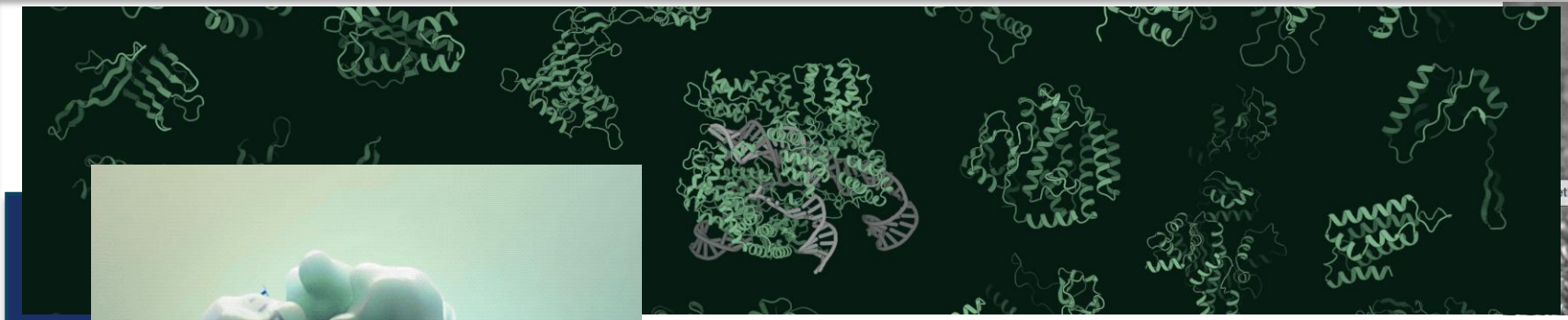
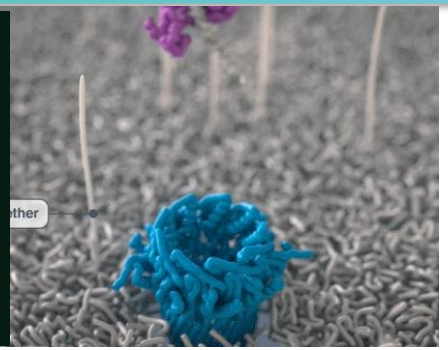
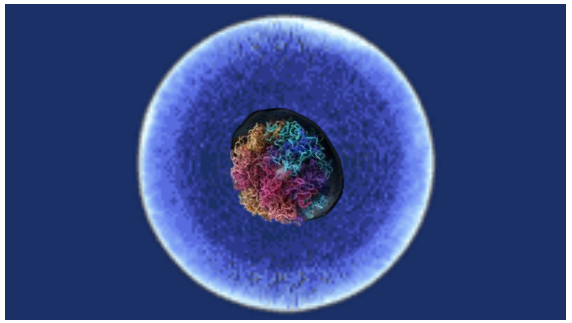







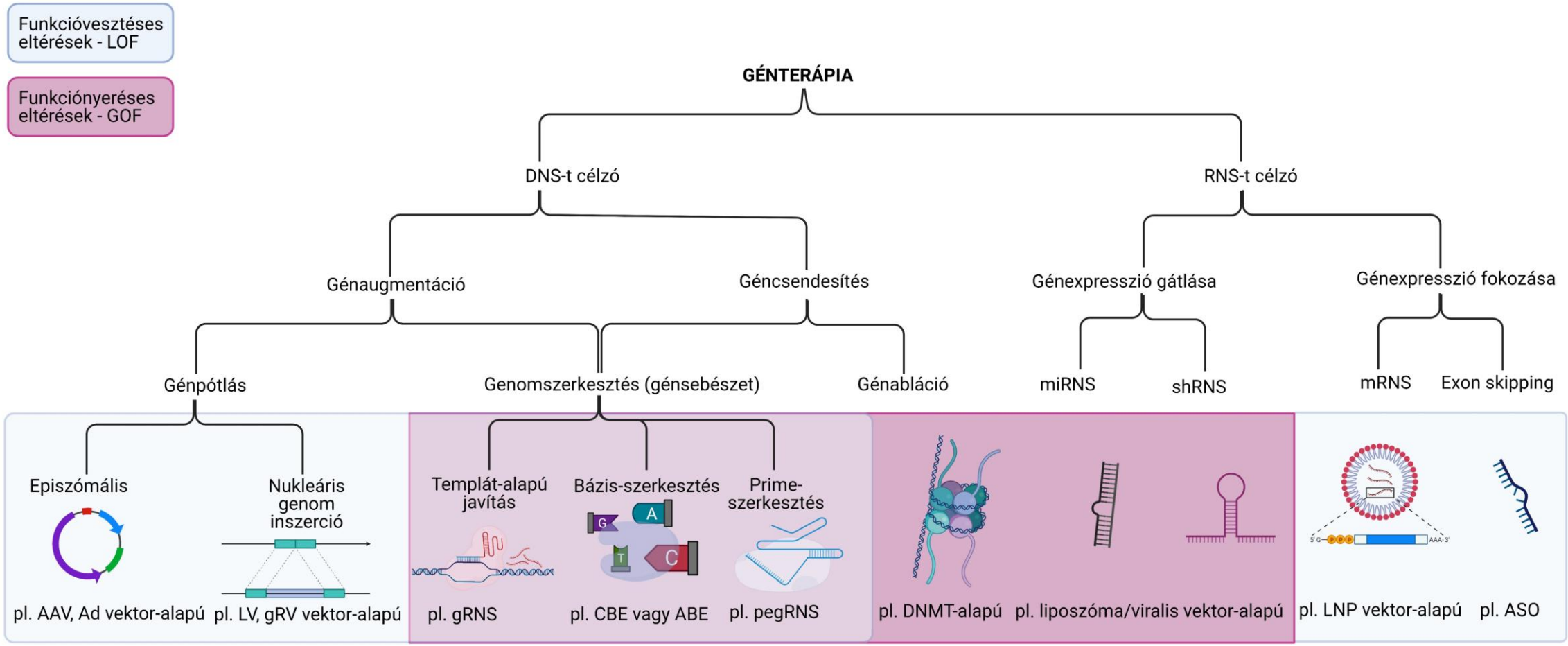
# Genomszerkesztés a génsebészet hajnalán

