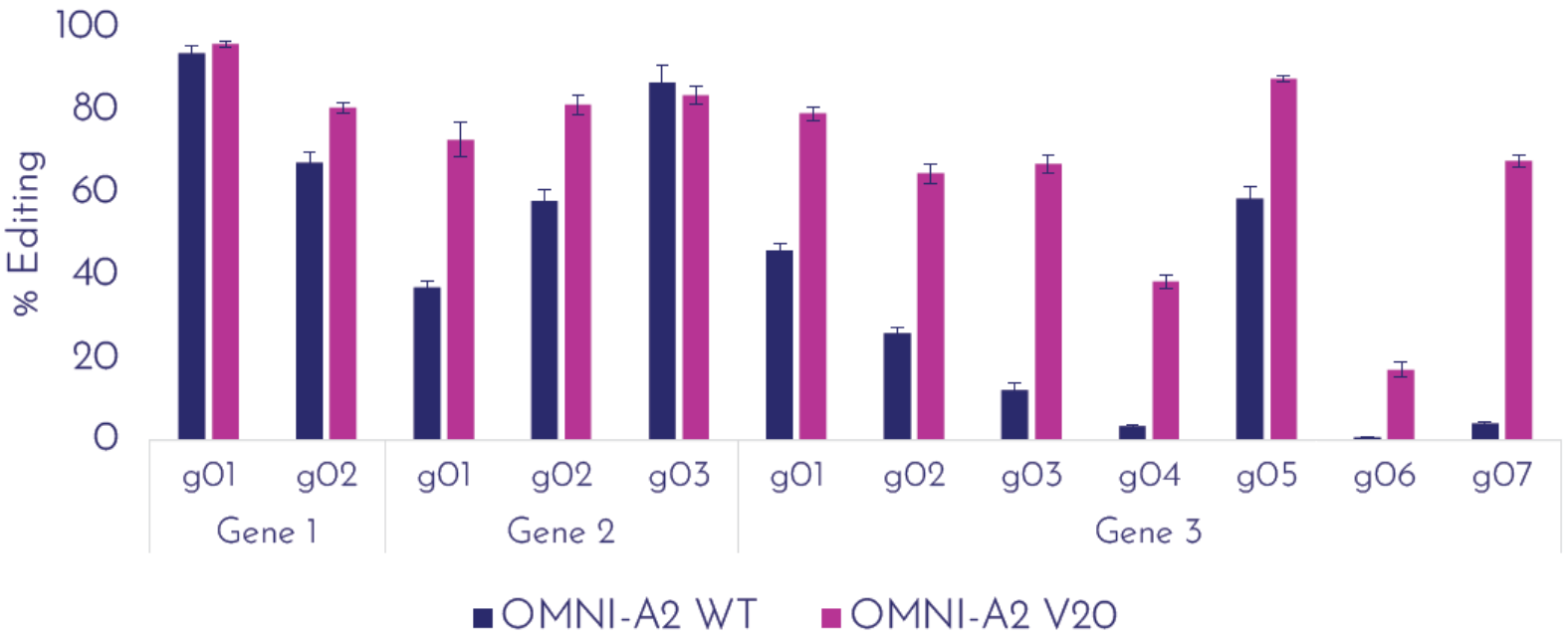
Short, highly active, AAV packaging compatible nucleases available

AAV-based vectors



Limited payload capacity

Editing by OMNI-A2-V20™ (1,050aa)

