A Panel of Novel Engineered Nucleases Unlocks the Full Potential of Genome Editing

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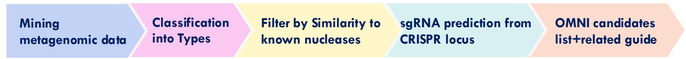
ABSTRACT

A successful CRISPR based gene editing strategy requires developing an optimized composition of nuclease and gRNA per target gene per organ. Different editing strategies require different gene editing tools with specific nuclease characteristics, such as nuclease size, diverse PAM recognition, compatibility with delivery systems and high activity and specificity to the target site. A panel of nucleases, the OMNI nuclease series, was developed by EmendoBio to overcome such key challenges in the field. The OMNI nucleases recognize different PAM sequences that cover approx. 80% of the human genome; they vary in size; and they are compatible with all common delivery modalities, including AAV. OMNI nucleases are engineered to be as active as industry gold standard nucleases while displaying enhanced specificity, which eliminates off-target effects and enables allele specific editing. EmendoBio's technology creates tailor-made nucleases by combining a discovery pipeline and cutting-edge protein-engineering capabilities, which is supported by extensive computational tools, including proprietary AI.

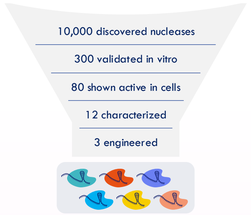
The specificity and efficiency of the OMNI nucleases enabled an achievement of high HDR efficiency in multiple target cells including HSCs and more, and recently OMNI editors were development to achieve efficient DNA writing efficiency.

EmendoBio's panel of novel nucleases, and its proprietary techniques to customize such nucleases, enables expansion of the existing CRISPR toolbox and overcomes major gene editing challenges, offering solutions for a wide range of diseases.

OMNI discovery pipeline

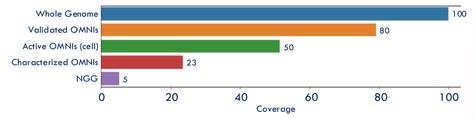


Nuclease Portfolio

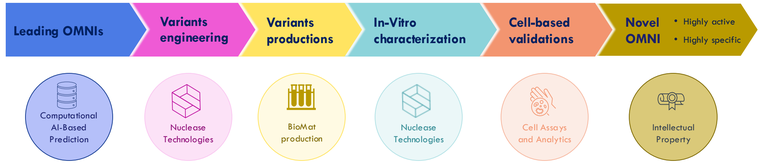


OMNI™ Genomic PAM Coverage

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



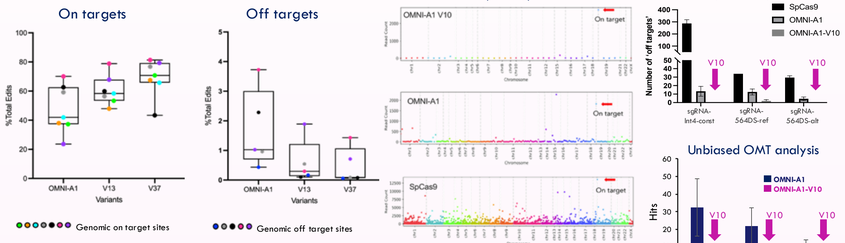
OMNI engineering pipeline



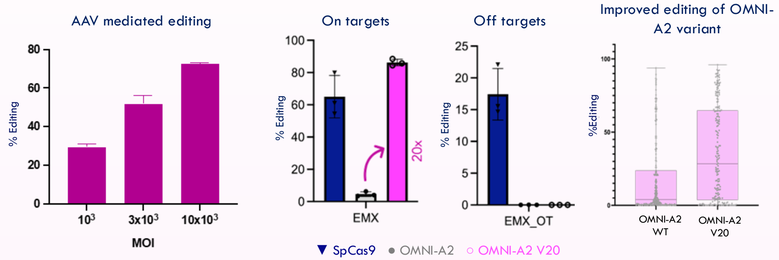
Engineered OMNI variants demonstrate improved capabilities compared to non-engineered nucleases

The OMNI Platform – combining discovery and engineering for the generation of a broad portfolio of nucleases

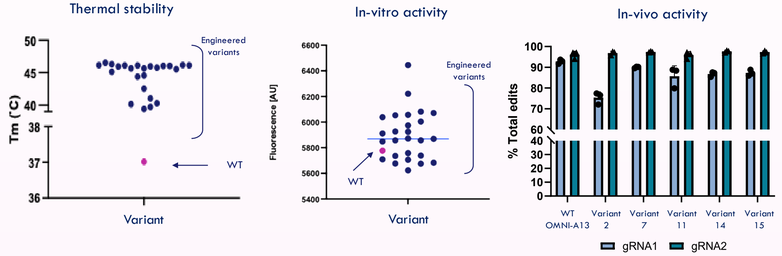
1. OMNI-A1 – Increased specificity



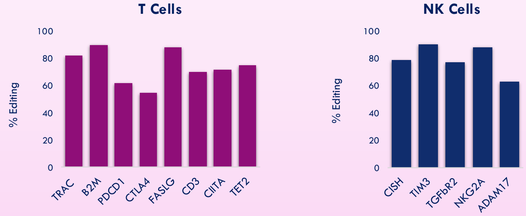
2. OMNI-A2 – AAV compatible nuclease with increased activity



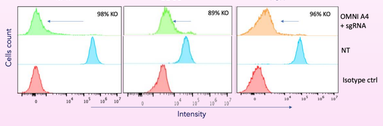
3. OMNI-A13- Applying AI-based engineering to improve protein stability



Non-NGG-PAM nuclease enables efficient editing to overcome IP constrains while maintaining efficiency and safety



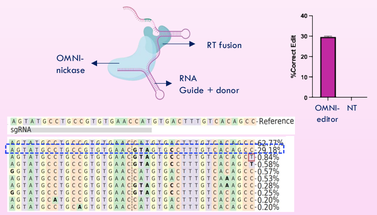
Efficient protein knock-out



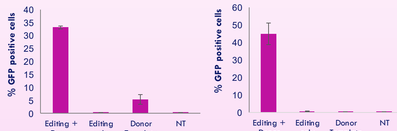
No off-target detected

Next-Generation OMNI-based tools for DNA writing and HDR

1. OMNI-editor- enables effective DNA writing



2. High HDR efficiency using OMNI-nucleases



Safe harbor site - locus 1
HepG2 cells

Safe harbor site - locus 2
Primary HSCs

3. OMNI-off systems are in development