

THE CHALLENGES OF THE RESEARCH ON SIALIC ACID O-ACETYLATION

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O-Acetylated sialic acids (Sia) are highly preserved in the animal kingdom, from the echinoderms onwards [1]. They also occur in many bacteria species and in pathogenic fungi. They represent components of glycoproteins, gangliosides, lipopolysaccharides and oligosaccharides and bear one or several acetic acid ester groups at the pyranose ring, at C-4, or at the Sia side-chain, at C-7, C-8 and C-9, although the 9-mono-O-acetylated sialic acid is prevailing. The amount and type of O-acetylated sialic acid depends on the tissue and animal or bacteria species. Especially rich sources are mucins and immunocompetent cells. Remarkably, in various tumours the expression of esterified sialic acids is upregulated and, more rarely, decreased.

O-Acetylated sialic acids are potent regulators of cell biological and pathological events [2]. The O-acetyl groups hinder the activity of enzymes degrading sialic acids and they have a negative effect on the interactions of sialic acids with various receptors on mammalian cells, microorganisms and viruses. Thus, they enhance the protective role of sialic acids, are components of the innate immune system and hinder apoptosis. Furthermore, they represent differentiation and tumour markers as well as virulence factors. In the latter case O-acetylated sialic acids serve as recognition signals for many viruses, which initiate the infection of cells by binding to these monosaccharides. Prominent examples are influenza C virus and corona viruses including mouse hepatitis virus, which use 4- or 9-O-acetylated sialic acids as targets.

Two sialic acid-specific enzyme systems are known transferring acetyl groups specifically either to C-4 or to various positions of the Sia side-chain, preferably to C-7. From there the ester group may migrate to the primary hydroxyl (C-9). The sialate-4-O-acetyltransferase preferably uses gangliosides as substrates, while the 7(9)-O-acetyltransferase, as studied with human colon and bovine submandibular gland, modifies free Neu5Ac and CMP-Neu5Ac with highest activity. These enzymes are located in the Golgi-membranes, from where they were solubilized and partially purified. Enzyme activity was also detected in other mammalian tissues, in bacteria, and in the starfish. So far, the eucaryotic O-acetyltransferases resisted structural investigation, while a few bacterial O-acetyltransferases were cloned, however, they could not yet be expressed and characterized.

[1] Tiralongo, J., Schauer, R. *Trends Glycosci. Glycotechnol.* **2004**, *16*, 1-5.

[2] Schauer, R. *Zoology* **2004**, *107*, 49-64.