International Research Journal of Biochemistry and Bioinformatics Vol. 13(4) pp. 1-3, August, 2023
Available online http://www.interesjournals.org/IRJBB

Mini Review

Utilization of Sialic Acid by Gut Microorganisms

Fennec Ken*

Medical University of Vienna, Center for Medical Biochemistry, Vienna, Austria

*Corresponding Author's E-mail: kenfennec@rediff.com

Received: 01-Aug-2023, Manuscript No. IRJBB-23-110216; **Editor assigned:** 03-Aug-2023, PreQC No. IRJBB-23-110216 (PQ); **Reviewed:** 17-Aug-2023, QC No. IRJBB-23-110216; **Revised:** 22-Aug-2023, Manuscript No. IRJBB-23-110216 (R); **Published:** 29-Aug-2023, DOI: 10.14303/2250-9941.2023.73

Abstract

Sialic acids are essential molecules with a wide range of structural variations. They have been found in higher creatures like Echinoderms, Hemichordata, Cephalochorda, and Vertebrata, as well as lower species like Platyhelminthes, Cephalopoda, and Crustaceae. Plants are known to be deficient in sialic acid. However, they have been observed in viruses, bacteria, protozoa, and fungus. Although deaminated neuraminic acid exists in both vertebrates and microorganisms, it is known to be abundant in lower vertebrates (Proudfoot 2009). Sialic acids are usually found at the terminals of glycoproteins and glycolipids, in capsular and tissue polysialic acids, in bacterial lipooligosaccharides/polysaccharides, and in other forms that determine their significance in biology (Olusegun et al., 2019).

Keywords: Sialic acid, Immunodetection, Neurobiology, Immune reactions, Viral infection, Microbiome, Diseases

INTRODUCTION

Sialic acids are a group of structurally similar sugars found on mucosal surfaces such as the human gut. Sialic acids play a variety of biological activities in the gut, particularly at the contact between the host epithelium and the microbiota. The most researched sialic acid, N-acetylneuraminic acid (Neu5Ac), provides a nutrition supply for bacteria and, when shown on the cell surface, a binding site for host immunological components, viruses, and bacterial toxins. Neu5Ac is widely changed by host and microbial enzymes, and the effects of Neu5Ac derivatives on host-microbe interactions, as well as human and microbial biology in general, are unknown (Hend et al., 2014).

Sialic acids are a diverse class of nine-carbon sugars with over 50 structurally and chemically different modifications. Sialic acids are major components of vertebrate glycoproteins, glycolipids, and milk oligosaccharides, as well as some microbial surface glycans, where they mediate a variety of functions such as glycan-protein, cell-cell, and microbe-host recognition. N-acetylneuraminic acid (2-keto-5-acetamido-3,5-dideoxy-D-glycero-D-galactononulopyranos-1-onic acid) (Neu5Ac) is the most frequent type of sialic acid in humans. Neu5Ac can be further changed by adding O-acetyl groups at the C-4, -7, -8, and -9 positions, or by hydroxylation of the N-acetyl group at the C-5 position to generate N- glycolylneuraminic acid (Neu5Gc). So far, the only enzyme known in humans that can O-acetylate Neu5Ac is capsule structure 1 domain 1 (CasD1), and its activity has been directly involved in the alteration of locations C-7 and C-9 (Morteza et al., 2013). Furthermore, it has been demonstrated that acetyl groups in position 7 may migrate spontaneously to locations C-8 and C-9, with the latter being the most stable form. CasD1 is hypothesized to add acetyl groups at C-7 before migrating to the C-9 position (Neu5, 9Ac2) under physiological conditions. This would allow CasD1 to add an extra acetyl group to C-7 to generate the di-O-acetylated Neu5, 7,9Ac3, albeit this has yet to be proven experimentally. CasD1 has been shown to act directly on cytidine-5-monophospho (CMP)-Neu5Ac prior to the transfer of the sialic acid moiety onto the acceptor target, implying that Neu5Ac is modified before sialylation, however, the ability of CasD1 to accommodate other acceptors such as sialoglycans has not been investigated. Additional O-acetyl modifications at the C-4 position can also be added to form Neu4, 5Ac2, although the enzyme mediating this process has yet to be discovered (Mohamed 2017).

