Editas Medicine Reports New Data Characterizing Novel Properties of Staphylococcus aureus Cas9 as a Tool for CRISPR-Based Genome Engineering

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Poster Presented at Keystone Symposium for Precision Genome Engineering and Synthetic Biology

Cambridge, Mass., January 12, 2015 – Editas Medicine, a leading genome editing company, today presented new data characterizing the Cas9 enzyme isolated from the bacterium *Staphylococcus aureus* for CRISPR-based genome engineering. This newly emerging version of Cas9 is structurally distinct from the most common version of Cas9 used in scientific research to date, and it has a number of favorable characteristics for developing medicines. *S. aureus* Cas9 expands the repertoire of DNA sequences that can be targeted and may also overcome some limitations related to viral–based therapeutic delivery of CRISPR/Cas9. The data were presented at the Keystone Symposium for Precision Genome Engineering and Synthetic Biology in Big Sky, MT.

"Cas9 is a very powerful genome editing tool, but there are significant opportunities to improve its characteristics in order to develop therapeutics," said Katrine Bosley, chief executive officer, Editas Medicine. "Editas is committed to rigorously enabling the full potential of genome editing by developing advanced systems with expanded platform capabilities. We believe this will allow us to develop meaningful new medicines that address a broad range of genetically-driven diseases."

The poster presentation, titled *Staphyloccocus aureus Cas9: An Alternative Cas9 for Genome Editing Applications,* presents the use and characterization of a Type II CRISPR endonuclease Cas9 isolated from the bacterium *S. aureus*, as opposed to the most commonly used Cas9 which is derived from *Streptococcus pyogenes*. Editas demonstrated several key characteristics of *S. aureus* Cas9:

- **Efficiency:** *S. aureus* Cas9 exhibits DNA cleavage rates comparable to *S. pyogenes* Cas9 in human tissue culture cells.
- **Protospacer Adjacent Motif (PAM) sequence identity:** Cas9 enzymes recognize target DNA sequences based on two elements: the sequence of the guide RNA (gRNA) associated with the Cas9 and the PAM sequence for a given Cas9. While the gRNA can be engineered to any desired sequence, the PAM for a given species of Cas9 is inherent to the protein and does not change when a different gRNA is used. The PAM is a short sequence that must be present in the target DNA in order for the Cas9 enzyme to engage and edit a DNA sequence. The PAM for *S. aureus* Cas9 was shown to be distinct from the PAM for *S. pyogenes* Cas9, expanding the range of DNA sites that can be targeted.
- **Guide RNA length optimization:** gRNA targeting sequences ranging from 15 to 24 nucleotides were tested, identifying differences in on-target DNA cleavage efficiency as well as off-target activity. Sequences greater than 18 nucleotides in length were active with maximal activity achieved in the 20-24 nucleotide range.
- **Size:** *S. aureus* Cas9 is 315 amino acids smaller than *S. pyogenes* Cas9, which is too large to fit into the commonly used AAV (adeno-associated virus) delivery vectors together with a gene encoding a guide RNA (gRNA). In contrast, *S. aureus* Cas9 is sufficiently small to be co-delivered with one or more gRNA gene in a single AAV vector. Together, the findings demonstrate that the *S. aureus* Cas9 is an effective, yet significantly smaller, tool for genome editing with key properties distinct from the more widely used *S. pyogenes* Cas9. Thus, the characterization of *S. aureus* Cas9 could represent a significant step towards the development of CRISPR/Cas-based therapeutics. The scientific poster will be available on Editas Medicine's website.

About Genome Editing

Genome editing is a method to perform sequence-targeted modifications at the DNA level. Recent advances in the field 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.

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 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 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 is a leading genome editing company and part of a transformational new area of health care – genomic medicine. The company was founded by pioneers and world leaders in genome editing bringing specific expertise in CRISPR/Cas9 and TALENs technologies. The company's mission is to translate its proprietary technology into novel solutions to treat a broad range of genetically-driven diseases. For more information, visit www.editasmedicine.com.

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