



Novel Glycosyltransferases and Improved Methods of Creating Glycosylated Nucleotides for Drug Discovery

[View U.S. Patent No. 8,637,287 in PDF format.](#)

WARF: P100340US02

Inventors: Jon Thorson, Richard Gantt

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a method of efficiently synthesizing novel nucleotide diphosphate sugars for use in research and drug discovery.

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). In this method, at least one aglycon and a pool of nucleotide diphosphate (NDP)-sugars are incubated with a glycosyltransferase enzyme to produce glycorandomized structures.

However, a huge hurdle in the production of these compound libraries is the generation of the glycosylated nucleotides that serve as sugar donors. Synthesis of sugar nucleotides is expensive, difficult and time-consuming.

The Invention

UW–Madison researchers have developed novel glycosyltransferases and improved methods of synthesizing NDP-sugars. The methods exploit the reversibility of glycosyltransferases to rapidly generate exotic NDP-sugars. These nucleotides are a starting material in the generation of glycosylated drug compounds using the glycorandomization methodology.

The researchers discovered that in addition to transferring sugar groups from an NDP-sugar to another molecule, glycosyltransferases can catalyze the removal of sugars from glycosylated natural products and the transfer of a sugar from one natural product backbone to a different natural product backbone, thus allowing sugars and aglycons to be exchanged with ease.

Applications

- Preparation of NDP-sugar libraries for biochemical research and drug discovery
- Preparation of ^{13}C labeled sugars for research
- Microscale glycosyl scanning to rapidly assess large compound libraries

Key Benefits

- Libraries of novel NDP-sugars can be prepared rapidly and efficiently.



Stage of Development

Milligram quantities of 22 fully characterized NDP-sugars were generated in a matter of hours.

Additional Information

Related Technologies

- [See WARF reference number P04020US for more information about glycorandomization.](#)

Tech Fields

- [Drug Discovery & Development : Compound libraries](#)

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