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Model-based Optimization of Neu5Ac Synthesis

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PURPOSE OF THE ABSTRACT

Sialic acids (SAs) are a group of more than 50 structurally distinct α-keto acids found in viruses, mammalian cells, and microorganisms1. They control various biological functions such as development, recognition, cell signaling, cell-cell interactions, and adhesion2. Sialylation of neural cell adhesion molecules during embryonic development is crucial for proper neural tissue development, while in certain cancers, sialylation is correlated with tumorigenesis and metastasis3. Pathogenic bacteria use sialylated glycoproteins and glycolipids to mask their presence from the host's immune system. There are over fifty molecules of sialic acid that carry diverse substituents at hydroxyl or amino groups, and their distribution is strongly regulated on a gene level and varies depending on the species of animal and cell's function4. N-Acetylneuraminic acid (Neu5Ac) is the most commonly occurring and studied SA, and its biosynthesis is controlled by Neu5Ac synthase, which catalyzes the aldol-like condensation of phosphoenolpyruvate (PEP) to N-Acetylmannosamine (ManNAc) to yield Neu5Ac.

In this work, a thorough kinetic analysis of Neu5Ac synthase (NeuB) catalysed synthesis of Neu5Ac was done in order to build the kinetic model and use it to find the bottlenecks of the system and optimize the reaction. The interdependent relationships between process variables of NeuB from Neisseria meningitidis and a promising NeuB homologue from metagenomic library were successfully investigated and evaluated for their potential use in SA synthesis5.

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FIGURES

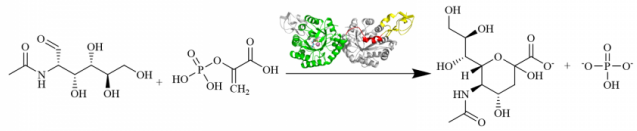

FIGURE 1

Scheme 1.

NeuS catalyzed Neu5Ac synthesis from ManNAc and PEP via aldol-like addition

FIGURE 2

KEYWORDS

Neu5Ac synthase | Enzyme kinetics | Optimization | Biocatalysis

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