Use of Glycorandomization to Produce Novel Glycosylated Products for Drug Discovery

**INVENTORS** • Jon Thorson

WARF: P04020US
View U.S. Patent No. 6,884,604 in PDF format.

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing combinatorial methods for rapidly generating a diverse library of novel glycosylated compounds for use in 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; however, current methods of generating novel glycosylated metabolites for testing as drug candidates have severe limitations.

**THE INVENTION**

A UW-Madison researcher has developed combinatorial methods for rapidly generating a diverse library of novel glycosylated compounds for use in drug discovery.

Glycorandomization is a chemoenzymatic strategy that overcomes the limitations in natural product derivatization associated with both chemistry-based approaches and in vivo engineering.

In the methods, at least one aglycon and a pool of nucleoside diphosphate (NDP)-sugars are incubated with a glycosyltransferase enzyme to produce glycorandomized structures. The pool of NDP-sugars may include difficult-to-produce or never-before-produced sugars, which can now be made easily and efficiently through a one-step nucleotidyltransferase-catalyzed conversion developed by the inventors. The glycorandomized structures may be incubated with the sugars and glycosyltransferase multiple times to generate additional compounds. The glycorandomized structures may also be incubated with at least one chemoselectively ligatable moiety to generate chemoselectively-ligated compounds.
APPLICATIONS

• Synthesis of large libraries of novel compounds for drug discovery

KEY BENEFITS

• Provides a next generation tool in drug discovery
• Enables rapid synthesis of compounds too complex for chemical synthesis and not amenable to biosynthesis
• For the first time, allows construction of large libraries of diverse macrolides with varied carbohydrate attachments
• Since the novel compounds are generally based on biologically-active, natural products, the potential for generating compounds with novel and useful activities is high.
• Compounds may be useful in clinical therapy, biomedical research, and chemical synthesis of downstream products.

STAGE OF DEVELOPMENT

Successfully used to generate novel novobiocin derivatives and erythromycin analogs.

ADDITIONAL INFORMATION

Related Technologies
These methods have also been successfully used to generate a large library of vancomycin derivatives (WARF reference number P04116US).

Tech Fields
Drug Discovery - Drug production & design
Drug Discovery - Libraries
Materials & Chemicals - Synthesis

CONTACT INFORMATION

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