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Sysmex Corporation
National Institute of Advanced Industrial Science and Technology (AIST)

Technology Development Utilizing Sugar Chain Functions

The World's First Reagent to Determine the Progression of Hepatic Fibrosis by Measuring Changes in the Sugar Chain

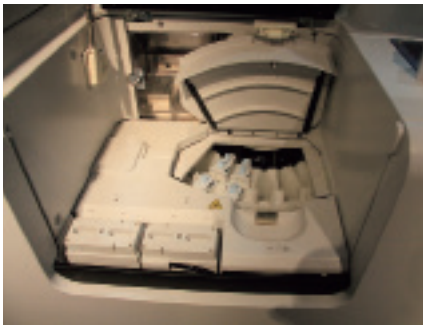
Measurement of a Hepatic Fibrosis Glycosylation Marker in Blood Within 17 Minutes Development of Fast and High-Precision Measurement Technology Which Received Approval for Health Insurance Coverage in January 2015

The most common cause of chronic hepatitis in Japan is infection with the hepatitis B virus and hepatitis C virus. The number of infected people is said to be approximately three million nationwide, of which nearly two-thirds are asymptomatic carriers. Chronic hepatitis that develops from infection with the hepatitis virus causes chronic cell destruction in the liver, and can advance to hepatic cirrhosis in 20 to 25 years due to fibrosis of the liver (hepatic fibrosis), and can eventually lead to liver cancer or serious disease. The progression of chronic hepatitis and the likely therapeutic efficacy of treatment can be determined by checking the level of hepatic fibrosis.

Today, the mainstay test for hepatic fibrosis is a biopsy in which the state of hepatic fibrosis is ascertained by collecting liver tissue with an inserted needle. However, the test imposes a heavy burden on patients, such as the necessity of hospitalization. Therefore, there is a public need for the development of a simple and high-precision liver fibrosis test such as blood testing. A technology that meets this need is Sysmex Corporation's HISCL M2BPGi reagent which uses a hepatic fibrosis glycosylation marker, a biomarker using sugar chains.

NEDO has implemented the world's most advanced research and development projects related to sugar chains since the Technology for the Production and Utilization of Glycoconjugates project started in 1991. The National Institute of Advanced Industrial Science and Technology (AIST), which has led these projects, found a new glycosylation marker involved in the progression of hepatic fibrosis. In order to utilize this achievement, AIST started to work with Sysmex Corporation, a manufacturer of clinical examination devices and test reagents, for the practical application of the hepatic fibrosis glycosylation marker, and then developed the HISCL M2BPGi reagent. This reagent received manufacturing and marketing approval in December 2013, was released in March 2014, and received approval for health insurance coverage in January 2015. It is expected to be widely used in the future.

Automatic immunoassay system used in testing HISCL-5000
(Photo courtesy of Sysmex Corporation)



Reagents placed in HISCL-5000
Twenty-four R1 to R3 reagent sample sets can be tested at the same time.

Q. Why did this project start?

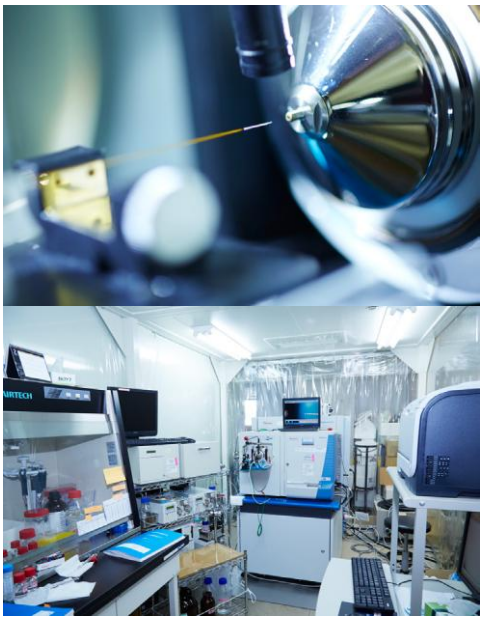
In accordance with the policy of the Ministry of Economy, Trade and Industry, NEDO has promoted technology development in the life science field, including medical care and diagnostic techniques, to address the problems of Japan's aging society and low birth rate and also improve the quality of life. In particular, NEDO has focused its attention on sugar chains that bind to protein in a living organism and perform important functions. It started a project on sugar chains in the early 1990s to improve drug discovery and diagnostic technologies and explore related seeds.

Q. What was the aim of the project?

NEDO started the Technology for the Production and Utilization of Glycoconjugates project in 1991 with the aim of developing fundamental technology to produce and utilize glycoconjugates (substances consisting of sugar chains, proteins, and other substances), which are basic structural substances in a living organism having major functions, including recognizing substances that are not realized by proteins and fat alone. The project was carried out for ten years and NEDO subsequently implemented the Technology Development to Create Functional Sugar Chain Composite Materials project for five years from FY1999 with the aim of developing technology to effectively synthesize complex sugar chains having sophisticated functions and fundamental technology to create functional composite materials that control the molecular density, orientation, and other properties of sugar chains.

In addition, to strengthen the foundation of sugar chain research and promote further advances in the future, NEDO carried out the Construction of a Human Glycogene Library project from FY2000 to FY2003. In this project, NEDO comprehensively cloned human glycogenes necessary for glycosylation and analyzed their functions to construct a database. To promote this project, the Research Center for Medical Glycoscience (today's Glycomedicine Technology Research Center) was established by AIST and libraries for numerous sugar chain-related genes were constructed. Two-thirds of new sugar chain-related genes reported around the world over the last three years were found and developed in this project.

In the Sugar Chain Structure Analytic Technology Development project undertaken from FY2002 to FY2005, NEDO developed fundamental technologies to analyze sugar chain structure. In particular, one of the developed fundamental technologies using a mass spectrometry method evolved into sugar chain structure profiling technology having the highest sensitivity in the world. Analyzers using this profiling technology are now exported.



Mass spectroscope installed in a laboratory
Sugar chain structure analysis using the mass spectroscope has generated a number of revolutionary technologies.

In the Technology Development Utilizing Sugar Chain Functions project implemented from FY2006 to FY2010 as a compilation of previous sugar chain research and development projects, NEDO analyzed the functions of sugar chains and proteins from biological samples using technologies and resources from previous projects for industrial application, accelerated the utilization of sugar chain functions through the development of a manufacturing method for a specific sugar chain recognition probe, and developed a method for synthesizing human sugar chains in large volumes. Industrially useful new sugar chain materials were also developed.

Q. What is the role of NEDO?

HISCL M2BPGi is an example showing how NEDO projects characteristically involve the world's most advanced research and development, construct industrial foundations, and promote practical application and commercialization through industry-academia-government collaboration. Practical application was realized because NEDO started research on sugar chains in the early 1990s ahead of other countries, and subsequently accumulated a foundation for sugar chain technologies in Japan.