Various PMST1 Mutants and the Synthesis of a Library of Sialyl Lewis X Containing Different Sialic Acid Forms

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ABSTRACT

Researchers at the University of California, Davis have developed a new method of obtaining a library of sialyl Lewis x and other sialosides containing different sialic acid forms. This method utilizes engineered mutants of sialyltransferase PmST1. These novel mutants show lower donor hydrolysis activity and/or sialidase activity without compromising the sialyltransferase activity.

FULL DESCRIPTION

Sialic acids are a family of monosaccharides that are commonly found as terminal residues on cell surface glycoproteins/glycolipids of higher animals. They have a vital role in cellular communication and recognition.

To a much lesser degree, they are also found in microorganisms and their presence is often linked with pathogenicity. To study the importance of various sialic acid forms in nature, an efficient synthetic approach is required to obtain a library of sialyl Lewis x and other sialosides containing different sialic acid forms.

UC Davis researchers have discovered a novel method of creating a library of sialyl Lewis x that contains different sialic acid forms using a chemoenzymatic approach. This new method proceeds through the addition of a sialic acid analog to a fucosylated Lewis x structure. The *Pasteurella multocida* alpha-2-3-sialyltransferase (PmST1) was engineered to tolerate the Lewis x as its substrate. The resulting PmST1 mutant (PmST1_M144D) was successfully utilized to synthesize the library of interest.

UC Davis researchers also generated three other engineered mutant forms of PmST1: E271F, R313Y, and E271F/ R313Y. The three resulting mutants (E271F, R313Y, and E271F/ R313Y) all showed lowered sialidase activity without compromising the desired sialyltransferase activity. To summarize, the use of these novel PmST1 mutants sheds new light on glycosyltransferase-catalyzed reactions, provides a novel strategy to improve glycosyltransferase substrate promiscuity, and supplies novel catalysts for efficient synthesis of complex sialosides.

APPLICATIONS

Useful for:

- $PmST_1$ mutants (E271F, R313Y, and E271F/ R313Y): Optimizing sialyltransferase-catalyzed reactions by lowering sialdase activity
- Creating a library of sialyl Lewis x that contains different sialic acid forms efficiently

FEATURES/BENEFITS

- Enzymatic sialylation avoids tedious protection and deprotection processes required by chemical sialylation
- More efficient approach to generating a library of sialyl Lewis x that contains different sialic acid forms
- $PmST_1$_M144D: easy to obtain, robust sialyltransferase, efficient
- Decreased sialidase activity
- $PmST_1$ mutants (E271F, R313Y, and E271F/R313Y

OTHER INFORMATION

KEYWORDS

Synthesis of sialosides, sialyltransferase, Sialyl Lewis x, sialic acid, PmST

CATEGORIZED AS

- **Biotechnology**
  - Industrial/ Energy
  - Other
- **Materials & Chemicals**
  - Chemicals
- **Medical**
  - Research Tools
  - Screening
- **Research Tools**
  - Reagents

RELATED CASES

2011-790-0, 2011-791-1

- Powerful sialyltransferases with decreased sialidase activity
- Good for sialylation when the reactions are not practical to monitor

PATENT STATUS

Country	Type	Number	Dated	Case
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