A Powerful Tool for the Observation of Living Things

Microscopy has a long and fascinating history, and it continues to evolve and improve. The microscope is a powerful tool for observing the smallest details of living things. It allows us to see structures that are invisible to the naked eye, providing insights into the complex world of biology.

The microscope has played a crucial role in scientific discovery, from the discovery of microorganisms to the understanding of cellular processes. It has enabled researchers to make new discoveries and advance our knowledge of the natural world.

In recent years, advances in technology have made microscopes even more powerful. Digital microscopes, for example, allow for high-resolution images and the ability to capture video footage. This has opened up new possibilities for research and education.

Despite its importance, microscopy is not without its challenges. Techniques such as immunofluorescence require careful sample preparation and specialized equipment. However, with the right tools and training, these challenges can be overcome.

As technology continues to develop, we can expect to see even more powerful microscopes in the future. These will undoubtedly help us to learn more about the living world and solve some of the greatest mysteries of science.

References:


For more information on microscopy and its applications, please visit the websites listed above. 

December 2008
December 2009

Title: "Dehydration and Tests in Drug Discovery: Protein Structure"

Abstract:

Protein structure is crucial for understanding the function of proteins and for designing drugs that interact with them. Dehydration is a common phenomenon in protein structure studies, as it can affect the stability and conformation of the protein. In this work, we investigated the effects of dehydration on protein structure using X-ray crystallography and NMR spectroscopy. We found that dehydration can lead to significant changes in the protein's three-dimensional structure, which can be observed through changes in the protein's electron density map. These changes can be explained by alterations in the hydrogen bonding network and the solvent-accessible surface area of the protein. We conclude that dehydration should be carefully controlled in protein structure studies to ensure accurate structural determination.

Keywords: Protein structure, dehydration, X-ray crystallography, NMR spectroscopy.

Reference:

March 2010

**From the Journal of Life Phenomena**

In recent years, there has been a growing interest in the study of life phenomena. This field encompasses a wide range of disciplines, from biology and chemistry to mathematics and physics. The aim is to understand the fundamental processes that give rise to life as we know it.

One of the key questions in this area is how life originated on Earth. Scientists have been exploring this topic through various approaches, including abiogenesis, which is the study of how life emerged from non-living matter.

Recent studies have suggested that the conditions on early Earth were more conducive to the development of life than previously thought. This includes the presence of a reducing atmosphere, a high concentration of volatiles, and a warm climate. These conditions allowed for the formation of complex organic compounds, which are the building blocks of life.

However, the exact timeline and mechanisms of these processes are still the subject of much debate. Researchers are using a combination of experimental and theoretical approaches to unravel these mysteries.

In addition to the study of life on Earth, there is also a growing interest in the search for extraterrestrial life. This involves looking for signs of life in other parts of the solar system and beyond. The discovery of water on Mars and the search for biosignatures in exoplanet atmospheres are just two examples of this.

Overall, the study of life phenomena is a dynamic and rapidly evolving field. As our understanding of the origins and evolution of life increases, so too does our appreciation of the complexity and richness of the natural world.
Development of a Next-Generation 4D Radiation Therapy System That Enables Irradiation of a Moving Cancer

Irradiation Precision Error: ± 0.1 mm
Realization of High-Precision and Safe Cancer Therapy

Today, the most common cause of death in Japan is cancer, which accounts for one out of every three deaths. Against this backdrop, NEDO has contributed to a reduction in the number of cancer patients through early social reintegration of cancer patients and improved quality of life (QOL) as a result of the development of cutting-edge medical equipment that enables early cancer diagnosis and therapy. There are three types of cancer therapy: surgery, chemotherapy, and radiation therapy. Among them, greater expectations are placed on technological advancement of radiation therapy because it puts the least strain on the body and is highly effective as a cure. The greatest challenge in radiation therapy is to avoid damaging normal cells when irradiating cancer cells.

Mitsubishi Heavy Industries, Ltd. carried out NEDO’s Fundamental Technology Research Facilitation Program/Development and Research on a High-Precision 4D Radiation Therapy System project for four years from 2003 in collaboration with Kyoto University Hospital’s Department of Radiation Oncology and Image-applied Therapy and its Clinical Research Center for Medical Equipment Development to establish fundamental technology. It subsequently carried out the Subsidized Project for Practical Development of Next-Generation Strategic Technology (Analysis of the Behavior of Affected Parts) and Development and Research of Feedback Technology Toward Adaptive 4D Radiation Therapy project for two years to resolve technical issues for practical application. This then led to the VerO4DRT, a next-generation 4D radiation therapy system that made it possible to irradiate a moving cancer for the first time in the world.

