Metagenomi Presents AI-Enabled Advancements of SMART Editing Platform at the Cold Spring Harbor Laboratory CRISPR Frontiers Conference

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AI-generated, compact SMART nucleases demonstrated robust genome editing activity in vitro in mammalian cells at multiple therapeutically relevant loci

Compact SMART genome editing tools that fit within delivery technologies constrained by cargo size may enable broad disease targeting

EMERYVILLE, Calif., Aug. 29, 2024 (GLOBE NEWSWIRE) -- Metagenomi, Inc. (Nasdaq: MGX), a precision genetic medicines company committed to developing curative therapeutics for patients using its proprietary gene editing toolbox, today presented a poster titled "Unlocking the Therapeutic Potential of Compact SMART Nucleases through Ancestral Reconstruction, Structure-Guided Engineering, and Generative AI" at the tenth meeting on Genome Engineering: CRISPR Frontiers at Cold Spring Harbor Laboratory, hosted in Cold Spring Harbor, NY from August 27-31, 2024. The work leverages the company's metagenomics-derived gene editing tools and a variety of AI methods to rapidly develop novel programmable CRISPR nuclease and base editing systems.

"Gene editing is a revolutionary technology and novel gene editing tools are needed to address limitations with current systems, including the need for small systems that are compatible with currently available delivery technologies," said Brian C. Thomas, CEO and founder of Metagenomi. "While there is no shortage of naturally occurring proteins that we can discover using our metagenomics platform, AI is one of several approaches we leverage to generate novel systems capable of highly efficient in vivo gene editing. We believe our metagenomics-based, AI-enhanced approach will allow us to achieve our goal of having the most effective gene editing tools to address any genetic disease anywhere in the human genome."

In today's poster presentation, Metagenomi demonstrated that metagenomics-informed synthetic sequence generation, including ancestral sequence reconstruction and generative AI techniques, can produce novel nucleases and base editors. These AI-based gene editing system variants show high editing efficiency in mammalian cells and include compact base editors that are less than 1,000 amino acids in length. Other key points from the presentation include:

- Both the SMART nucleases and base editors fit well within the carrying capacity of viral vector-based delivery systems.
- Compact SMART nucleases are promising for genome editing due to their small size but are extremely rare in nature, significantly limiting engineering efforts based on similar proteins.
- De novo, AI-generated, synthetic nucleases expand on natural systems and demonstrate robust activity in mammalian cells.
- Rational engineering further improved activity based on a newly solved structure of the enzyme and achieved saturating levels of editing in human cells (Ocampo, Rodrigo Fregoso, et al. "DNA targeting by compact cas9d and its resurrected ancestor." *bioRxiv*, https://doi.org /10.1101/2024.04.08.588528).

"While other groups use generative AI to focus on creating systems very similar to SpCas9, our work highlights how Metagenomi is uniquely positioned to combine the incredible diversity from our metagenomics database of over 11 billion proteins with our understanding of both SMART biochemistry and generative AI to create gene editing tools that open up new capabilities and therapeutic applications," said Christopher Brown, Head of Discovery at Metagenomi. "Combining metagenomics and generative AI is in its early stages, but our poster at today's CRISPR Frontiers Conference suggests the potentially significant value we seek to realize by training generative AI models with our vast collection of proteins recovered from the natural environment. Large datasets such as ours allow generative AI algorithms to find novel solutions with even greater precision and speed, and are valuable resources for accelerating drug development."

About Metagenomi

Metagenomi is a precision genetic medicines company committed to developing curative therapeutics for patients using its proprietary, comprehensive metagenomics-derived toolbox. Metagenomi is harnessing the power of metagenomics, the study of genetic material recovered from the natural environment, to unlock four billion years of microbial evolution to discover and develop a suite of novel editing tools capable of correcting any type of genetic mutation found anywhere in the genome. Its comprehensive genome editing toolbox includes programmable nucleases, base editors, and RNA and DNA-mediated integration systems (including prime editing systems and clustered regularly interspaced short palindromic repeat associated transposases). Metagenomi believes its diverse and modular toolbox positions the company to access the entire genome and select the optimal tool to unlock the full potential of genome editing for patients. For more information, please visit https://metagenomi.c.

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This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements, which are often indicated by terms such as "anticipate," "believe," "could," "estimate," "expect," "goal," "intend," "look forward to," "may," "plan," "potential," "predict," "project," "should," "will," "would" and similar e include, but are not limited to, any statements relating to our growth strategy and product development programs, including the timing of and our ability to conduct IND-enabling studies, make regulatory filings such as INDs, statements concerning the potential of therapies and product candidates, statements concerning the timing of data presentations and publications, and any other statements that are not historical facts. Forward looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition, and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; our ability to obtain, perform under, and maintain financing and strategic agreements and relationships; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials; uncertainties relating to preclinical and clinical testing; our dependence on third party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual property matters; competition; as well as other risks described in "Risk Factors," in our most recent Form 10-K and our most recent 10-Qs on file with the Securities and Exchange Commission. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and we claim the protection of the safe harbor for forward-looking statements contained in the Private

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