SHIMADZU
Excellence in Science

C10G-E075A

Collaborative Research & Development for Advanced Healthcare

ADVANCED HEALTHCARE

Developing Technology for Current and Future Challenges

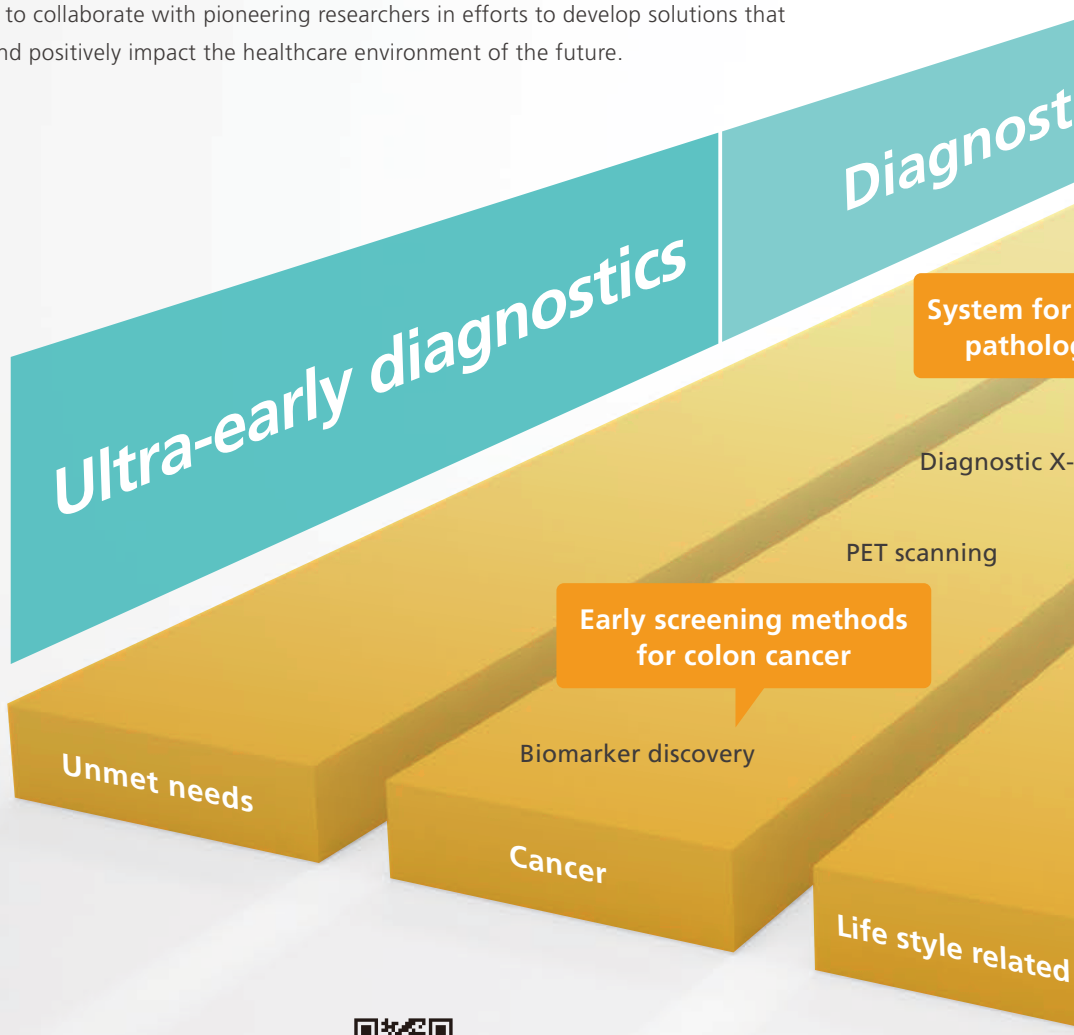
- Pioneering Partnerships for Advanced Healthcare -

As society enters an era of aging demographics, there is a growing concern about how to maintain health at these advanced ages. Maintaining a healthy lifestyle as long as possible involves prevention, ultra-early diagnosis, medical treatment that minimizes the burden on the body and mind, and managing prognosis appropriately.

How can Shimadzu Corporation help?

As a pioneer in diagnostic X-ray imaging and a leader in mass spectrometry, Shimadzu has been working daily with researchers to develop solutions that will significantly change the future of healthcare, based on visualization using our medical and imaging technology and quantitative analysis using mass spectrometers.

Moving forward, we will continue to collaborate with pioneering researchers in efforts to develop solutions that extend healthy life expectancies and positively impact the healthcare environment of the future.



