## Proposed EC/sub-subclass

2.4.1.102

## Accepted name

Core 2 beta-1,6-N-acetylglucosaminyltransferase

## Synonyms

Core 2-branching enzyme; Core2 GlcNAc-transferase; Leukocyte type core 2 beta-1,6-N-acetylglucosaminyltransferase

## Phylogeny

GCNT1 is conserved across various mammalian species, including mouse, rat, and cattle, indicating its essential role in mucin-type O-glycosylation pathways (gupta2020asystematicreview pages 15-17, taniguchi2014handbookofglycosyltransferases pages 149-151). It shares significant sequence identity (approximately 40–50%) with isoenzymes such as Core2GlcNAcT-III, reflecting preserved catalytic mechanisms among core-branching glycosyltransferases (taniguchi2014handbookofglycosyltransferases pages 146-148). Phylogenetic analyses place GCNT1 within a group of glycosyltransferases involved in the elongation and branching of O-glycans, highlighting its evolutionary conservation across metazoans (schjoldager2020globalviewof pages 6-6, taniguchi2014handbookofglycosyltransferases pages 149-151).

## Glycosyltransferase family

GT14

## Reaction Catalyzed

GCNT1 catalyzes the transfer of an N-acetylglucosamine (GlcNAc) unit from UDP-N-acetylglucosamine (UDP-GlcNAc) to the 6-hydroxyl group of the galactose residue in a mucin-type core 1 O-glycan, resulting in the formation of core 2 O-glycans. The reaction can be summarized as follows:  
UDP-GlcNAc + Galβ1-3GalNAcα-Ser/Thr → UDP + Galβ1-3(GlcNAcβ1-6)GalNAcα-Ser/Thr (taniguchi2014handbookofglycosyltransferases pages 143-146, taniguchi2014handbookofglycosyltransferases pages 149-151).

## Cofactor Requirements

GCNT1 operates independently of metal ions, distinguishing it from many glycosyltransferases that require divalent metal ions (taniguchi2014handbookofglycosyltransferases pages 149-151, cheng2011mucinoglycanbranching pages 4-6).

## Substrate Specificity

GCNT1 preferentially acts on mucin-type core 1 O-glycan motifs, specifically recognizing Galβ1-3GalNAc structures linked to serine or threonine residues (taniguchi2014handbookofglycosyltransferases pages 143-146, taniguchi2014handbookofglycosyltransferases pages 149-151). It can also transfer GlcNAc to glycolipid substrates, such as GalGb4Cer globosides, contributing to the biosynthesis of stage-specific embryonic antigen 1 (SSEA-1) determinants (gupta2020asystematicreview pages 15-17, taniguchi2014handbookofglycosyltransferases pages 149-151).

## Structure

GCNT1 is a type II transmembrane protein characterized by a short N-terminal cytosolic tail, a single transmembrane domain, a stem region with potential N-linked glycosylation sites, and a large lumenal catalytic domain (cheng2011mucinoglycanbranching pages 2-4, taniguchi2014handbookofglycosyltransferases pages 146-148). The catalytic domain adopts a GT-A fold, featuring a central mixed β-sheet and α-helices, with key catalytic residues including a free cysteine (Cys217) and glutamic acid (Glu320) that facilitate substrate binding and catalysis (unknownauthors2010structuralandfunctional pages 25-30, pak2011structuralandmechanistic pages 11-12).

## Regulation

GCNT1 expression is regulated at the transcriptional level by factors such as Sp1 and cytokines (IL-2, IL-4, IL-15) in activated T-cells (unknownauthors2010structuralandfunctional pages 30-36). Post-translational modifications, including N-linked glycosylation, influence its stability and localization within the Golgi (cheng2011mucinoglycanbranching pages 2-4, taniguchi2014handbookofglycosyltransferases pages 146-148). Additionally, substrate availability and competition with other glycosyltransferases can modulate GCNT1 activity (taniguchi2014handbookofglycosyltransferases pages 143-146, taniguchi2014handbookofglycosyltransferases pages 149-151).

## Function

GCNT1 is crucial for synthesizing mucin-type core 2 O-glycans, which serve as scaffolds for complex glycan structures, including selectin ligands essential for leukocyte adhesion and migration (taniguchi2014handbookofglycosyltransferases pages 154-156, taniguchi2014handbookofglycosyltransferases pages 149-151). It is predominantly expressed in leukocytes, particularly activated T-cells, highlighting its role in immune responses (unknownauthors2010structuralandfunctional pages 30-36).

## Disease relevance

GCNT1 has been implicated in various cancers, with increased expression correlating with aggressive tumor behavior and altered glycan structures affecting cell adhesion and immune interactions (gupta2020asystematicreview pages 14-15, dimitroff2019ibranchedcarbohydratesas pages 3-4). Dysregulation of GCNT1-mediated glycosylation may contribute to immune-related syndromes, including AIDS and Wiskott-Aldrich syndrome (taniguchi2014handbookofglycosyltransferases pages 154-156, taniguchi2014handbookofglycosyltransferases pages 149-151).

## Other Comments

GCNT1 demonstrates substrate flexibility, acting on both protein and glycolipid substrates, which contributes to the diversity of glycoconjugates (cheng2011mucinoglycanbranching pages 1-2, hodgson2023theroleof pages 9-10). Recombinant expression systems have been utilized for biochemical analyses, and viral homologs with high sequence identity suggest evolutionary adaptations in glycosylation pathways (taniguchi2014handbookofglycosyltransferases pages 154-156).

## References

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