Dr. Kovács Árpád Ferenc

**Design of highly functional genome editors by modeling the universe of CRISPR-Cas sequences** Jeffrey
A. Ruffolo, Stephen Nayfach, Joseph Gallagher, Aadyot Bhatnagar, Joel Beazer, Riffat Hussain, Jordan Russ, Jennifer Yip, Emily Hill, Martin Pacesa, Alexander J. Meeske, Peter Cameron, Ali Madani
bioRxiv 2024.04.22.590591; doi: https://doi.org/10.1101/2024.04.22.590591

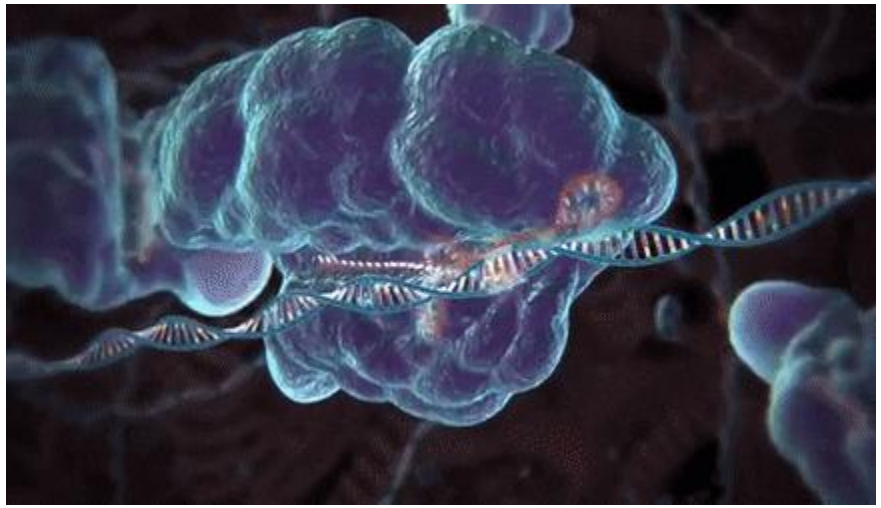
**2024.04.29.**

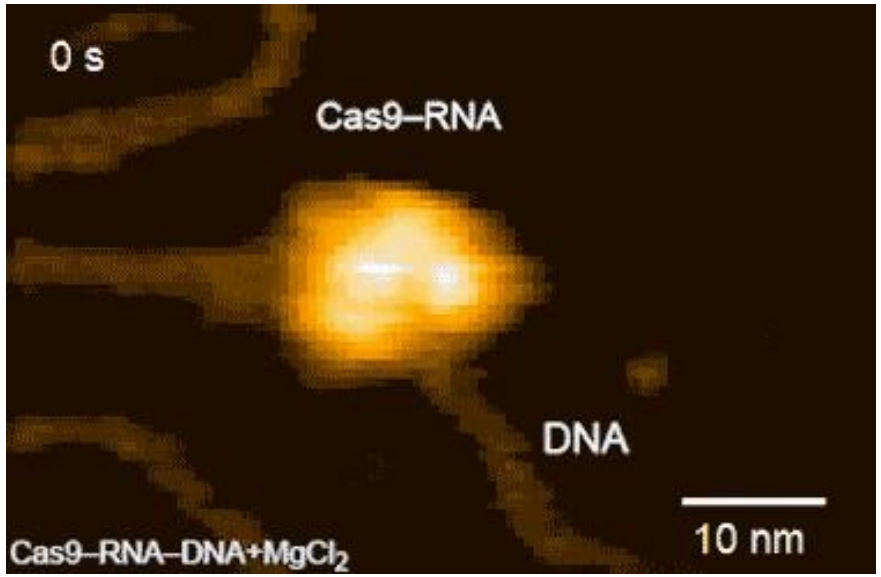
# HÁTTÉR




Kovács, Orsolya Tünde ; Szalai, Renáta ; Fekete, Nóra ; Haltrich, Irén ; **Kovács, Árpád Ferenc** Elérhető génterápiás készítmények az Európai Unióban GYÓGYSZERÉSZET 67 : 2023/11 pp. 581-589. , 9 p. (2023)

