Title of Project : Exploration of Novel Markers on Cancer and Development of a Technology for the Diagnosis Utilized by Comprehensive Glycomics

Shin-Ichiro Nishimura
(Hokkaido University, Faculty of Advanced Life Science, Professor)

Research Area :   Complex systems
Keyword :   Searching diagnosis chemicals

【Purpose and Background of the Research】

Serum biomarkers are important to detect diseases in early stage and useful for decision of treatment easily and quickly. In this study we will focus on gastrointestinal cancers including hepatocellular carcinoma, pancreatic cancer and colon cancer, and urological cancers including renal cell carcinoma and prostate cancer, to explore highly sensitive- and disease/pathologically specific- biomarkers by means of novel, large scale and comprehensive glycomics approach. We have developed automated system for pre-treatment and glycoblotting, "Sweetblot" (Japan Science and Technology Agency JST, 2003-2011). Utilized by the system, we will construct a highly reliable database of patients' glycans, which allows us to explore glycobiomarkers with clinical information provided from longitudinal/cross-sectional studies. It is believed to enable us to achieve practical study for clinical applications.

【Research Methods】

"SweetBlot" is an automated system, which utilizes glycoblotting method (*Angew. Chem. Int. Ed.* 2005, 44, 91-96), allowing us to enrich glycans specifically from crude mixtures from biological materials, such as serum. Once we set 10 μL of serum onto 96-well micro plate, extraction, modification, label with tag, spot onto a target plate and analysis by MALDI-TOF/MS will be perfoemed automatically. Glycan profiles from 96 patients will be obtained in almost a day.
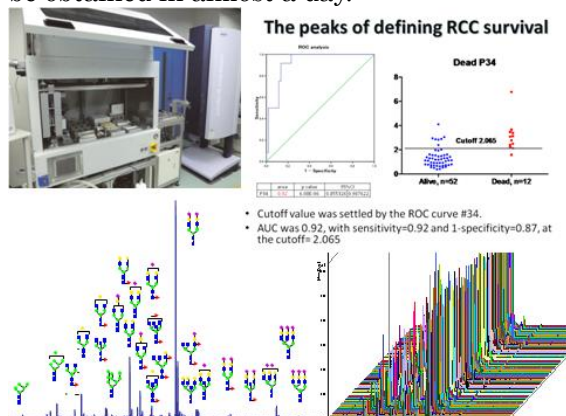

The peaks of defining RCC survival

- Cutoff value was settled by the ROC curve #34.
- AUC was 0.92, with sensitivity=0.92 and 1-specificity=0.87, at the cutoff= 2.065

Figure1. Exploration of glycan biomarkers utilized by automated system for large scale glycomics

Here we will apply 200-300 samples from patients in each region of disease, including serum, urine, tissues and cultured cells, to "Sweetblot". We will analyze the samples which are sequentially obtained from the same individuals, and also from the same disease patients in the distinct hospitals. Potential glycan biomarkers will be found from the accumulated glycan data, which will provide us the efficiency of medicines and/or prognosis, following to an evaluation by comparison with conventional markers.

【Expected Research Achievements and Scientific Significance】

Not only early detection of cancers but also drug susceptibility and diagnosis which are difficult to be determined by conventional markers are expected to be enabled by this study. If the relationship between balance of immune system and homeostasis including changes of glycan structures is clarified, we might understand the mechanism of diseases deeply from the view point of biogenic networks, i.e, systems biology, which will have an great impact in the field of basic biology and development of medicines focusing on the significance of post-translational modification.

【Publications Relevant to the Project】

・ Nishimura, S.-I., et al., "High-Throughput Protein Glycomics: Combined Use of Chemoselective Glycoblotting and MALDI-TOF/TOF Mass Spectrometry" *Angew. Chem. Int. Ed.* 44, 91-96 (2005)
・ Kamiyama, T., et al., "Identification of novel serum biomarkers of hepatocellular carcinoma using glycomic analysis" *Hepatology* 57, 2314-2325 (2013)

【Term of Project】 FY2013-2017

【Budget Allocation】 152,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://altair.sci.hokudai.ac.jp/g4/index.html