O-GlcNAc Biology

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While it is the DNA sequence which holds the information deciding the amino acid sequence of the resulting proteins, in order to fully comprehend the entirety of the structures and functions of proteins in an organism, further information than just the amino acid sequence is a necessity. Of the numerous modifications that occur on proteins, glycosylation is a field in the limelight in post-genome research. In February of 2003 the Massachusetts Institute of Technology published an article on "10 Emerging Technologies that will change the world" – glycobiology was selected in the field of biotechnology, therefore its potential and merit acknowledged, and since then research in the field has been burgeoning in the USA and Japan. Before Dr. Gerald Hart of Johns Hopkins University School of Medicine had discovered the existence of nuclear and cytosolic O-GlcNAc modification in 1984, complex carbohydrates were known to exist only in the endoplasmic reticulum, the Golgi apparatus and outside the cell, thus until now researches conducted on complex carbohydrates were limited to the endomembrane system. However, when O-GlcNAc modification was revealed to be closely involved with diabetes, Alzheimer's disease and tumorigenesis, as well as that it competes against phosphatase for the modification sites on serine and threonine residues, the biological functions of O-GlcNAc modification, more specifically its role in cell signal transduction became the focal point of researches on molecular and individual levels. 3% of all glucose that enter the cell pass through the hexosamine biosynthesis pathway and are converted into UDP-GlcNAc. Utilizing UDP-GlcNAc as its substrate, O-GlcNAc modification is a modification unlike its predecessors in that its level is dynamically regulated by O-GlcNAc trasferase (OGT) which attaches O-GlcNAc onto target proteins, and reversibly removed by O-GlcNAcase (OGA). Proteomics and glycomics research technologies have determined that over 1,800 proteins are modified by O-GlcNAc, but due to a slowed development of technological infrastructure with which to recognize and study the function of O-GlcNAc modification, locating O-GlcNAc modification sites of a protein has only recently become an active field of research. There are only around 100 proteins of which the exact modified amino acid and its resulting functions are known – a vastly small number compared to the number of proteins known to possess O-GlcNAc modification as aforementioned.

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