## GÉNSZERKESZTÉS

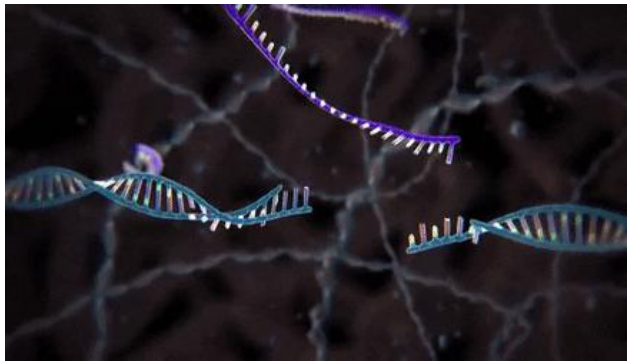






2020, NIH

## GÉNPÓTLÓ TERÁPIA



# Design of highly functional genome editors by modeling the universe of CRISPR-Cas sequences

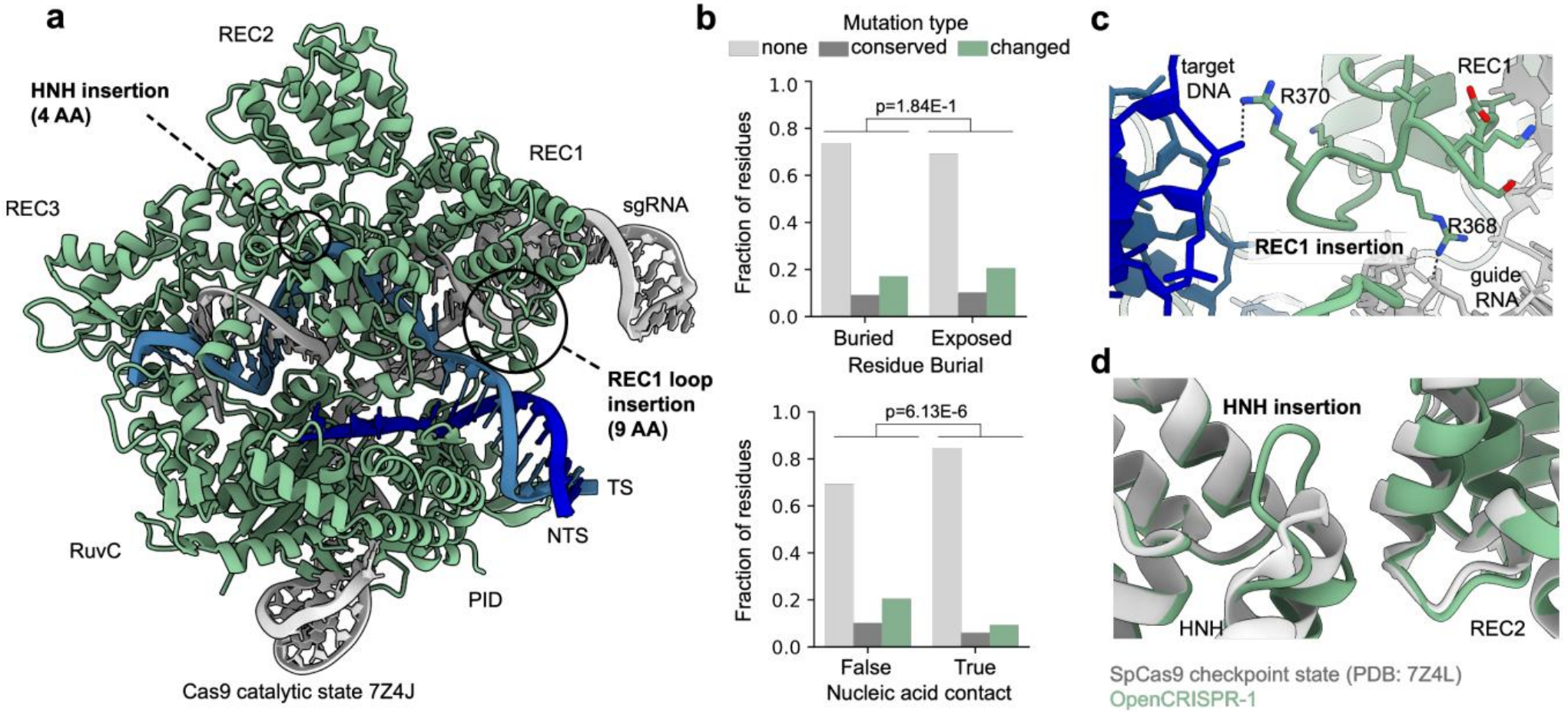
**Jeffrey A. Ruffolo[1,*], Stephen Nayfach[1,*], Joseph Gallagher[1,*], Aadyot Bhatnagar[1,*], Joel Beazer[1], Riffat Hussain[1], Jordan Russ[1], Jennifer Yip[1], Emily Hill[1], Martin Pacesa[1,2], Alexander J. Meeske[1,3], Peter Cameron[1], and Ali Madani[1,†]**

[1]Profluent Bio, Berkeley, CA, USA; [2]Laboratory of Protein Design and Immunoengineering, École Polytechnique Fédérale de Lausanne and Swiss Institute of Bioinformatics, Lausanne, Switzerland; [3]Department of Microbiology, University of Washington, Seattle, WA, USA

