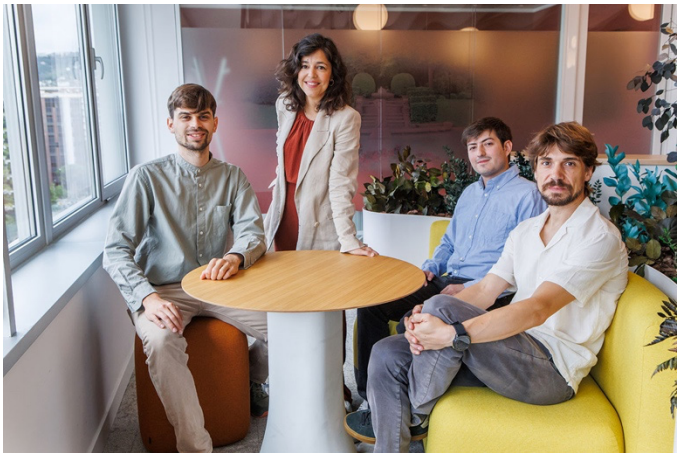
**PRESS RELEASE - EMBARGOED UNTIL OCTOBER 2 2025 at 10:00 (London time) / 05:00 (US Eastern Time)**

# Generative AI is more efficient than nature at designing proteins to edit the genome

**Researchers at Integra Therapeutics, in collaboration with Pompeu Fabra University and the Center for Genomic Regulation in Barcelona, have published this finding in the journal *Nature Biotechnology*.**

**After studying the diversity of mobile elements in the genome to feed and train generative AI tools, researchers have been able to design and lab validate new synthetic proteins that can edit the genome more efficiently than natural proteins.**



Dimitrije Ivančić (co-first author of the paper), Avencia Sanchez-Mejías (CEO of Integra Therapeutics), Alejandro Agudelo (co-first author of the paper) and Marc Güell (ICREA researcher and CSO of Integra Therapeutics)

*Barcelona, Spain, 2 October 2025*. Researchers at Integra Therapeutics, in collaboration with the Pompeu Fabra University (UPF) Department of Medicine and Life Sciences (MELIS) and the Center for Genomic Regulation (CRG), have designed and experimentally validated new synthetic proteins that can edit the human genome more efficiently than proteins provided by nature. This work, a **global pioneer published today in the journal *Nature Biotechnology***, will be of great use in improving the current gene editing tools used in biotechnology research and personalized medicine by developing cellular (CAR-T) and gene therapies, especially **to treat cancer and rare diseases**.

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The ability to insert large DNA sequences into genomes in a safe, targeted manner has been a revolution in the research and development of advanced therapies in recent years. Among the most promising systems are transposases, such as PiggyBac, which *copies and pastes* DNA to introduce therapeutic genes into patient cells. However, their potential has been limited by the scarce diversity of known transposases and their lack of precision.

## Exploring biodiversity

The researchers used computational bioprospecting to screen more than 31,000 eukaryotic genomes and discovered more than 13,000 new, previously unknown PiggyBac sequences. After performing experimental validation in cultured human cells, **10 active transposases** were identified, demonstrating that there is a large functional diversity that has not yet been explored. Two of these new transposases showed activity comparable to versions already optimized for laboratory and patient use, and one of them even exhibited high activity in human primary T cells, a crucial cell type for cancer therapies.

## Designing with generative artificial intelligence

In the second phase, researchers went beyond nature and used a protein large language model (pLLM), a form of generative artificial intelligence. They trained the model with the 13,000 PiggyBac sequences discovered to generate completely new sequences with enhanced activity. This approach not only optimized one of the existing transposases, but also demonstrated that AI-engineered variants are **compatible with advanced gene editing technologies such as the FiCAT platform**.

“Publishing this paper in *Nature Biotechnology* opens the way to *revolutionizing* the field of gene editing and advanced therapies and cements Integra Therapeutics’ position at the forefront of gene therapies and the use of innovative tools like AI for protein design in our development,” notes Dr. Avencia Sánchez-Mejías, CEO and co-founder of Integra Therapeutics.

“For the first time, we have used generative AI to create synthetic parts and expand nature. Like the cognitive power of ChatGPT can be used to write a poem, we have used the protein-based large language models to generate new elements that comply with the physical and chemical principles of genes,” explains Dr. Marc Güell, scientific director at Integra Therapeutics and ICREA researcher at MELIS-UPF where he heads up the Translational Synthetic Biology Lab.

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"These AI models are trained with all known protein sequences on earth and learn the internal language or 'grammar' of proteins. Using this grammar, they are able to speak this language perfectly, generating completely new proteins that maintain structural and functional meaning," says Dr. Noelia Ferruz, who leads the Artificial Intelligence for Protein Design Group at the CRG.

To accelerate and expand its FiCAT technology and pipeline of therapeutic products, Integra Therapeutics forges strategic partnerships with leading companies and research centers like UPF and CRG.

**Reference paper**

**Discovery and protein language model-guided design of hyperactive transposases**

Dimitrije Ivančić, Alejandro Agudelo, Jonathan Lindstrom-Vautrin, Jessica Jaraba-Wallace, Maria Gallo, Ravi Das, Alejandro Ragel, Jorge Herrero-Vicente, Irene Higueras, Federico Billeci, Marta Sanvicente-García, Paolo Petazzi, Noelia Ferruz, Avencia Sánchez-Mejías, Marc Güell. *Nature Biotechnology*, 2025. DOI: 10.1038/s41587-025-02816-4

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**About Integra Therapeutics**

Integra Therapeutics is a biotech company that creates cutting-edge gene writing tools to improve the safety and efficacy of advanced therapies. Integra was founded in 2020 by Dr. Marc Güell and Dr. Avencia Sánchez-Mejías as a spinoff of Pompeu Fabra University (UPF). It has secured the backing of international investors (AdBio Partners, Columbus Venture Partners, Invivo Capital and Takeda Ventures), the European Commission, the Government of Spain and other organizations in the health and biomedical sector. It earned My Green Lab sustainability certification in 2023. The company has its corporate headquarters in Barcelona and its lab in the Advanced Therapies Platform at Hospital Sant Joan de Déu in Esplugues de Llobregat (Barcelona). More information: integra-tx.com

**About Pompeu Fabra University**

MELIS is a research-intensive department at Pompeu Fabra University (UPF), distinguished with three María

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de Maeztu awards (2014, 2018, 2024). Located within the Barcelona Biomedical Research Park (PRBB) — one of the city's leading biomedical hubs— MELIS hosts over 340 researchers across 40 groups, covering a broad spectrum of biological research topics.

The department demonstrates strong scientific productivity: in 2023, MELIS researchers published 477 articles in indexed journals, with 52% in D1 and 78% in Q1. Beyond publications, MELIS fosters innovation and collaboration, submitting 6 EU priority patent applications, securing 3 competitive technology transfer grants, and signing 32 industry contracts worth over €779K in the past year. The department also leads numerous outreach initiatives, enhancing both its global scientific visibility and societal impact. More information: https://www.upf.edu/web/biomed/inici

**About the Center for Genomic Regulation**

The Centre for Genomic Regulation (CRG) is a renowned international biomedical research center located in Barcelona. Founded in December 2000, the CRG houses an interdisciplinary research team of more than 400 scientists focused on understanding the complexity of life, from the genome to the cell and the entire organism. The CRG is a research center with a unique research model, focused on recruiting internationally recognized leaders in the field. The CRG forms part of the Barcelona Institute of Science and Technology (BIST) and is a CERCA research center of the Government of Catalonia. More information: www.crg.eu

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