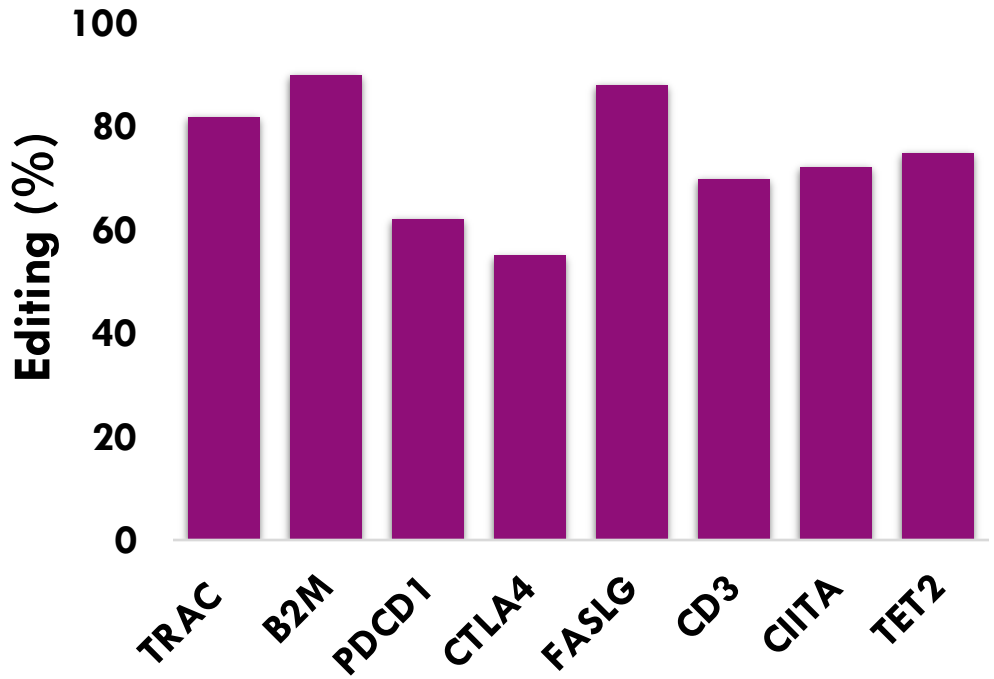


OMNI-A4™ Presents High Activity and Specificity Profile

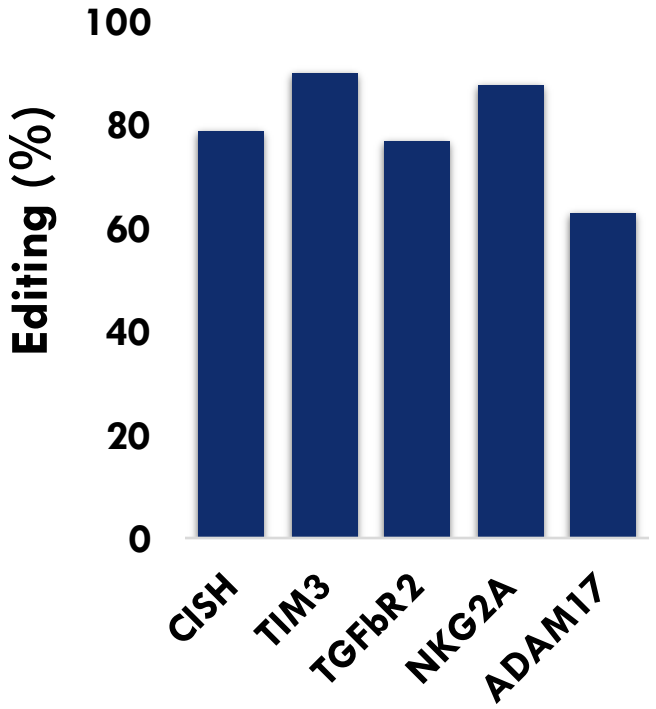
Non-NGG PAM nuclease compositions for major cell therapy and immuno-oncology targets

OMNI-A4™	
Protein Length (AA)	1349 (161.9 KDa)
gRNA length (nt)	107+22=129
PAM (TXTL results)	NNRACT

T cells



NK cells



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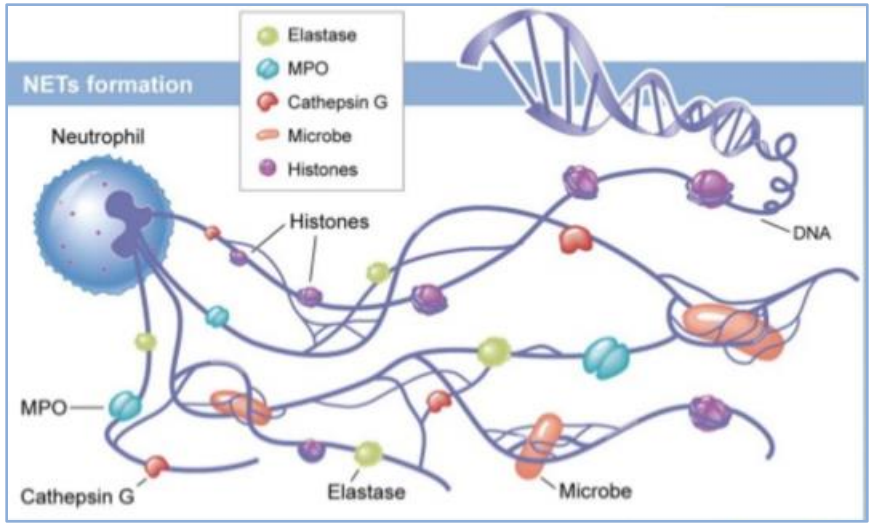
PRODUCT CANDIDATE AVAILABLE FOR LICENSING

