

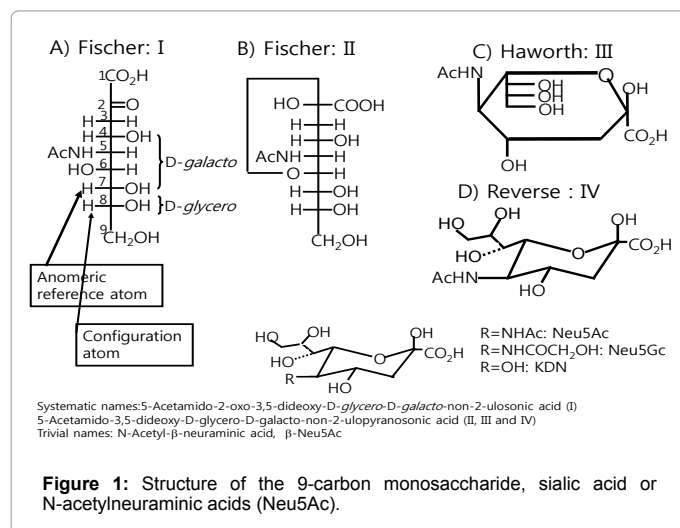
Sialic Acid (N-Acetylneuraminic Acid) as the Functional Molecule for Differentiation between Animal and Plant Kingdom

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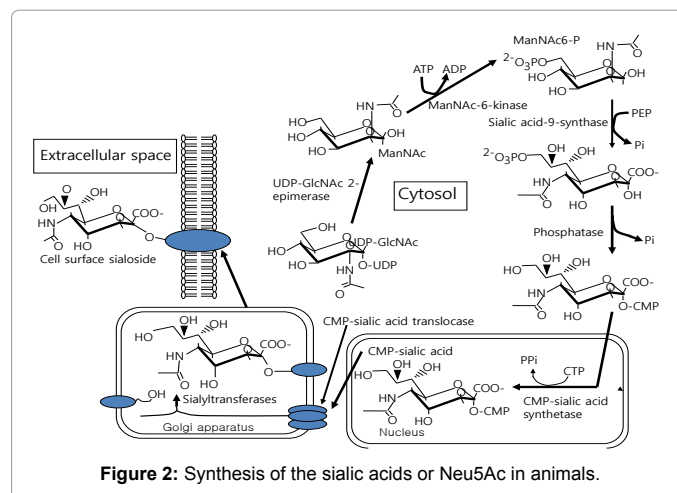
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Organisms synthesize saccharides for carbohydrates, amino acids for proteins, fatty acid for lipids and nucleotides for nucleic acids for the basic molecules. Recently, carbohydrates have been recognized as the 3rd life chain molecule in eukaryotic cells. One of the biggest differences between the plant and animal kingdom would be the existence of the 9-carbon monosaccharide, sialic acid or N-acetylneuraminic acids (Neu5Ac) (Figure 1). Even some enterobacterial species produce the sialic acids, although their origins are postulated to be probably derived from the bacteria-host interactions during long evolution. Some sialic acid-like saccharides such as legionaminic acid were also found in bacteria. The interesting point will be then what is the motivation of the acquisition of the 9-carbon sialic acid from the carbohydrate biosynthesis and functional distribution of these animals and bacteria. This fundamental question is linked to the paradoxical question why do not the plants contain the sialic acids? Interestingly, these two organisms of bacterial and animals can move to place to place as the behavioral characters, where the process is indeed called “biological adaptation” or “evolution”. The organism’s movement process needs their consideration, thought, memory, learning and education, as these processes are specialized for the mobile organisms. Actually the contents of sialic acids of human brain is the most highest among those of the current organisms through all the animals, as human is the mostly evolved organism. The more the content of sialic acids is high the more the organism is evolved. Then the sialic acids are thought to be the movement-related molecules. How do the molecules play their roles in cells, tissues, organs, and organisms? If the sialic acids are such functional? The prospective answer will be based on the molecular interactions of the sialic acids and their counterparts in each specific cell or site of each organism [1-3].