SHIMADZU's Research Development for Advanced Healthcare
https://www.shimadzu.com/advanced-healthcare/

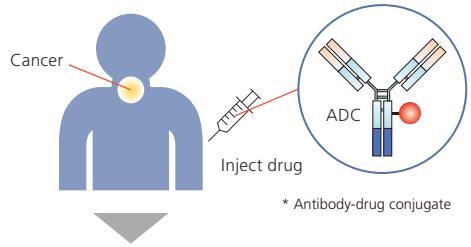

ics
Medical treatment
Prognosis
Monitoring drug levels in blood
Tumor-tracking for radiotherapy
Confirming treatment effectiveness
Support for cancer photoimmunotherapy research
Observation of drug accumulation and treatment areas
Metabolite quantitative analysis
Quantitative analysis of hormones in blood
supporting rapid gical diagnosis
Development of support system for primary aldosteronism
Using angiography system to confirm area for blood collection
ray imaging
Diagnostic X-ray imaging
Biomarker measurement
Development support for Alzheimer's drug discovery
Biomarker discovery
Bone metabolic marker analysis
disease
Neurocognitive Disorders
Locomotive syndrome

Case Study #1: Cancer Photoimmunotherapy Research

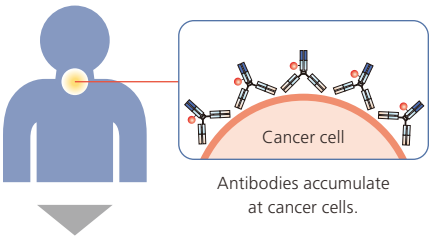
Cancer photoimmunotherapy is a new treatment technique that involves selectively binding the antibody portion of a therapeutic drug to proteins uniquely present on the surface of cancer cells and then killing only the cancer cells by irradiating the area with near-infrared light, so that the photosensitive portion of the therapeutic drug reacts to the light.
Given that the treatment method also helps the immune system attack cancer cells by stimulating immune cells, practical applications are anticipated. During basic research, an NIR-PIT near-infrared camera was used to create a system for evaluating the therapeutic effects in real time.

Mechanism of Cancer Photoimmunotherapy

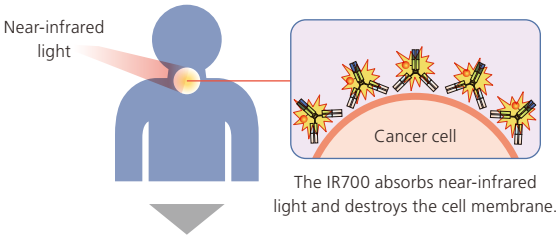
(1) A therapeutic drug conjugate, with antibodies bound to a photosensitive chemical substance (IR700), is administered.



(2) The therapeutic drug accumulates only at proteins uniquely present on the surface of cancer cells.



(3) Near-infrared light irradiation activates the chemical substance, which destroys the cancer cells.



(4) Excitation light from the chemical substance attenuates.

Near-Infrared Fluorescence Imaging System for Visualizing Progression of Chemical Reaction to Near-Infrared Light

This system creates an image of the chemical reaction to the near-infrared light applied during treatment, and evaluates and records the therapeutic effects.

Mass Spectrometer for Confirming Therapeutic Effects Based on Urine and Blood Analysis

We are searching for a metabolomic method of evaluating therapeutic effects.

Note: These measures are still currently in research and development.
FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC PROCEDURES.

Joint Research Partner

U.S. National Cancer Institute,
National Institutes of Health

Dr. Hisataka Kobayashi

Trying to be effective without damaging the body is the concept of NIR-PIT. It can selectively kill cancer cells without damaging or killing many normal cells. Also, this therapy can decrease the number of cancer cells and then increase and activate the host immunity to better fight the cancer. SHIMADZU has the strength in chemistry and we have the strength in biology. That is the reason why we have a very good collaboration in this research.

Case Study #2: Development of AVS Support System for Primary Aldosteronism

Sampling the adrenal vein is an effective means of determining a treatment plan for primary aldosteronism, but it can take several days to obtain results. Furthermore, samples are acquired from multiple locations. That has resulted in problems due to the difficulty in integrating image information with measurement results and managing the data.
The AVS support system for primary aldosteronism marks adrenal vein images with the locations where blood was acquired from adrenal veins during sampling and displays measurement results linked to those marked locations. Consequently, the system enables an accurate understanding of measurement results at each adrenal vein location from only a glance.