EMD-101 Targeting *ELANE*

For The Treatment of Severe Congenital Neutropenia

Target Indications and Market Opportunity

ELANE-related severe congenital neutropenia (SCN)



A neutrophils depletion disorder (<0.5×10^{9}cells/L), causing severe recurrent infections

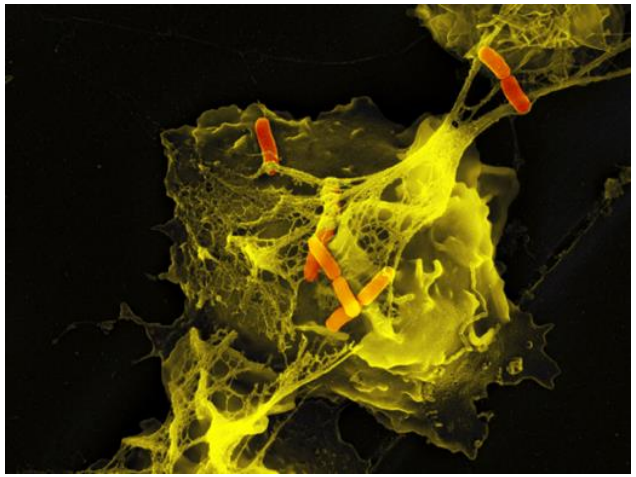
- Neutrophil Elastase (NE), a serine protease, part of the NET trap
- Dominant mutations cause protein misfolding, ER stress and maturation arrest
- Prevalence 1:200,000*, under-diagnosed

Patient Population

- **1,600 patients in the U.S., 40,000 patients worldwide**

Market Size

- **$ 2-3B in the U.S.**



*Genetic Home Reference, NIH US National Library of Medicine: https://ghr.nlm.nih.gov/condition/severe-congenital-neutropenia#statistics.
Colored scanning electron micrograph showing stimulated neutrophil with NETs and trapped Shigella bacteria. ©Max Planck Institute for Infection Biology.

