## Proposed EC/sub-subclass

B4GALNT1 is classified under EC 2.4.1.92, indicating its role in transferring hexosamine residues via a β-linkage (kellokumpu2016glycosyltransferasecomplexesin pages 3-4, petit2021aphylogeneticview pages 10-11). This classification is based on its specificity for glycolipid substrates (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Accepted name

The accepted name for the enzyme is Beta-1,4 N-acetylgalactosaminyltransferase 1, with synonyms including GM2 synthase and GalNAc-T (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Phylogeny

B4GALNT1 is conserved across vertebrates, with orthologs in humans, mice, and rats (taniguchi2014handbookofglycosyltransferases pages 183-187). It shares sequence conservation with other glycosyltransferases involved in ganglioside synthesis (petit2021aphylogeneticview pages 6-7).

## Glycosyltransferase family

B4GALNT1 belongs to the CAZy glycosyltransferase family GT31, characterized by a GT-A fold and conserved motifs like the DXD motif (petit2021aphylogeneticview pages 4-5).

## Reaction Catalyzed

B4GALNT1 catalyzes the transfer of N-acetylgalactosamine from UDP-GalNAc to glycolipid acceptors, converting GM3, GD3, GT3, and GA3 into GM2, GD2, GT2, and GA2, respectively (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Cofactor Requirements

The enzyme requires Mn²⁺ ions for its activity, which are essential for coordinating the UDP-GalNAc donor substrate (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Substrate Specificity

B4GALNT1 specifically acts on glycolipid substrates, such as GM3, GD3, GT3, and GA3, and does not act on glycoproteins (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Structure

B4GALNT1 is a type II transmembrane protein with a catalytic domain containing a DXD motif for Mn²⁺ coordination. It forms homodimers and has three N-glycosylation sites essential for activity (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Regulation

Regulation includes transcriptional control, alternative splicing, and N-glycosylation. Increased expression is observed in certain cancers (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Function

B4GALNT1 is crucial for ganglioside biosynthesis in neural tissues, impacting cell recognition and signaling. It is highly expressed in the brain and retina (taniguchi2014handbookofglycosyltransferases pages 183-187).

## Disease relevance

Alterations in B4GALNT1 are linked to hereditary spastic paraplegia and various cancers, affecting ganglioside biosynthesis and cell signaling (hennet2002thegalactosyltransferasefamily pages 12-13).

## Other Comments

B4GALNT1’s activity is restricted to glycolipid substrates, and it requires Mn²⁺ for catalysis. Its role in ganglioside biosynthesis is significant for neural function and cancer biology (taniguchi2014handbookofglycosyltransferases pages 183-187).

## References

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