Biological function of Sialic Acids

The sialic acids or Neu5Ac are a group of 9-carbon monosaccharide and synthesized in animals (Figure 2) [1]. Sialic acid-containing glycoconjugates are initially synthesized from the deuterostome lineage of the echinoderms such as starfish and sea urchin up to the higher mammals. The echinoderms emerged some 500 million years ago. In insects and gastropod, the content of sialic acids are extremely low [4-6] and protostome animals do not produce the sialic acids as forms of glycoconjugates [7]. In sialic acid-producing organisms, they occur as terminal residues in the glycoconjugates of cell surface and are components of glycoproteins, glycolipid such as ad gangliosides and glycosaminoglycan ubiquitously present in mammals and lower vertebrates (Figure 3) [8]. Due to their terminal location, sialic acids in glycoconjugates function as ligands or receptors for cell-cell or host-parasite interaction [9,10]. For example, 9-O-acetyl Neu5Ac and 4-O-acetylated Neu5Ac are reported to be ligands for the agglutinin of influenza virus C [11] and for the agglutinin of murine hepatitis S virus [12], respectively. Sialylated glycolipids named gangliosides are functioned as the receptors for pathogenic bacterial infection on the gut epithelial cells [13]. Acidically modified sialic acids including acetylated and sulfated sialic acids are known as receptors for viral

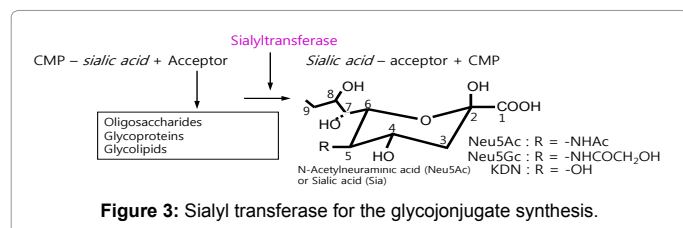


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infections when compared with the neutrally modified sialic acids such as methylated one [14,15]. Actually, the non-acidic sialic acids such as methylated sialic acids seem not to be used for those receptors, although it has been remained unclear yet.

Structure Diversity of Sialic Acids

Figures and schemes should be embedded in the main text. Embedding should be carried out by copy & paste or insert function. Number all figures in Arabic numerals 1,2, etc. Include photographs as part of the consecutive figures. There are various modifications of sialic acids with at least 25 differently substituted structures and 40 naturally occurring forms in nature during evolutionary stage [16]. The resulting structural diversity of the sialic acids is directly related with the broad functions of the chemical molecules in cell differentiation and species evolution [17]. Structurally, sialic acids exhibit diversity differing in the position 5 of an amino group (neuraminic acid derivatives) or an hydroxyl group (3-deoxy-D-glycero-D-galactononulosonic acid (Kdn)), different acylations of the NH_2 group at position 5 (glycolyl, acetyl) and various substituents of the different hydroxyl groups (phosphate, sulphate, methyl, acetyl, etc.) [18]. In echinoderms including starfish and sea urchin, N-glycolylneuraminic type such as Neu5Gc is predominant for diverse specialized sialo glycoconjugate structures specific for this phylum [19-22]. The di sialo-glycoconjugates have the additional Neu5Gc, O-methyl-Neu5Gc, N-acetyl-O-methylneuraminic acid and N-glycolyl-O-methyl neuraminic acid [23,24]. For example, the starfish *Asterias rubens* expresses the specific 8-O-methyl-5-Neu5Gc (Neu5Gc8Me) [25]. Within these organisms, the most common sialic acids are Neu5Ac, Neu5Gc and their O-acetylated derivatives, although certain starfish additionally possess 8-O-methylated sialic acids [26]. Therefore, it is suggested that from the structural modifications, sialic acids give a clear species specificity depending on organisms. For example in human, N-glycolylneuraminic acid (Neu5Gc) (but not Kdn) or N-glycolysialic acid is absent from human and chicken [27], although it was found in all other mammalian species. In the NeuGc, the terminal sialic acid residue is linked through the hydroxy group of the glycolic acid unit. The biosynthesis of Neu5Gc is carried out from Neu5Ac by the enzymatic catalytic reaction of a CMP-N-acetylneuraminic acid (CMP-Neu5Ac) hydroxylase (CMAH) in animals even in lower animals [27,28]. This enzyme is highly evolved, as oxygen and reduced pyridine nucleotide are required for enzyme activity with an effective cofactor NADH and the substrate CMP-Neu5Ac. The enzyme is activated by cytochrome b5.

Conclusion and Prospective

From the above diversity relationship between structure modification and expression of sialic acids in the bacterial and animal kingdoms, it was concluded that the sialic acids as 9-carbon sugars lead to the biodiversity and animal-specific characters during evolution.

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