Development of Novel Fluorescent Puromycin Derivatives

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BACKGROUND

Puromycin is an aminonucleoside antibiotic produced by the bacterium *Streptomyces alboniger.* Its mode of action is to inhibit protein synthesis by disrupting peptide transfer on ribosomes, leading to premature chain termination during protein translation. Puromycin blocks protein synthesis in both eukaryotes and prokaryotes and is routinely used as a research tool in cell culture. The native Puromycin is also used assays such as mRNA display. As such, derivatives have been synthesized in which the amino acid of the 3' end of adenosine based antibiotics is altered to change the compound's antibiotic activity. Other compounds have been synthesized with differing amino acids and functionalities to examine the effect it has on bacterial viability. The majority do not show useful absorption or emission profiles. What is needed is a method to track the compounds in biological systems.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have synthesized derivatives of puromycin in which a fluorophore is incorporated into the core skeleton of the molecule. These compounds have incorporated adenosine nucleobases with red-shifted absorbance and emission that provide a facile method to track the compounds in biological systems. We believe that these derivatives will also show altered photophysical signals, which will facilitate real time monitoring of translation-related events.

The invention provides the puromycin analogs incorporating a thieno[3,4-d]pyrimidine heterocycle replacing the native adenosine skeleton. These compounds exhibit antibiotic activity. The photophysical properties demonstrate that the compounds are able to be tracked using absorption and emission and the nucleobase has been tested and exhibits desirable photophysical properties.

APPLICATIONS

These derivatives may potentially be used clinically for the treatment of infectious diseases. The additional benefit of installing fluorescence in nucleoside based antibiotics is the possibility for introducing a novel quantitative method for measuring bacterial viability *in vivo* or to facilitate the discovery of new analogs via high throughput fluorescence-based assays.

ADVANTAGES

Various nucleoside-based antibiotics have been developed to enhance and investigate antibiotic activity. Our molecule has incorporated adenosine nucleobases with red-shifted absorbance and emission that may provide a facile method to track the compounds in biological systems.

STATE OF DEVELOPMENT

A puromycin derivative incorporating a theino[3,4-d] pyrimdine nucleus has been synthesized, and exhibits antibiotic activity. Probing the photophysical properties is also necessary to ensure the compound is able to be tracked using absorption and emission. The nucleobase itself has been tested and exhibits desirable photophysical properties.

INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

Antibiotic, protein synthesis, ribosome, translation, fluorescence-based assays, photophysical signals, puromycin, red-shifted absorbance

CATEGORIZED AS

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