Primary Aldosteronism

Primary aldosteronism causes high blood pressure due to excessive excretion of the hormone aldosterone from the adrenal gland. About 5 to 10 % of high blood pressure cases are said to be caused by primary aldosteronism, which can be resolved in nearly 50 % of cases through adrenal gland surgery.

AVS Support System for Primary Aldosteronism

(1) Insert a catheter into the adrenal vein for venography.

(2) Based on an X-ray image, insert a catheter in the adrenal vein to acquire blood at multiple locations and read the sample ID information from each blood collection tube.

(3) Use the sample ID information to record the blood collection location information on the X-ray image.

(4) Read the sample ID information from each blood collection tube and analyze the samples by mass spectrometry.

(5) Use the sample ID information to associate the LC-MS/MS analysis results with each blood collection location and then prepare an AVS examination report.

Angiography System that Reads Sample ID Information from Blood Collection Tubes and Links it to Blood Collection Locations on X-Ray Images

Registers sample ID information from blood collection tubes and the corresponding blood collection locations.

Mass Spectrometer for Quantitating Aldosterone and Cortisol Levels in the Blood (Research Use Only)

Quickly and accurately measures a wide variety of substances from a small quantity of blood samples.

Software for Displaying Measurement Results Associated with Blood Collection Locations on X-Ray Images

X-ray images (morphology information) with different characteristics can be integrated with measurement results (biological information) and managed as a single set of information.

Note: This system is intended for research use (scheduled for release only in Japan).
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Joint Research Partner

Tohoku University Hospital
Dr. Kei Takase

Using a combination of diagnostic imaging technology and measurement technology for component analysis, the AVS support system enables faster and more accurate diagnostic capabilities. The ability to determine, on-the-spot from a localization diagnosis, where the problem is located in the adrenal vein will lead to less invasive treatments in the future. This type of sampling technique can be used not only for the adrenal gland but also for various other endocrine organs and endocrine disorders. Therefore, I think that our development experience can also be deployed for other endocrine disorders in the future.

Case Study #3: Alzheimer's Drug Discovery Support

The beta-amyloid deposition level in the brain, which gradually changes as Alzheimer's disease progresses, is used as an indicator for determining and monitoring how far the disease has progressed. Currently, PET imaging scans and cerebrospinal fluid examinations are the only two methods currently available for detecting beta-amyloid levels. However, PET scans are expensive and only available from a limited number of facilities, whereas acquiring cerebrospinal fluid is a highly invasive procedure. Therefore, in response to a growing need for a low-cost and easy examination method, we developed a method that can be used to screen a larger number of people based on blood tests. In 2014, Shimadzu Corporation and the National Center for Geriatrics and Gerontology discovered a peptide ratio that is effective as a blood biomarker for detecting Alzheimer's lesions by IP-MS. Furthermore, a composite biomarker was developed by combining that biomarker with another peptide ratio.

Blood Biomarker for Alzheimer's Beta-Amyloid Deposit

Mass spectrometry was used to successfully discover 22 biomarkers, including 8 newly discovered biomarkers. During that process, we also discovered that the ratio between two biomarkers, Aβ1-42 and APP669-711, correlates to the progression of Alzheimer's disease.

Mechanism of IP-MS Method

IP-MS combines immunoprecipitation (IP), which achieves selective separation based on an antigen-antibody reaction, with mass spectrometry (MS). In this case, an anti-beta amyloid monoclonal antibody was used to extract beta-amyloids from blood plasma, with the beta-amyloids measured using a matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MALDI-TOF MS).

(1) React the magnetic beads bound to anti-beta amyloid antibodies with the blood plasma sample.

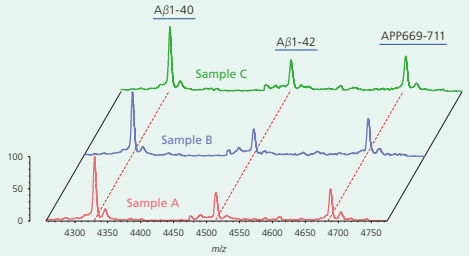
(2) Elute the beta-amyloid in the blood plasma from the magnetic beads.

(3) Analyze the eluate solution in the MALDI-TOF MS system.

