OPEN ACCESS Freely available online

Journal of Glycobiology

Commentary

Brief Note on Clinical Manifestations Involved in Genetic Disorders of Glycosylation

Aalten JK*

Department of Biochemistry and Molecular Biology and the Center for Blood Research, University of British Columbia, British Columbia V6T 1Z3, Canada

DESCRIPTION

Genetic Disorders of Glycosylation (GDDs) are a group of rare inherited metabolic disorders characterized by abnormalities in the glycosylation process. Glycosylation is the enzymatic addition of sugar molecules (glycans) to proteins or lipids, which is crucial for proper protein function and cellular processes. When glycosylation is impaired due to genetic mutations in specific genes, it can lead to a wide range of clinical symptoms and health problems.

Types of GDDs in glycosylation

Congenital Disorders of Glycosylation (CDG) are the most well-known and studied group of GDDs. They are further classified into two main subgroups:

- CDG-I disorders involve defects in the early stages of glycan synthesis and attachment, primarily affecting N-linked glycosylation. Examples include *PMM2*-CDG (formerly known as CDG-Ia) and *ALG1*-CDG.
- CDG-II disorders involve defects in glycan processing and maturation, typically affecting the later stages of N-linked glycosylation. Examples include *MGAT2*-CDG (formerly known as CDG-IIa) and *ALG8*-CDG.

O-linked glycosylation disorders: These disorders affect O-linked glycosylation pathways. Mutations in genes like *B3GALTL* cause defects in mucin-type O-glycosylation, leading to disorders like *B3GALTL*-CDG.

Sialic acid disorders: These disorders involve defects in the synthesis or transport of sialic acid, a key component of glycans. Sialic acid disorders can lead to conditions such as Salla disease and infantile sialic acid storage disease.

Defective glycan degradation disorders: In some cases, GDDs can result from mutations in genes involved in the degradation of glycan molecules. Examples include disorders like Schindler disease and Kanzaki disease.

Glycosylation pathways

There are two main types of glycosylation pathways namely N-linked glycosylation and O-linked glycosylation, each with its own subpathways and specific enzymes involved. Both pathways are essential for proper protein function and are tightly regulated processes. They influence protein stability, localization, interactions, and biological activity. Dysregulation of these pathways can lead to various diseases and disorders, highlighting the importance of understanding glycosylation in cellular biology and medicine.

N-linked glycosylation is a common type of protein glycosylation that involves the attachment of glycans to asparagine (Asn) residues within the consensus sequence Asn-X-Ser/Thr (where X can be any amino acid except proline). The N-linked glycosylation pathway occurs primarily in the Endoplasmic Reticulum (ER) and Golgi apparatus.In the early stages of N-linked glycosylation, a high-mannose glycan structure is added to the protein. This structure consists of multiple mannose residues.In the Golgi apparatus, high-mannose glycans are modified into complex N-glycans by adding various sugar residues (e.g., N-acetyl glucosamine, fucose, sialic acid). These modifications are crucial for glycan diversity and function.

O-linked glycosylation involves the attachment of glycans to serine (Ser) or threonine (Thr) residues on proteins. Unlike N-linked glycosylation, O-linked glycosylation is more diverse and less conserved. This is the most common form of O-linked glycosylation and involves the addition of N-acetylgalactosamine (GalNAc) to Ser or Thr residues. It can further lead to the formation of mucin-type O-glycan's, which are abundant in mucins and other secreted proteins.

Clinical manifestations and diagnosis

The clinical presentation of GDDs varies widely, but common symptoms include developmental delays, intellectual disability, seizures, muscle weakness, growth retardation, and various organ abnormalities. The severity of symptoms can also vary, from mild

Correspondence to: Aalten JK, Department of Biochemistry and Molecular Biology and the Center for Blood Research, University of British Columbia, British Columbia V6T 1Z3, Canada, E-mail: aal.k@gmail.com

Received: 15-Jun-2023, Manuscript No. JGB-23-26978; **Editor assigned:** 19-Jun-2023, PreQC No. JGB-23-26978 (PQ); **Reviewed:** 4-Jul-2023, QC No. JGB-23-26978; **Revised:** 11-Jul-2023, Manuscript No. JGB-23-26978 (R); **Published:** 19-Jul-2023, DOI: 10.35841/2168-958X.23.12.248.

Citation: JK Aal (2023) Brief Note on Clinical Manifestations Involved in Genetic Disorders of Glycosylation. J Glycobiol. 12:248.

to severe, and can affect multiple systems in the body. Diagnosis of GDDs typically involves a combination of clinical evaluation, biochemical testing, and genetic analysis. The analysis of serum glycoproteins, glycosylation profiles, and genetic sequencing can help identify the specific GDD subtype.

Treatment

There is no cure for GDDs, and treatment focuses on managing the symptoms and complications associated with the disorder. Therapies may include physical therapy, occupational therapy, speech therapy, and dietary management. In some cases, specific glycan supplements or medications may be used to alleviate symptoms.

CONCLUSION

It's important to note that GDDs are extremely rare and can manifest with a wide range of clinical symptoms, including developmental delays, intellectual disability, seizures, muscle weakness, and organ abnormalities. Diagnosis typically involves a combination of clinical evaluation, biochemical testing, and genetic analysis to identify the specific subtype and underlying genetic mutations. Management of GDDs focuses on symptom relief and support for affected individuals and their families.