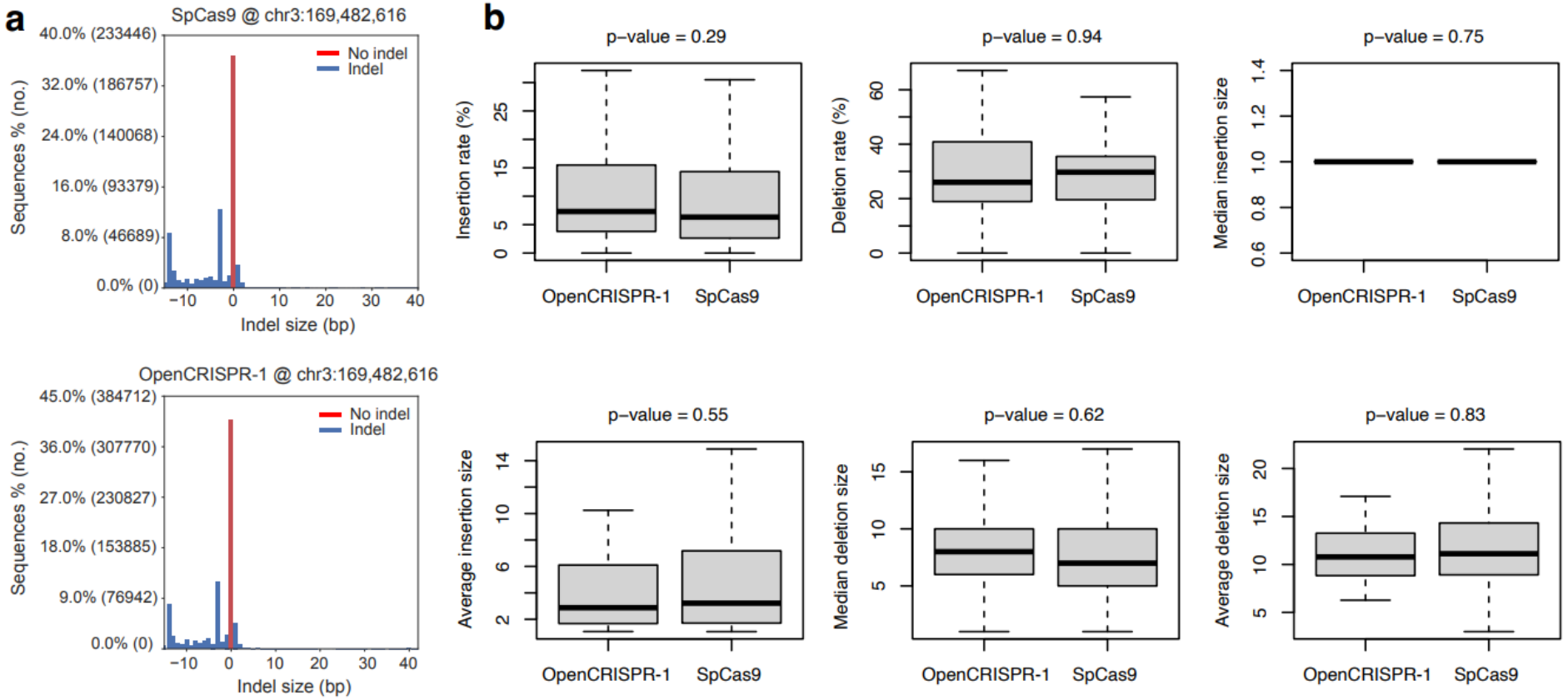
**Gene editing has the potential to solve fundamental challenges in agriculture, biotechnology, and human health. CRISPR-based gene editors derived from microbes, while powerful, often show significant functional tradeoffs when ported into non-native environments, such as human cells. Artificial intelligence (AI) enabled design provides a powerful alternative with potential to bypass evolutionary constraints and generate editors with optimal properties. Here, using large language models (LLMs) trained on biological diversity at scale, we demonstrate the first successful precision editing of the human genome with a programmable gene editor designed with AI. To achieve this goal, we curated a dataset of over one million CRISPR operons through systematic mining of 26 terabases of assembled genomes and meta-genomes. We demonstrate the capacity of our models by generating 4.8x the number of protein clusters across CRISPR-Cas families found in nature and tailoring single-guide RNA sequences for Cas9-like effector proteins. Several of the generated gene editors show comparable or improved activity and specificity relative to SpCas9, the prototypical gene editing effector, while being 400 mutations away in sequence. Finally, we demonstrate an AI-generated gene editor, denoted as OpenCRISPR-1, exhibits compatibility with base editing. We release OpenCRISPR-1 publicly to facilitate broad, ethical usage across research and commercial applications.**

genome editing | large language models | protein design

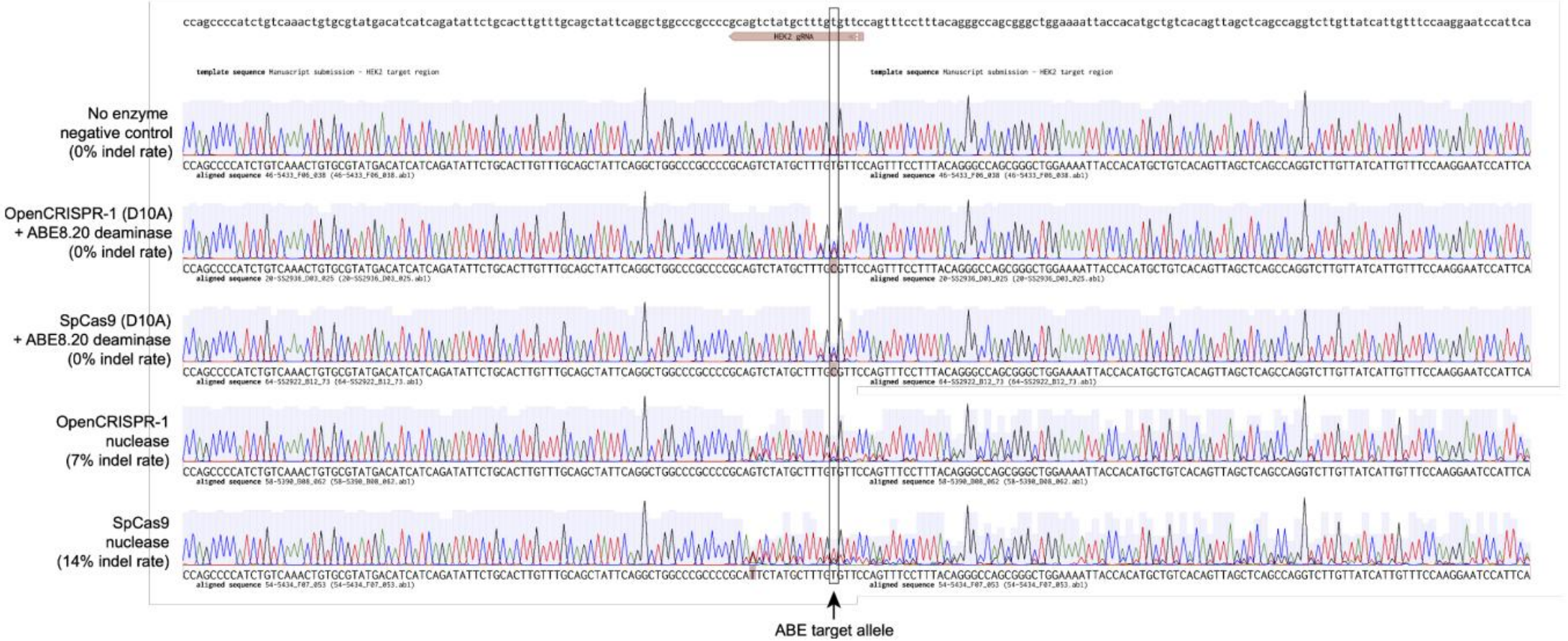
## OpenCRISPR-1 fehérje szerkezetének tervezése – jobb sgRNS kötés és hasítási hatékonyság



