Universal Nucleotidyltransferases Expand Sugar Substrate Families Available for Glycorandomization

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing mutant enzymes that expand the types of substrates that can be used in enzymatic glycorandomization, thereby increasing the diversity of chemical libraries for drug screening.

OVERVIEW

Many of the compounds used in drug discovery by pharmaceutical companies are glycosylated, bacterial secondary metabolites. A glycosylated metabolite consists of a central core structure (aglycon) and various sugar (glycosyl) attachments.

Because the sugar moieties of many of these metabolites define their biological activities, altering the carbohydrate ligands can lead to valuable new pharmaceuticals. A UW-Madison researcher previously developed a glycorandomization method for rapidly generating a diverse library of novel glycosylated compounds for use in drug discovery (see WARF reference number P04020US). This method uses nucleotidyltransferases to efficiently produce a large pool of sugar molecules that then can be combined with various aglycons. However, no known nucleotidyltransferase utilizes all eight naturally occurring nucleotide triphosphates (NTPs), limiting the types of sugar substrates that can be used in enzymatic glycorandomization.

THE INVENTION

The UW-Madison researcher has discovered that the nucleotidyltransferase protein RmlA is capable of utilizing all naturally occurring NTPs. He used X-ray crystallographic protein structures to design variations of RmlA with mutations at a specific amino acid in the active site of the enzyme. These mutants have an increased purine/pyrimidine bias in NTP substrate specificity. They can be used in the production of diverse purine-based sugar nucleotide libraries.
APPLICATIONS

• Creation of more diverse libraries of sugar substitutes that can be used in enzymatic glycorandomization to create libraries of novel compounds that in turn can be screened for use as pharmaceuticals, food ingredients, fine chemicals or agricultural products
• Conversion of purine-based nucleotides into glycosyl nucleotides

KEY BENEFITS

• Utilizes purine-based nucleotides more efficiently than wild-type RmlA
• Expands the types of substrates that can be used in the inventor’s enzymatic glycorandomization method
• May increase the diversity of chemical libraries created using this method

ADDITIONAL INFORMATION

Related Technologies
See WARF reference number P04020US for more information about glycorandomization.

Publications

Tech Fields
Drug Discovery - Drug production & design

CONTACT INFORMATION

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847.