HDR-CRISPR - Precision Genome Editing

Cas9 fusion platform with improved efficiency

Technology

CRISPR-Cas9 technology enables gene editing in a sequence specific manner. Precise editing requires the resolution of nuclease-induced DNA double strand breaks (DSBs) by homology-directed repair (HDR) which is typically much less efficient than the non-homologous end-joining (NHEJ) repair and often far below the desired clinically relevant frequencies.

We present a novel high precision CRISPR platform consisting of a Cas9 fused to DNA repair factors to synergistically inhibit NHEJ and favor HDR for precise repairing of Cas-induced DSBs. Compared to canonical CRISPR/Cas9, the increase in error-free editing is up to 7-fold in multiple cell lines and in primary human cells. This novel CRISPR/Cas9 platform accepts clinically relevant repair templates, such as oligodeoxynucleotides and adeno-associated virus-based vectors, and has a lower propensity to induce chromosomal translocations as compared to benchmark CRISPR/Cas9. The observed reduced mutational burden provides a remarkable gain in safety and advocates this novel CRISPR system as an attractive tool for therapeutic applications depending on precision genome editing.

Innovation

- Precision Cas9 nuclease
- Fusion with critical DNA repair factors for improved safety
- Ability to enhance HDR and inhibit NHEJ only at the DSB site
- Increased editing fidelity
- Low mutational burden
- Low off-target effects
- Improved safety

Application

- Clinically relevant human primary hematopoietic cells
- Acceptance of various donors

Responsible Scientist

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