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Novel Small Molecule Inhibitors of Endosomal Trafficking for the Treatment of Viral and Bacterial Infection

Tech ID: 23631 / UC Case 2013-466-0

SUMMARY

Researchers at UCLA have identified a class of novel small molecule inhibitors of endosomal trafficking. This inhibitor can be used to block the cellular entry of bacterial toxins and viruses that require trafficking to acidified endosomes.

BACKGROUND

The endocytic pathway is a vital host cell process consisting of several distinct compartments that internalize molecules and recycle them back to the cell surface or target them for degradation. Many viruses and bacteria have evolved mechanisms to take advantage of this pathway to gain entry into and/or transport proteins (such as toxins) into the cytosol of host cells. Small molecules that disrupt the binding, entry and trafficking of bacterial toxins or viruses could be developed as novel therapeutics for the prevention and treatment of certain infectious diseases.

INNOVATION

A cross-disciplinary team of investigators at UCLA including Dr. Ken Bradley in the Department of Microbiology, Immunology & Molecular Genetics and Dr. Michael Jung in the Department of Chemistry and Biochemistry have identified a series of novel small molecule inhibitors of endosome trafficking. These compounds were initially identified in a small molecule screen for inhibitors of anthrax lethal toxin (LT), a toxin known to be trafficked and activated through the endocytic pathway. Validation studies demonstrated the compounds work by blocking trafficking of LT to acidified endosomes, and are well-tolerated by cells at therapeutic doses. The compounds inhibit multiple intracellular toxins and viruses that share a requirement for trafficking to acidified endosomes including: diphtheria toxin, exotoxin A, LCMV and influenza.

APPLICATIONS

- Lead compounds for therapeutic development
- Research tools

ADVANTAGES

- Non-cytolytic and well tolerated in vitro (cell culture)
- Capable of inhibiting entry of various viruses and bacterial toxins
- Novel mechanism

STATE OF DEVELOPMENT

The lead compound was identified using a high throughput screen. Its activity has been validated in cell culture. Many structural analogues have been prepared in a structure-activity relationship (SAR) study and the parameters for activity identified. We have also been able to identify a new analog with higher activity than the original lead.

RELATED MATERIALS

Novel Small Molecule Inhibitors of Endosomal Trafficking for the Treatment of Viral and Bacterial Infection. Proc Natl Acad Sci U S A.

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Contact Our Team



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INVENTORS

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OTHER INFORMATION

KEYWORDS pharmaceutical, therapeutic, small molecule, anthrax, LCMV, influenza, endosomes, endocytotic pathway, endosome trafficking. infectious disease

CATEGORIZED AS

- Medical
 - Disease: Infectious
 - Diseases
 - ▶ New Chemical Entities,
 - Drug Leads
 - Research Tools
 - Therapeutics

RELATED CASES 2013-466-0

PATENT STATUS

Country	Туре	Number	Dated	Case
United States Of America	Issued Patent	10,730,848	08/04/2020	2013-466

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