As a newcomer in the medical equipment business, Mitsubishi Heavy Industries initially carried out medical-related activities through intrapreneurship. In this situation, it was able to realize an innovative and safe high-precision radiation therapy system in which the irradiation precision error of therapeutic X-rays (referred to as “therapeutic beams”) is within ±0.1 mm. This was accomplished by combining technologies obtained through an industry-academia partnership, such as image diagnosis, with its technology for system integration of large equipment and its globally competitive technology for accelerating tubes.

In order to cure a cancer that moves because of respiration or some other movement, the VerO4DRT was designed as a 4D high-precision radiation therapy system by adding temporal axes to the concept of 3D therapy that enables irradiation from various angles. As a result, the system has numerous new advanced functions not seen in previous radiation therapy systems.

As of February 28, 2015, 24 units of the system were installed in hospitals not only in Japan but also in Europe, the US, and Asian countries. These hospitals have successfully performed irradiation of lung, liver, and pancreatic cancers. The VerO4DRT is attracting attention as an innovative therapy system that enables a radical cure without putting much strain on the body.

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.
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A University-Launched Venture Develops New Market for Commercial Cerebral Infarction Risk Assessment Through Industry-Academia Collaboration

Cerebral infarction, which causes paralysis, inability to move as well as other aftereffects, prevents patients from performing daily life activities. Thus, it has been hoped that an early detection method would be established in order to improve the quality of life of patients. However, among the three major diseases of cancer, heart disease, and cerebral infarction, the biomarker for cerebral infarction has been the most difficult one to find. This is why diagnosis of this disease is difficult. Although magnetic resonance imaging (MRI) is used as a test for the early diagnosis of cerebral infarction, it is difficult to conduct mass screenings because of the relatively high cost and a test time as long as 50 minutes.

Under these circumstances, NEDO decided to aim for practical application of a simple cerebral infarction risk assessment technology. It subsequently supported the development of biomarkers by Professor Kazuaki Igarashi of the Graduate School of Pharmaceutical Sciences at Chiba University for three years from 2005 through its University-Launched Business Creation and Practical Application Research and Development Project/Cerebral Infarction and Renal Failure Biomarker: Acrolein Measurement Kit Development Project. Hoping to use the research results obtained in his university work to benefit society, Professor Igarashi established Amine Pharma Research Institute Co., Ltd., shortly after he left the university in April 2007. It was a university-launched venture, and he took up the post of president. Amine Pharma Research Institute Co., Ltd., applied the results of basic research on the physiological action of polypeptide conducted at the Graduate School of Pharmaceutical Sciences at Chiba University and succeeded in developing the world’s first practical application of a simple and very precise cerebral infarction risk assessment based on biomarker measurement using a blood test.

Cerebral infarction is a disease in which a blood vessel in the brain is blocked, and thereby surrounding cells are destroyed. Polymers in the cells leak out, and the level of acrolein as a metabolite increases in the blood. The increase of acrolein induces L-6 [interleukin-6] from neurons and macrophages, and then L-6 induces the production of CRP (C-reactive protein) in the liver. In this way, cerebral infarction causes the levels of acrolein, L-6, and CRP in the blood to increase. By measuring these levels and using a unique risk calculation method in which the subject’s age is considered, it has become possible to assess the risk of cerebral infarction (silent cerebral infarction).

In 2013, 17,000 people used this cerebral infarction risk assessment service, and the total number of users from the introduction of the assessment exceeded 60,000 as of FY2014, allowing profitability to be achieved. This university-launched venture is steadily moving forward and creating a new commercial medical testing market referred to as cerebral infarction risk assessment.

Specimen inserted in measurement system

Amount of acrolein, which is produced when brain cells are destroyed, is measured to assess risk of cerebral infarction.
Traditionally, most laboratory animals have been used to investigate new substances that are potential candidates for new medicines. However, these substances are verified using laboratory animals which can be affected by a disease that also affects humans. When investigating the efficacy of medicine that treats or alleviates the symptoms of a human disease, the animals in the experiment must be able to be affected with the same human disease. Therefore, a new method for evaluating zebrafish human disease models was developed in order to make experimentation convenient. There are long and difficult processes in order to make new medicines. Enormous effort and costs are required for the development of new medicines. The procedures and structures of such substances are investigated, the effectiveness and safety of an enormous number of new substances are verified using laboratory animals, and then the candidates are narrowed down. Separating candidates by investigating the efficacy of medicine that treats or alleviates the symptoms of a human disease, the animals in the experiment must be able to be affected with the same human disease.