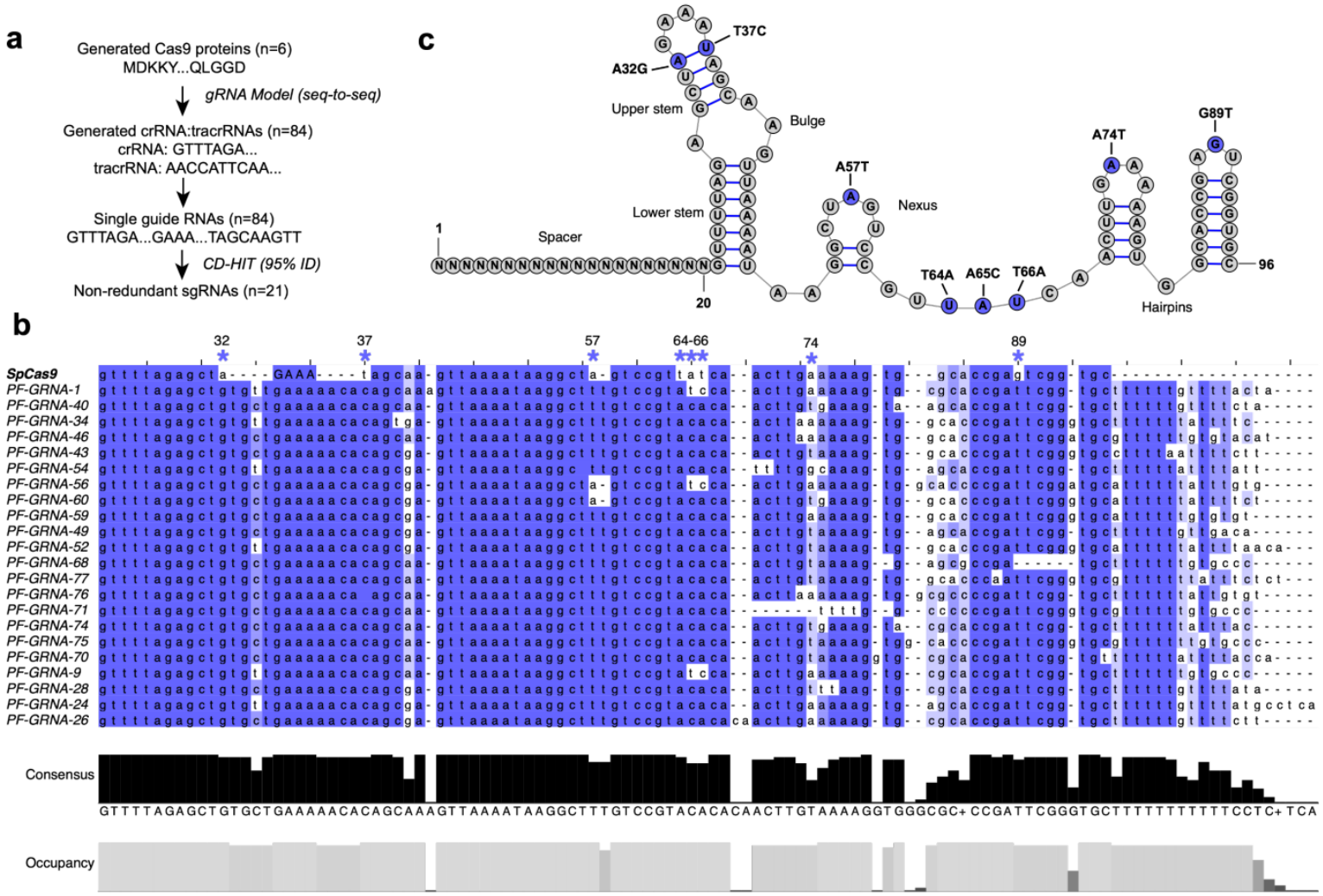
# OpenCRISPR-1 és spCas9 genomszerkesztési hatékonysága



