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Novel method of searching for glycosylation-regulating compounds

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Many studies are accomplished about the relationship between carbohydrate structure and disease. It had been reported that some kinds of disease make the carbohydrate structure of glycoconjugates change. on the other hand, recently, there are 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 cabohydrate 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.

Biography

Kenichi Hatanaka has completed his Ph.D. at the age of 27 from the University of Tokyo and postdoctoral studies from University of Texas Health Science Center at San Antonio. He is a professor of biomaterials at Institute of Industrial Science, the University of Tokyo.

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