Professor Toshio Tanaka of the Mie University Graduate School of Medicine speculated that if it is possible to use a large amount of zebrafish in drug development screening, then drug development should be able to be performed more conveniently and broadly. At the time, he was participating in NEDO’s Grant for Practical Application of University R&D Results program, and he started working to develop a zebrafish human disease model. He developed the Zebrafish (ZF) Plate which is capable of observing many zebrafish long before the start of the project. Investigating drug efficacy with large volume observations of zebrafish human disease models Around that time, a technology called genome editing was being established by American researchers. Using new technology that pinpoint and deletes DNA in a genome, it became possible to develop a model organism more simply than in the past. Using this new technology, Professor Tanaka succeeded in creating various zebrafish human disease models.

However, he was not satisfied with the results that he obtained. He believed that in order to realize the type of large-scale drug development screening he had envisioned, it would be necessary to have research tools that can evaluate the results of a large number of potential candidates for new medicine by observing a large number of zebrafish. This process would also need to be automated in the future.

Therefore, as a first step, Professor Tanaka developed the Zebrafish (ZF) Plate which is capable of observing many zebrafish at the same time. He also selected HASHIMOTO ELECTRONIC INDUSTRY CO., LTD. from Matsusaka City in Mie Prefecture to be a collaborator in the development work. He selected the company because he had heard about their technology to manipulate fine particles and their advanced knowledge of zebrafish.

Next, NEDO adopted the development of the ZF Plate under its Innovation Commercialization Venture Support Project which was continued from 2013. Through repeated trial and error by developers at Hashimoto, a general purpose ZF Plate was developed. This then led to the development of a procedure for a commonly used centrifugal separator which could be used without expensive accessories. This made it possible to easily perform experiments anywhere using a large number of zebrafish.

For The Future
Using the new technology to develop functional foods and personalized cancer treatment

NEDO’s Role
For research and development venture companies, development for practical application is an extremely risky phase before reaching commercialization. Therefore, support for superior advanced technology seeds that make use of promising original technology is provided to projects with a specific plan to achieve practical application within three to five years.

When adopting a project, NEDO considers the novelty of the technology, the level of goal setting, the superiority of patents and know-how, as well as the possibility for practical application. Goals, problems, and steps needed to solve problems are also clarified, and the suitability of research planning, including cost-effectiveness, is evaluated.

Furthermore, in addition to the potential for a new market creation, the understanding of market needs, and the priority of developed products and services, the reliability of the system for commercialization and business planning are also reviewed as part of NEDO’s evaluation process. Evaluations are carried out from various points of view, such as the contributions to revitalization of regional economies, in order to strengthen the foundation of creative innovation.
Enabling high-precision examinations without inflicting pain

At first glance, Elmammo appears to have the shape of a bed. On the top, there is a single opening with a diameter of approximately 18.5 cm where the examination takes place. A female patient receiving the examination lies face-down. The examination is performed with the patient positioning one breast in the opening at a time and then having a PET image of each breast taken. Currently, with mammography used for breast cancer examinations, a patient’s breasts are pressed tightly together before images are taken, resulting in a heavy burden for the patient as she may experience pain and other discomfort. In comparison, using Elmammo does not require a patient to press her breasts together, so she will not experience any pain. Also, the device is capable of taking 3D tomographic PET images of the breasts when they are not pressed together. Furthermore, the device is extremely effective, offering about twice the resolution and ten times the sensitivity of current whole-body position emission tomography/computed tomography (PET/CT) devices.

The biggest contributing factor to realization of such high resolution and sensitivity is that the detectors are arranged in a ring structure. On a side note, Elmammo was originally developed in cooperation with the National Institute of Radiological Sciences for brain examinations. A NEDO project led to it also being used for breast cancer examinations. Among cancer incidence rates for Japanese women, breast cancer is the highest (see accompanying graph), so early detection can mean the difference between life and death. Shimadzu Corporation determined that its device could be used for breast cancer examinations, and therefore applied to participate in NEDO’s project.

For The Future

Listening to user opinions and taking the technology overseas

During the early stage of development of the device, it was difficult to simultaneously achieve high resolution and high sensitivity. However, after improvements in technology, hardware, and software, it became possible to achieve both high resolution and high sensitivity. Furthermore, through medical-engineering cooperation with Kyoto University Hospital, the opinions of doctors using the device and patients undergoing examinations were reflected in the development process, making the device more user-friendly. There are future plans to develop domestic and overseas markets for early-stage detection and treatment of breast cancer, which is increasing every year.