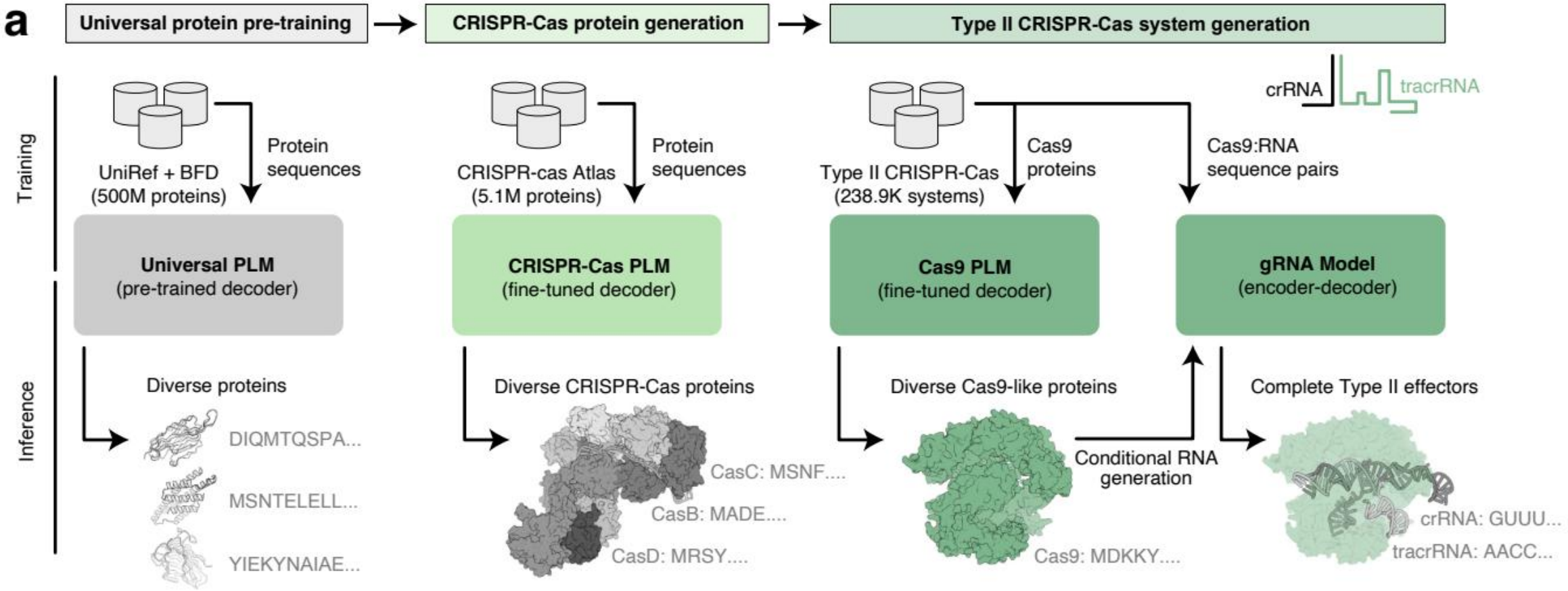
# Egy bázis szerkesztése T → C a *HEK2* génben OpenCRISPR-1 D10A mutáció létrehozásával



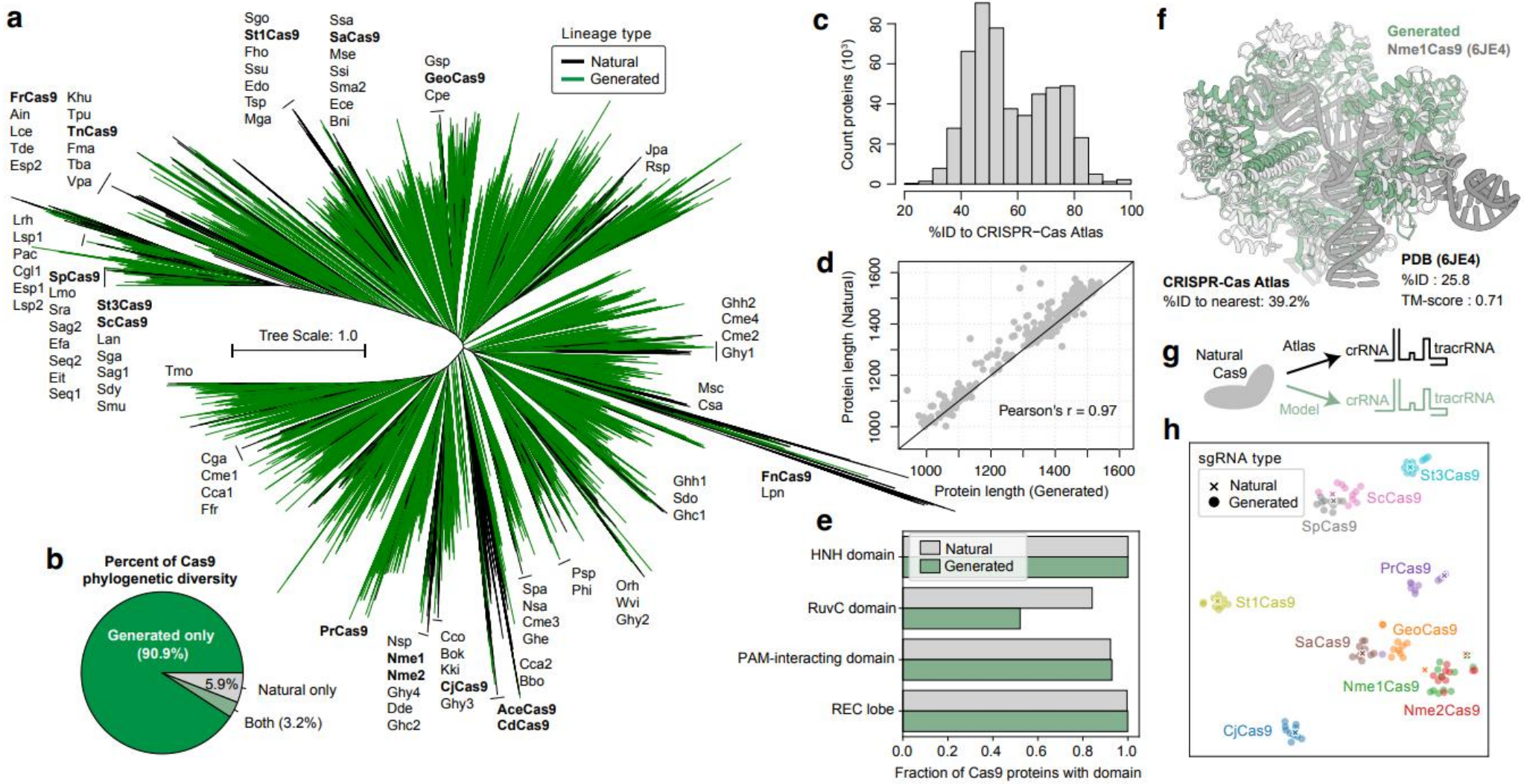
# Mesterséges intelligencia vezérelt irányító RNS tervezés



