

CRISPR-Cas Inhibiting Polypeptides

Tech ID: 32880 / UC Case 2018-166-0

TECHNOLOGY DESCRIPTION

The inventions introduce novel Cas nuclease inhibiting polypeptides with synthetic/ non-natural amino acids as well as techniques to conjugate it to an antibody or PEG for easy delivery to targeted cells. Bacterial cells respond to phage attack by activating CRISPR-Cas nuclease to digest phage genome; to escape it, phages encode anti-CRISPR-Cas proteins. **Broad-spectrum Cas enzyme inhibitors will allow for better post-translational regulation of CRISPR-Cas system for gene editing. These polypeptides were hitherto unknown** and their use along with CRISPR-Cas system for genetic manipulation will improve its efficacy and potential for translation to human applications.

VALUE PROPOSITION

- ▶ **Anti-CRISPR polypeptides are the tools which will efficiently target the genes being edited**
- ▶ Large number of clinical trials are currently using CRISPR-Cas systems to treat diseases- from hematological malignancies to treating HIV via permanent genetic modifications. **However, a major risk involved in using CRISPR-Cas based gene therapy are off-target effects, which may lead to permanent changes in patient genome at non-target sites.**
- ▶ **Anti-CRISPR polypeptides allow for long-term regulation of CRISPR-Cas therapy without any off-target effects.** They can be introduced independently of the CRISPR system, and they will maintain activity over longer durations.
- ▶ **Anti-CRISPR polypeptides act with a better specificity are easier to design and synthesize,** when compared to small molecule inhibitors.

RELATED MATERIALS

- ▶ Marino, N. D., Pinilla-Redondo, R., & Bondy-Denomy, J. (2022). CRISPR-Cas12a targeting of ssDNA plays no detectable role in immunity. *BioRxiv*, 2022.03.10.483831.
- ▶ Rauch BJ, Silvis MR, Hultquist JF, Waters CS, McGregor MJ, Krogan NJ, Bondy-Denomy J. Inhibition of CRISPR-Cas9 with Bacteriophage Proteins. *Cell*. 2017 Jan 12;168(1-2):150-158.e10.
- ▶ Mahendra C, Christie KA, Osuna BA, Pinilla-Redondo R, Kleinstiver BP, Bondy-Denomy J. Broad-spectrum anti-CRISPR proteins facilitate horizontal gene transfer [published correction appears in *Nat Microbiol*. 2020 Jun;5(6):872]. *Nat Microbiol*. 2020;5(4):620-629.

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OTHER INFORMATION

KEYWORDS

CRISPR, gene editing, Cas, anti-CRISPR

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Research Tools
 - ▶ Therapeutics
- ▶ **Research Tools**
 - ▶ Nucleic Acids/DNA/RNA

RELATED CASES

2018-166-0, 2017-057-0, 2020-001-0

PATENT STATUS

Country	Type	Number	Dated	Case
Japan	Issued Patent	7210029	01/13/2023	2017-057
United States Of America	Issued Patent	11,485,760	11/01/2022	2017-057
European Patent Office	Published Application	4055158	09/04/2022	2020-001
United States Of America	Published Application	20210363206	11/25/2021	2018-166

Additional Patents Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [Robust Genome Engineering in Primary Human T Cells using CRISPR/Cas9 Ribonucleoproteins](#)
- ▶ [Novel Small Protein Inhibitors for Rapid and Controllable CRISPR-Cas9 Interference](#)

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