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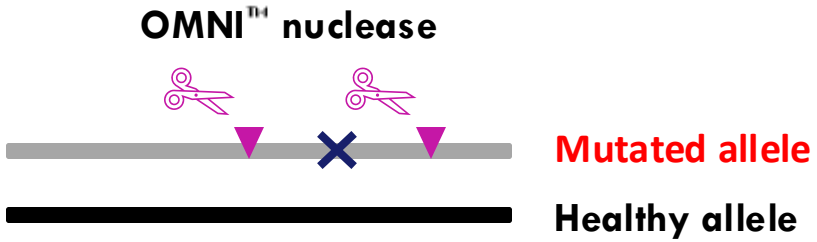
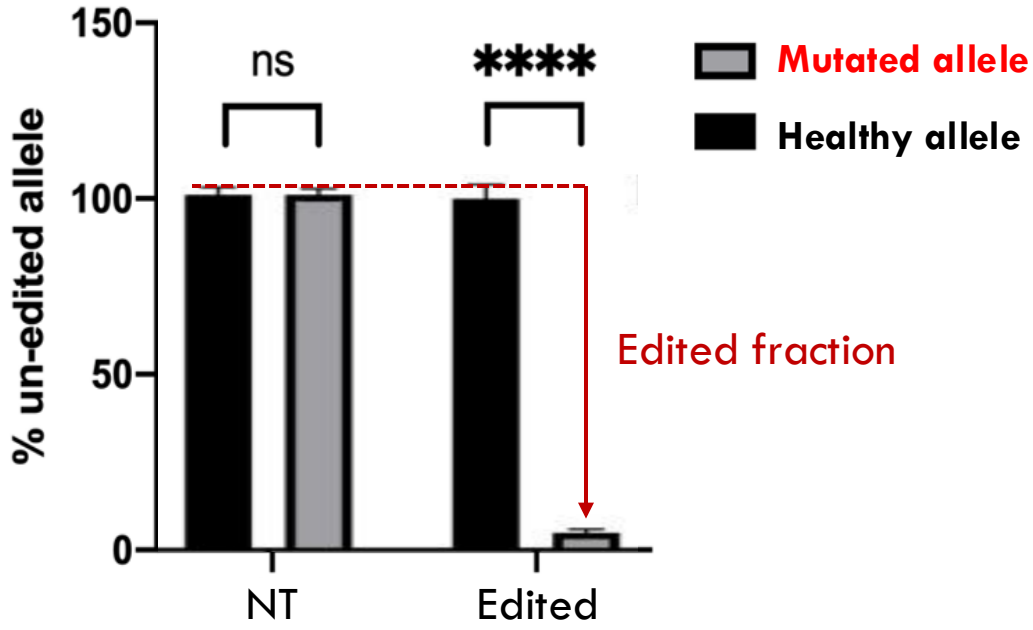
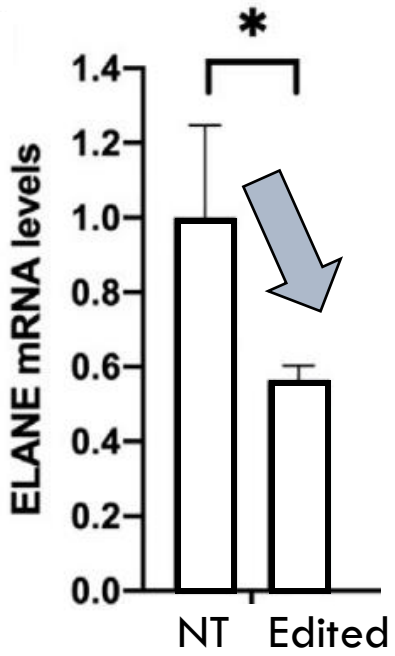
Mechanism of Action

ELANE gene



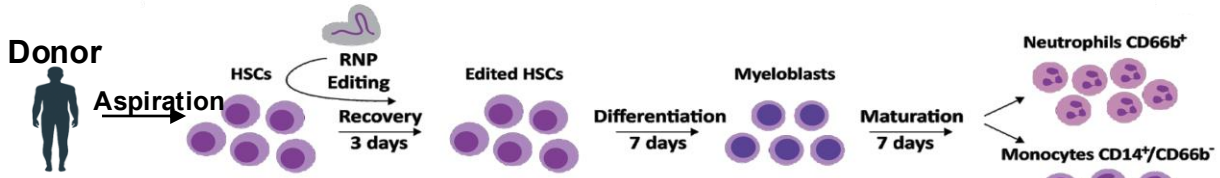
Mono allelic knockout of mutated *ELANE* gene caused the degradation of the mutated *ELANE* mRNA