# Mesterséges intelligencia a génszerkesztésben



# Mesterséges intelligencia a génszerkesztésben



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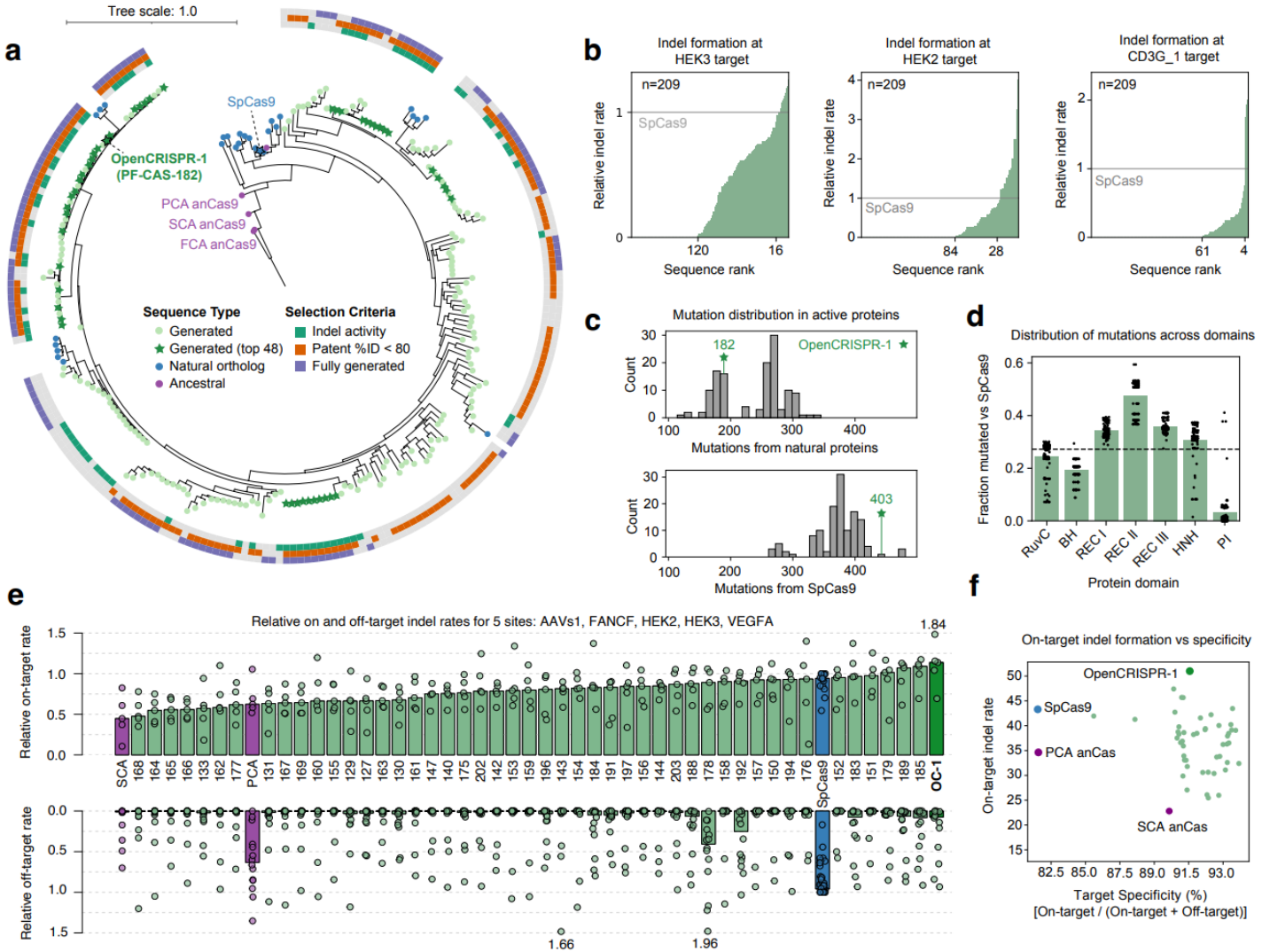

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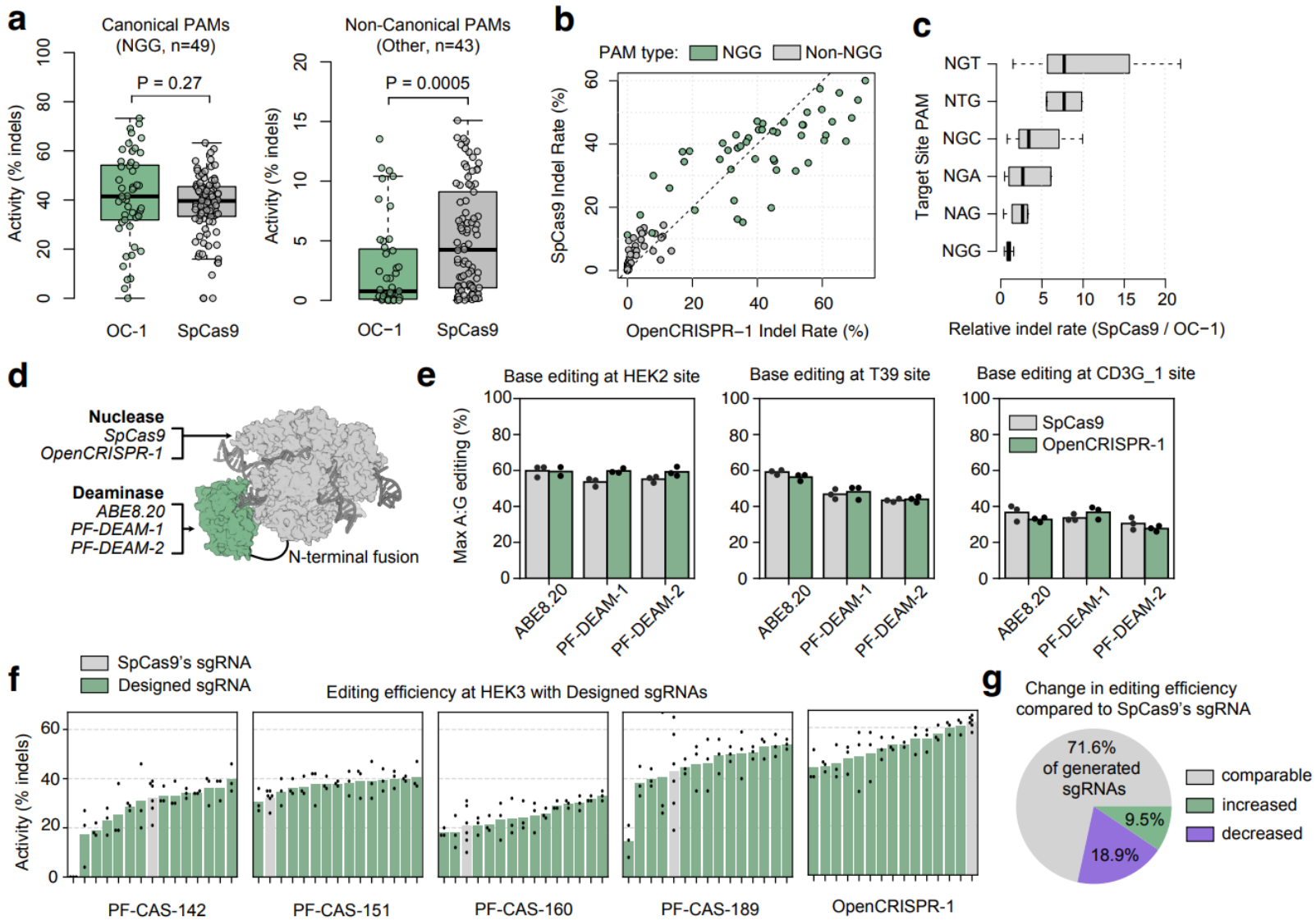