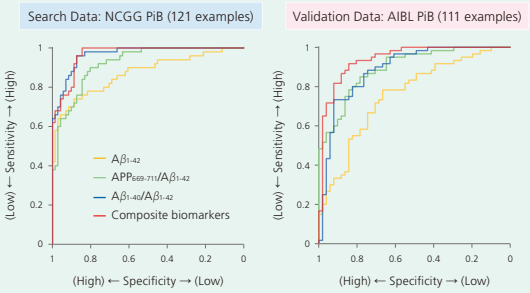
The results of this research were published in Nature volume 554, pages 249 to 254 (2018) "High performance plasma amyloid-β biomarkers for Alzheimer's disease" (doi:10.1038/nature25456).

MALDI-TOF MS for Estimating the Beta-Amyloid Deposition Level in the Brain

This system enables many types of beta-amyloids to be characterized and simultaneously detected with high sensitivity by analyzing only 0.6 mL of blood plasma. Of these beta-amyloids, Aβ1-42, Aβ1-40, and APP669-711 can be used in combination as biomarkers to estimate the deposition level with high accuracy.



MALDI-TOF MS Mass Spectra



Evaluation of Biomarker Accuracy (ROC Analysis)

Note: Offered as contract analysis service (only in Japan).
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Joint Research Partner

The Florey Institute,
The University of Melbourne

Prof. Colin L Masters

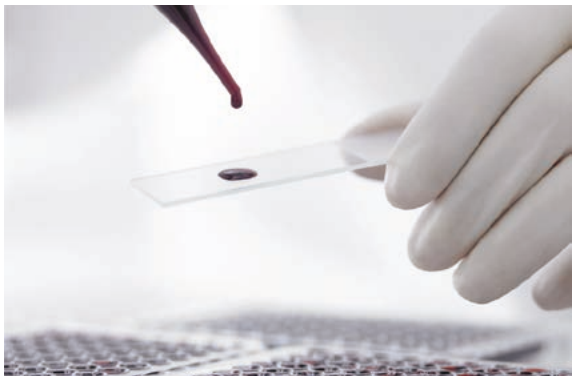
For more than 30 years, academics have been looking for a test that has high performance in predicting the development of Alzheimer's disease. This is one of the great unmet needs of our society. If a test that only requires taking a few drops of blood with just a minimal invasion really performs well, it will allow the early detection of Alzheimer's disease and assist in developing new therapeutics. SHIMADZU has a long history and a reputation of doing excellent work in developing high performance analytical technology. I'm very confident that this partnership between Industry and Academia is the only way that we can make real progress in this field.

Case Study #4: New Metabolic Profiling Research

If ultra-early diagnosis with minimal stress on the body can be achieved, then an increase in life expectancy will likely result. We intend to conduct research aimed at achieving methods that are less invasive and more informative.

Early Screening Methods for Colon Cancer (Kobe University and Shimadzu Corporation)

Multi-biomarkers that can be used for diagnosing colon cancer were discovered from metabolomic analysis. The diagnostic predictive algorithms created based on those research-use-only biomarkers have been shown to maintain high sensitivity, even for early-stage colon cancer patients. The ability to measure the biomarkers with minimally invasive blood tests means there is hope for the possibility of screening patients in a clinic, for example, without the effects of bleeding during examinations.



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New Technologies for Advanced Cancer Detection (University of Yamanashi and Shimadzu Corporation)

Currently, pathological diagnoses involve acquiring a localized sample, preparing a specimen, observing the specimen under a microscope, and then making a diagnosis. That process requires about 30 minutes. In addition to being time-consuming, it requires significant technical skill by the pathologist. Recently, we developed a new probe electrospray ionization (PESI) technology for mass spectrometry (MS) that enables analyzing data acquired from trace tissue samples. It is the basis for a rapid pathological diagnosis support system (PESI-MS), currently in development, that can complete the measurement process in about two minutes after local sampling.

Note: These measures are still currently in research and development.
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～ Research and Development for a Better Future ～

Our goal in supporting research and development around the world is to help develop technology with future tangible benefits. If ultra-early diagnosis is achieved, then it should be possible to start treatment earlier as well.
Based on that belief, we continue to challenge ourselves to ponder real possibilities and breakthroughs.

KYOLABS: SHIMADZU Healthcare R&D Center for Researching Advanced Solutions

The Healthcare R&D Center uses Shimadzu's technical strengths, including analytical instrument and medical diagnostic imaging technologies, to develop innovative solutions for healthcare applications. We encourage dialogue and joint research with customers in ongoing efforts to address both current and evolving challenges.
In addition, the center aims to create connections between people, and between intangible activities and tangible things, using science and technology as a bridge to satisfy unmet needs and develop powerful platforms that advance society.

KYOLABS
Shimadzu's collaborative laboratories

SHIMADZU

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