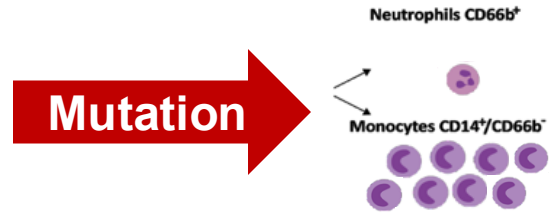


Preclinical Data of Proof of Concept

Recovery of neutrophils differentiation by editing of mutant *ELANE* allele

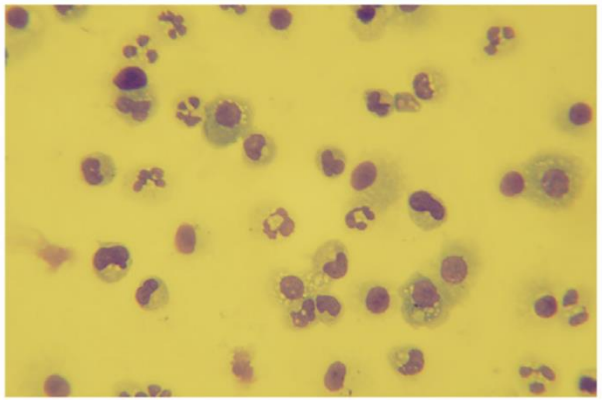


Normal

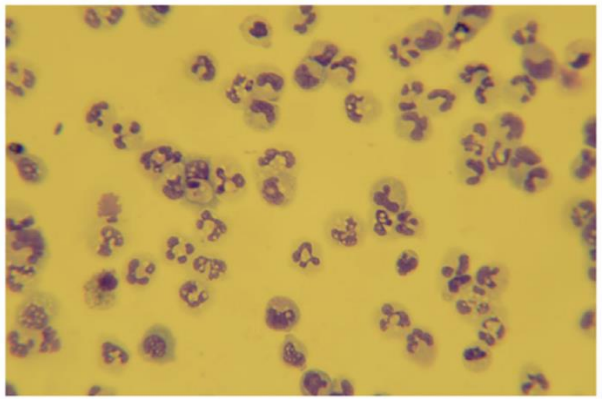


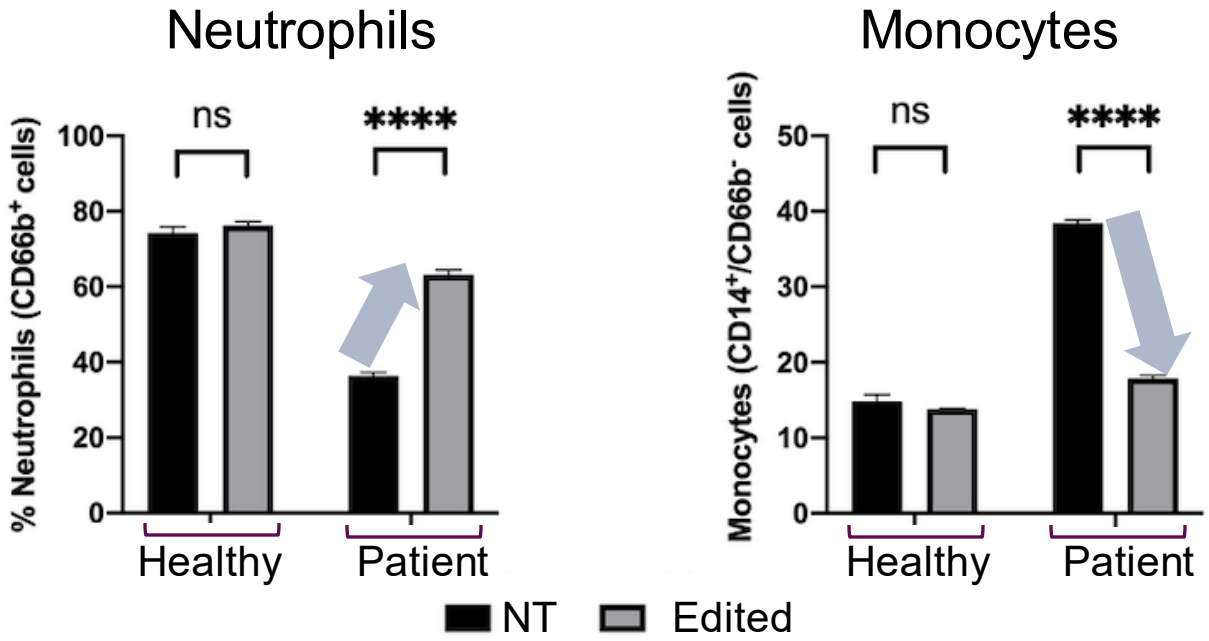
Patient

NT



Edited





EmendoBio's Service Offerings

- Gene editing services
  - Off-the-shelf compositions for target genes
  - Proprietary nucleases tailored to specific project needs
  - Consulting services for gene editing strategy, gRNA selection, off-target experiments and analysis
- License opportunities
  - Non-exclusive research use licenses for exploration, discovery and early development
  - Exclusive clinical/commercial use licenses for advanced development of defined products
- Strategic collaborations
  - Joint assessment of project needs
  - Optimization of OMNI™ nuclease and gRNA combination for specified applications
  - Joint development of product candidates