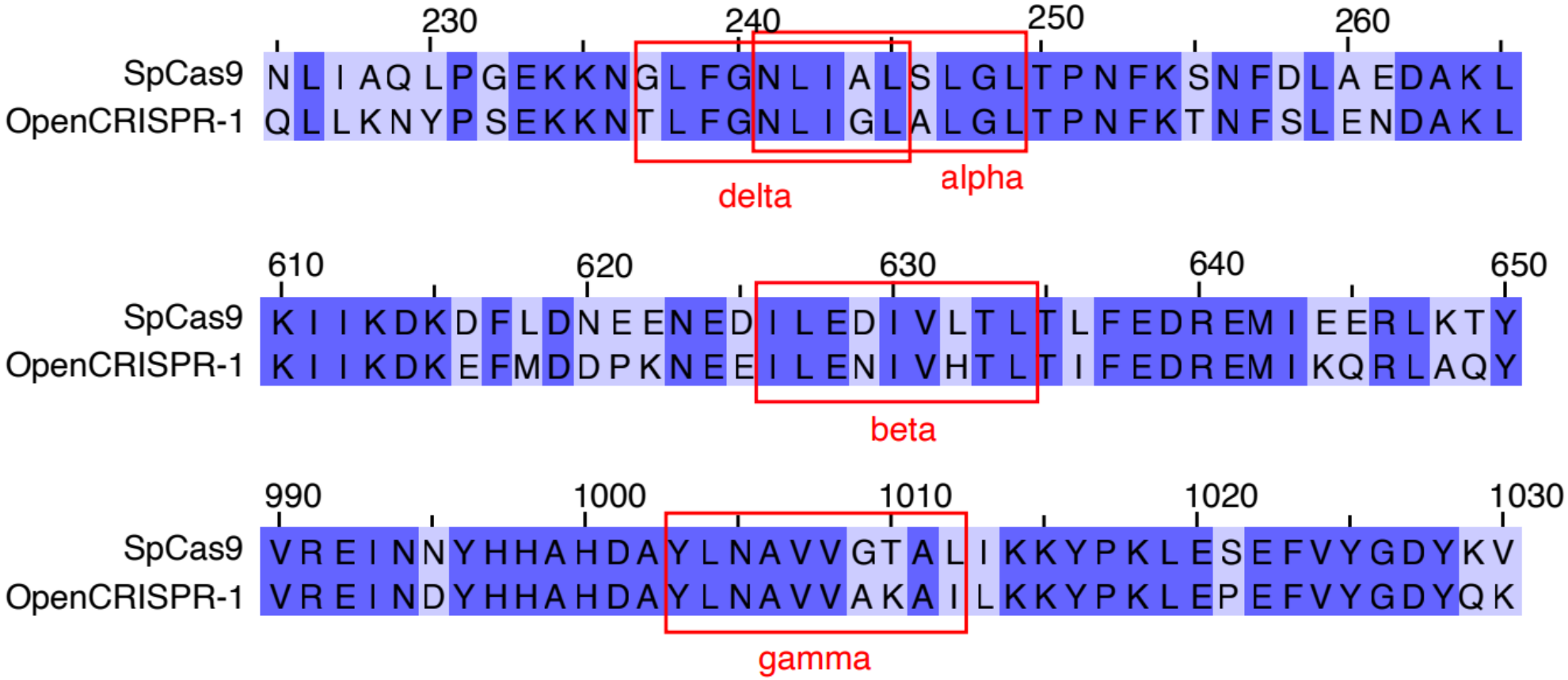


**Fig. S10. Comparison of SpCas9 immunogenic epitopes with OpenCRISPR-1.** Ferdosi et al. discovered four SpCas9 epitopes that elicit pre-existing B cell and T cell immune responses in healthy donors (36). Alignments to SpCas9 and OpenCRISPR-1 revealed one or more mutations in each of these epitopes.

# Köszönöm szépen a megtisztelő figyelmet!