O-Sulfation of sialic acid has received less attention than O-acetylation, and while sulfated sialic acids have recently been detected in vertebrate cells and tissues by immunodetection, and the sialate O-sulfo-transferases responsible for the sulfation have been identified, their presence in the gut remains unknown. Because of the inherent range of sialic acid changes, the Symbol Nomenclature For Glycans guidelines have been modified to reflect this natural variation (Nwangwa et al., 2016). Although humans lack the CMP-N-acetylneuraminic acid hydroxylase (CMAH) enzyme, which synthesizes the N-glycolyl modification in Neu5Gc, Neu5Gc may be metabolically absorbed into human tissues from Neu5Gc-rich diets such as red meat. Sialic acids are present in the GI tract at the terminal site of mucin glycan chains composing the mucus layer and in some human milk oligosaccharides (HMOs), and are an uncommon component of the cell surface of some bacterial species (Obembe et al., 2015).

Sialic acid plays important roles in human physiology such as cell-cell interaction, communication, cell-cell signaling, carbohydrate-protein interactions, cellular aggregation, development processes, immune reactions, reproduction, and in neurobiology and human diseases such as bacterial and viral infection, tumor growth and metastasis, microbiome biology, and pathology. It permits infections to use molecular mimicry to avoid host immune responses. Recently, sialic acid has been discovered to play a function in therapeutics. This chapter has focused on (i) sialic acid variety, (ii) their prevalence in many living forms, (iii) sialylation and sickness, and (iv) sialic acid and treatments.

Gut bacteria's ability to absorb sialic acids is dependent on their ability to release sialic acids from glycoproteins or oligosaccharides and transport them into cells, where they are further processed. In bacteria, the genes involved in sialic acid metabolism are typically located in so-called Nan clusters. The biochemical and structural features of the major sialic acid enzymes and transporters involved (Kingsley et al., 2016). The human intestinal mucus lining is much more than a physical barrier that prohibits direct interactions between bacteria in the gut microbiota and the host epithelium. Mucins, the primary constituents of mucus, are highly glycosylated proteins that actively contribute to the biology and ecology of the gut environment. The majority of mucin biomass is made up of post-translationally added sugars with a wide range of structure and composition (Brown et al., 2015). Mucin glycans play critical functions in gut homeostasis. They offer nourishment to commensal organisms, operate as biochemical "landing pads" for gut-colonizing microorganisms, and guard against pathogenic bacteria and mucin breakdown, a characteristic frequently linked with gut inflammatory disorders (Onyinyechukwu et al., 2017).

Blix isolated sialic acid from bovine submaxillary gland mucin for the first time in 19361, and more than 50 kinds of sialic acid have been found to date. Sialic acid is a generic term for neuraminic acid derivatives of negatively charged carboxyl group-containing nine-carbon acidic amino saccharides that can be divided into three types based on the carbon-5 position: N-acetylneuraminic acid (Neu5Ac), N-glycolylneuraminic acid (Neu5Gc), and deaminoneuraminic acid. Sialic acid is strongly linked to a variety of biological phenomena and is required for the development of the human brain and neurological system as well as the regulation of the immune system. Sialic acid has also been linked to the colonization of symbiotic microorganisms such as bacteria, viruses, and fungi. As a result, sialic acid is critical for comprehending the host-microorganism symbiotic connection.

CONCLUSION

The functional studies described above show that gut bacteria have evolved multiple pathways for releasing, transporting, and metabolizing sialic acid derivatives, underlining the importance of sialic acid as a valuable nutrient in microbial community adaptation to the gut. Although most research have focused on Neu5Ac as the primary form recognized by sialidases, sialic acid transporters, and sialic acid aldolases, studies are emerging that demonstrate specificities to alternative forms of sialic acid generated by gut bacteria, such as 2,7-anhydro-Neu5Ac. Furthermore, the majority of biochemical and structural understanding on sialic transporters to far has come from research on diseases or bacteria from other ecological niches. Given the great structural variety of sialic acid forms in the gut, many new routes are expected to be discovered in the coming years. Changes in sialic acid homeostasis levels in the gut have been linked to infection and inflammation in preclinical animals, but the underlying processes remain unknown. With the field of gut microbiota expanding beyond association studies and sialic acid being recognized as a key mediator of human health, it is critical to broaden our mechanistic insights into the range of sialic acid derivatives metabolized by gut microbes, as well as their role in signaling within and outside the gut. This will undoubtedly contribute to our understanding of human-microbe coevolution while also offering novel biomarkers and therapeutic targets.

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