Editas Medicine Co-founder Develops Novel Approach to Increase Specificity of CRISPR/Cas9 Technology; Findings Published in Nature Biotechnology

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Approach May Enhance Therapeutic Potential of Editas' Genome Editing Technology

Cambridge, Mass., January 27, 2014 – Editas Medicine, a transformative genome editing company, today announced new published research from company co- founder J. Keith Joung, M.D., Ph.D., demonstrating the ability of truncated guide RNAs (tru-gRNAs) to increase the specificity of the novel genome editing technology CRISPR (clustered, regularly interspaced short palindromic repeats)/Cas9 (CRISPR- associated protein 9). This approach has the potential to further refine Editas' CRISPR/Cas9 technology and enhance the company's ability to knock-out, knock- down or selectively edit disease-causing genes. The paper was published in the current online edition of *Nature Biotechnology*[1] and co-authored by Dr. Joung, who is associate chief of pathology for research and an associate pathologist at Massachusetts General Hospital and associate professor of pathology at Harvard Medical School.

"Despite recent enhancements to CRISPR-based systems, the development of additional methods to improve specificity has remained an important priority in our ongoing research," said Dr. Joung. "These results define a simple, effective way to minimize off-target effects and still impact on-target nucleotides of interest with high efficiencies, allowing us to manipulate CRISPR/Cas9 technology with greater control and accuracy, which will be extremely important as we continue to optimize genome editing technology for therapeutic use."

Tru-gRNAs behave similarly to standard guide RNAs (gRNAs), RNA sequences that direct CRISPR/Cas9 nucleases to genomic locations of interest in Editas' genome editing system, but bear shorter regions of target site complementarity. These findings demonstrate that tru-gRNAs substantially reduce the off-target effects of CRISPR/Cas9 nucleases without compromising on-target activities, and can improve Cas9 specificity by 5,000-fold or more at off-target sites. Tru-gRNAs achieved even greater reductions in off-target effects when combined with paired Cas9 variants that nick DNA, also known as paired nickases, which have been developed previously by other Editas co-founders. Tru-gRNAs have also been successfully used with other non-nuclease applications of Cas9, such as dCas9 gene regulatory proteins. These results show the overall approach is flexible and simple to implement, does not require any new vectors, and is an effective strategy to improve the specificities of Cas9 nucleases or paired nickases for genome editing.

About Genome Editing

Following an explosion of high-profile publications on CRISPR/Cas9 and TALENs, genome editing has emerged as one of the most exciting new areas of scientific research. These recent advances have made it possible to modify, in a targeted way, almost any gene in the human body with the ability to directly turn on, turn off or edit disease-causing genes. Editas Medicine's five founders have published much of the foundational work that has elevated genome editing technology to a level where it can now be optimized and developed for therapeutic use.

CRISPR (clustered, regularly interspaced short palindromic repeats)/Cas9 (CRISPR- associated protein 9) and TALENs (transcription activator-like effector nucleases) comprise novel gene editing methods that overcome the challenges associated with previous technologies. Early published research on CRISPR/Cas9, coupled with a growing body of work on TALENs, suggests the potential to pursue therapeutic indications that have previously been intractable to traditional gene therapy, gene knock-down or other genome modification techniques. The CRISPR/Cas9 system, the most recent and exciting approach to emerge, acts by a mechanism in which the Cas9 protein binds to specific RNA molecules. The RNA molecules then guide the Cas9 complex to the exact location in the genome that requires repair. CRISPR/Cas9 uniquely enables highly efficient knock-out, knock-down or selective editing of defective genes in the context of their natural promoters, unlocking the ability to treat the root cause of a broad range of diseases.

About Editas Medicine

Editas Medicine is a transformative genome editing company founded by five world leaders in the fields of genome editing, protein engineering, and molecular and structural biology, with specific expertise in CRISPR/Cas9 and TALENs technologies. The company's mission is to translate its genome editing technology into a novel class of human therapeutics that enable precise and corrective molecular modification to treat the underlying cause of a broad range of diseases at the genetic level. Editas Medicine was launched in November 2013 with funding from Flagship Ventures, Polaris Partners and Third Rock Ventures with participation from Partners Innovation Fund. For more information, visit www.editasmedicine.com.

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1. Fu Y., Sander J.D., Reyon D., Cascio V.M., Joung K.J. Improving CRISPR-Cas nuclease specificity using truncated guide RNAs. *Nature Biotechnology* , 2014 Jan 26; doi: 10.1038/nbt2808. [Epub ahead of print]