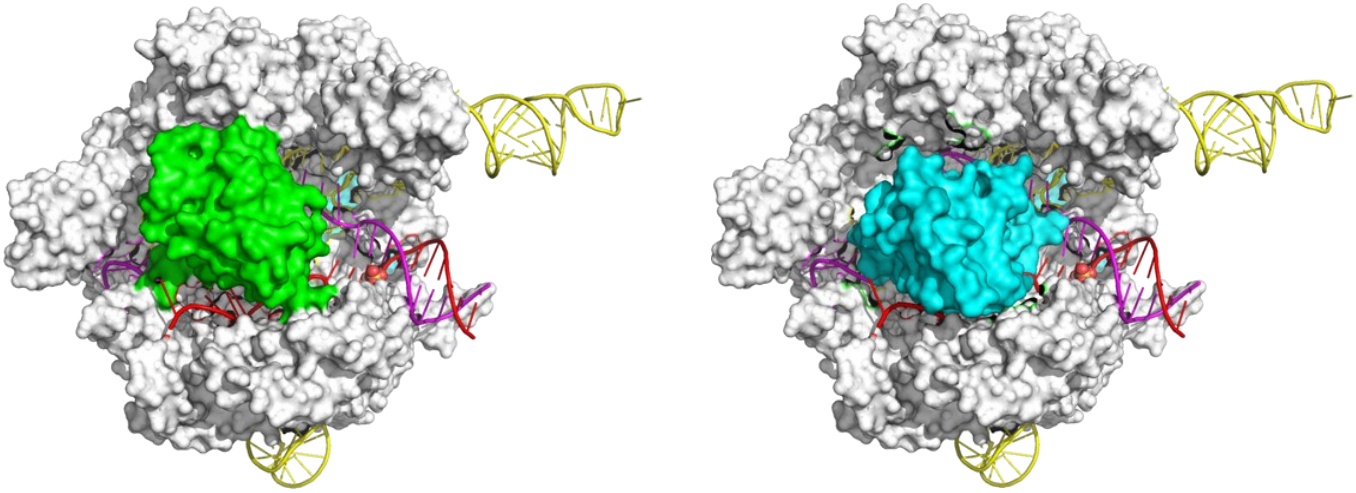
ETH zürich

# Licensing Opportunity

## Gene therapy for diseases caused by DNA mutations



*Structural data of hypothetical Cas9 constructs: (left) HNH domain (green) blocks access to certain parts of the single-stranded DNA, (right) TAdA deaminase (turquoise) replaces the HNH domain and makes additional loci accessible.*

### Application

Diseases caused by single base pair mutations can be repaired by base editing techniques. A chimeric Cas9 enzyme expands the toolbox for genome editing. Previously sterically inaccessible disease loci can now be targeted.

### Features & Benefits

- Gene therapy
- Targeted deamination of adenosine in mammalian DNA
- Significantly shifted base editing window compared to state-of-the-art Cas enzymes
- Smaller size: easy construction of single adeno-associated virus (AAV)-vectors

### Publications

- L. Villiger et. al., “Relacing the *Sp*Cas9 HNH domain by deaminases generates compact base editors with an alternative targeting scope”, preprint bioRxiv https://doi.org/10.1101/2020.11.09.371237
- Patent pending

### Background

Base editors are RNA-guided deaminases that enable the site-specific and precise conversion of A-to-G and C-to-T nucleobases or vice versa, and thus have great potential for research and therapeutic applications. Many disease causing mutations, however, cannot be targeted with state-of-the art CRISPR-Cas base editing techniques, because their genetic location falls outside the narrow base editing window. Hence, there is a need for techniques that aim at expanding the editing window without generating non-target nucleotide edits.

### Invention

This Cas9-deaminase has, compared to classical adenine base editors (ABE), a PAM-proximally shifted editing window. The HNH nuclease domain of Cas9 has been replaced by a deaminase; and in this position, the deaminase can now gain access to the previously inaccessible part of the single-stranded DNA, which is then deaminated. Providing proof-of-concept, in comparison to previous ABEs (with N-terminally fused deaminase), a considerably higher on-target editing for a known disease-causing mutation (FANCA gene) has been demonstrated.

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**Technology Readiness Level**