

Novel Method of Searching for Glycosylation-Regulating Compounds

Kenichi Hatanaka *

The University of Tokyo, Japan

*Corresponding author: Kenichi Hatanaka The University of Tokyo, Japan E-mail: hatanaka@iis.u-tokyo.ac.jp

some reports that carbohydrate chain abnormality causes a disease. Therefore, the regulation of the cellular glycosylation may lead to the treatment of the disease. In this investigation, a novel method of searching for glycosylation-regulating compounds was developed. The application to therapeutic drug searches to normalize carbohydrate chain abnormality that causes the disease by establishing the assay method suitable for the high-throughput screening is expected.

It is considerably difficult to check the quantitative change of the carbohydrate chains of various structures existing in a cell. Accordingly, a molecule that analyzes the carbohydrates in the cell was introduced. Dodecyl lactoside is incorporated to cell membrane, transported to Golgi apparatus, glycosylated by glycosyltransferases, and the saccharide-chain-elongated products are released from the cell to culture medium. Therefore, the released products reflect intracellular carbohydrate synthesis. The effect of a candidate compound on the carbohydrate synthesis can be detected by adding the candidate compound and dodecyl lactoside to the culture medium. Advantages of this method are (1) detection without cell homogenization, (2) amplification of the signal, (3) detecting the effect on carbohydrate synthesis right after addition of candidate compound, (4) expandability by using various kinds of cells and alkyl glycosides. Moreover, the glycosylated products by using azidododecyl lactoside could be conjugated with fluorescent molecule by click chemistry, and the obtained fluorescent oligosaccharides were quantitatively analyzed by HPLC.

Glycation (sometimes called non-enzymatic glycosylation) is the result of typically covalent bonding of a protein or lipid molecule with a sugar molecule, such as fructose or glucose, without the controlling action of an enzyme. All blood sugars are reducing molecules. Glycation may occur either inside the body (endogenous glycation) or outside the body (exogenous glycation). Enzyme-controlled addition of sugars to protein or lipid molecules is termed glycosylation; glycation is a haphazard process that impairs the functioning of biomolecules, whereas glycosylation occurs at defined sites on the target molecule and is required in order for the molecule to function. Much of the early laboratory research work on fructose glycations used inaccurate assay techniques that led to drastic underestimation of the importance of fructose in glycation.

These compounds are absorbed by the body during digestion with about 10% efficiency.[citation needed] Browning reactions (usually Maillard type reactions) are evidence of pre-formed glycations. Indeed, sugar is often added to products such as french fries and baked goods to enhance browning.[citation needed] Glycation may also contribute to the formation of acrylamide,[2] a potential carcinogen, during cooking. Until recently, it was thought that exogenous glycations and AGEs were negligible contributors to inflammation and disease states, but recent work has shown that they are important.

Food manufacturers have added AGEs to foods, especially in the last 50 years, as flavor enhancers and colorants to improve appearance.[4] Foods with significant browning, caramelization, or directly added preformed AGEs can be high in these compounds.[5] A very partial listing of foods with very high exogenous AGEs includes donuts, barbecued meats, cake, and dark colored soda pop.

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