THE ALCAS12A ENZYME THAT CUTS IN CIS AND TRANS: A NEW REVOLUTION IN DIAGNOSTICS AND GENE EDITING

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RESUMEN

Molecular Microbiology research group at the University of Alicante has described a new Cas12a endonuclease, named AlCas12a, derived from a wastewater metagenome. This protein is smaller than the usual variants and recognizes a PAM of only two nucleotides, which expands the number of target sequences and facilitates its delivery to cells.

AlCas12a cleaves both cis (at specific double-stranded DNA sequences) and trans (degrading any single-stranded DNA). This duality makes it a highly versatile tool for precise gene editing, epigenetic regulation, mutant selection, molecular diagnosis of diseases and pathogens, and the production of antimicrobial agents. In addition, the tool gives bacteria the ability to resist viral infections, whether or not they have specific target sequences, allowing bacterial cultures to be protected from existing and emerging viruses.

Companies interested in acquiring the technology for commercial exploitation through patent licensing agreements are sought.

VENTAJAS Y ASPECTOS INNOVADORES

ADVANTAGES OF THE TECHNOLOGY

This novel technology offers the following **advantages**:

1. The **small size** of the AlCas12a protein (1226 amino acids) facilitates administration via plasmid and viral vectors.
2. **Flexible PAM recognition** (5'-TTN-3' nucleotides) expands the number of editable sites.
3. **Trans-cutting activity** enables the creation of molecular diagnostic systems.
4. The **operating temperature range** (between 20-45 °C) allows its application in a wide variety of organisms, including plants and animals (both ectotherms and endotherms).
5. It enables **universal defence against invasive DNA** without the need for crRNA, protecting bacteria from DNA viruses regardless of their sequence.
6. **Dead AlCas12a mutants** with no cutting activity can be used as expression regulators, among many other applications.
7. **Potential as a sequence-specific antibacterial agent**, offering an alternative to antibiotics.
8. They have the potential to enable gene silencing or deletion, mutagenesis, and specific sequence corrections in the genome of any cell in an **easy, fast,** and **highly accurate** manner.
9. The inability of AlCas12a to process guide RNAs allows the use of **optimised guides with modified sequences** without the risk of them being altered by the effector protein.

INNOVATIVE ASPECTS OF THE TECHNOLOGY

AlCas12a is smaller than most commercial variants and is capable of recognising a very simple DNA pattern (PAM) (5'-TTN-3'), which broadens

the range of editable targets and facilitates its administration to cells.

AICas12a maintains cis and trans cleavage activity, as well as potent single-stranded DNA degradation without a guide, making it a versatile tool for gene editing, disease diagnosis, and the production of specific antibacterials. It also lacks ribonuclease activity, allowing modified crRNAs to be used without altering their sequence.

APLICACIONES DE LA OFERTA

The patent describes uses ranging from genetic editing in plants and animals to the development of virus-resistant bacteria and rapid pathogen detection. The combination of compact size, permissive PAM, and absence of ribonuclease activity positions AICas12a as a versatile tool that can be adapted to research and biotechnology needs more easily than current versions of Cas12a.

Among the main **fields of application**, the following stand out: Biology, Biotechnology, Biomedicine, and Agri-food, with the following uses being the most important:

- Genetic editing.
- Production of antibacterials.
- Non-specific degradation of single-stranded DNA sequences.
- Selection of mutants.
- Molecular diagnostics.
- Gene expression regulation.
- Epigenetic modification.

Its potential for precise editing, specific sequence detection, and protection against bacterial infections, especially when the bacteria are resistant to antibiotics, opens up new avenues for basic research and clinical application, consolidating the role of CRISPR-Cas systems as pillars of modern biology.

COLABORACIÓN BUSCADA

We are looking for companies interested in acquiring this technology for **commercial exploitation** through patent **licensing agreements**.

Company profile sought:

- Genetic editing companies.
- Molecular diagnostics laboratories.
- Manufacturers of antibacterial and antimicrobial agents.
- Pharmaceutical and biomedicine companies.
- Genetic administration vector companies.
- Research institutions and universities with synthetic biology and microbiology programmes.
- Biotechnology start-ups focused on infection control and bacterial resistance solutions.