Originating in the Tohoku region, reaching out to the world. New medical technology in creation and dissemination.
Disseminating cutting-edge medicine originating in the Tohoku region to the world

I was appointed as the Director of Tohoku University Hospital in April 2019. When the Clinical Research, Innovation and Education Center, Tohoku University Hospital (CRIETO) was established in 2012, it was a pioneer in Japan in aiming for practical application of results in life science R&D by conducting seamless support for basic research, translational research and clinical research and trials. In 2015 Tohoku University Hospital was selected as a Clinical Trials Core Hospital under the Medical Care Act. As such, CRIETO is responsible for furthering medical innovation in Japan, and it is providing for the powerful promotion of translational research, including world-class clinical research and investigator-initiated clinical trials in difficult diseases. Although CRIETO is an organization situated within Tohoku University Hospital, it is the university hospital at a comprehensive university. As such, the center’s role is to uncover and fosters the seeds of basic research from inside and outside the university and bring them to practical application. Tohoku University established the Promotion of Medical Science Committee as an interdepartmental organization for Tohoku University’s 16 departments, fostering a cross-pollination of Tohoku University’s vast wealth in research seeds. We are resolved to optimize our strengths as a multi-departmental university and disseminate the results of that effort from here in Tohoku outward to all the world. We hope to have your cooperation and support in our endeavor.

Integrated development of medical technology R&D and clinical applications. The future of university hospitals starts here.

The Power Supporting the Medicine of the Future

I was appointed as the Director of CRIETO in June, 2013. The mission of CRIETO is to promote clinical research and trials at Tohoku University Hospital as well as life science R&D at Tohoku University, from the early stage of planning to the final stage of clinical trials, aiming for their clinical applications. We also aim to support clinical research and trials throughout the Tohoku region and to develop human resources. In addition to CRIETO, life science research in general is expanding at Tohoku University, including the United Centers for Advanced Research and Translational Medicine (ART) of the Tohoku University Graduate School of Medicine, The Translational Research Program: Strategic Promotion for practical application of Innovative medical Technology (TR-SPRINT) (AMED), all of which are unified by the Promotion of Medical Science Committee of Tohoku University (PROMOT). In cooperation with these initiatives, CRIETO will accomplish its missions as the core center of clinical research in Japan. Your kind understanding of our work and cooperation with CRIETO will be greatly appreciated.

The Objectives of CRIETO

The objective of CRIETO is to aim for a practical application of results in life science R&D by conducting seamless support for basic research, translational research and clinical research and trials. In particular, as well as providing developmental support for medical devices that are one of Tohoku University’s strengths, we will also provide developmental assistance for developing new drugs and new diagnostic and treatment methods addressing difficult, rare diseases and childhood diseases. Furthermore, we will conduct clinical trials in collaboration with university hospitals and municipal hospitals in the Tohoku region.

Bringing innovative medical technology originating in Tohoku to the world

Role of CRIETO

Development of needs guidance at medical-engineering cooperation centers
Product development utilizing advanced technical skills and specialties
Development support that is conscious of the exit strategy
Support for intellectual property management and technology transfers
Large-scale post-marketing research, support for the implementation of joint international research
Securing ICH-GCP-compliant clinical trials system, ethics and credibility
Spread of and education in ICH-GCP-compliant clinical trials and implementation systems
CRIETO structure for support of research seeds

Various different ideas come into being in the course of everyday medical activities as well as fundamental and applied research. Among them may be potential “seeds” for research that will lead to the development of new drugs or medical devices. Based on its abundant record of performance in development, CRIETO addresses such seeds directly and actively.

In the case of medical devices, prototypes are fabricated to satisfy requirements that are derived from the original idea. Results of research and other achievements made up to that point are examined, and approaches to development (non-clinical trials, clinical trials, approval screenings, etc.) that are best suited to the particular seeds are designed. Development support is provided so as to facilitate speed while also pursuing continuous verification of safety and effectiveness.

In the pharmaceuticals field, animal testing is used to determine what effects a candidate drug has, whether people can feel safe using it, and other such matters. In the case of medical devices, too, non-clinical trials are used to verify effectiveness and safety. CRIETO also provides support for non-clinical trials so as to facilitate the transition to clinical trials.

Clinical trials involve the use of candidate drugs and medical devices on actual people (healthy people and patients) to confirm their effectiveness and safety. CRIETO provides support primarily to the departments conducting clinical research, while taking steps also to coordinate with other departments, so as to facilitate the smooth implementation of clinical trials in general, to include clinical testing, and to improve the quality of clinical trials.

After effectiveness and safety have been confirmed by clinical trials and other such procedures, all results obtained from fundamental research to clinical trials must be put together in organized form for approval screening by the Ministry of Health, Labour and Welfare. CRIETO provides support for applications and related matters so that pharmaceutical approval can proceed with certainty and speed.

In the case of medical devices, too, prototypes are fabricated to satisfy requirements that are derived from the original idea. Results of research and other achievements made up to that point are examined, and approaches to development (non-clinical trials, clinical trials, approval screenings, etc.) that are best suited to the particular seeds are designed. Development support is provided so as to facilitate speed while also pursuing continuous verification of safety and effectiveness.

To the seeds of research that are being developed at the related departments of Tohoku University, other universities and research institutions, corporations, and other such organizations, CRIETO provides support that is geared to every stage involved, making effective use of its know-how and knowledge. Using the appropriate development strategy, we provide support to take the seeds of potentiality with greater sureness and speed along the course to their practical application.

There are 16 departments at Tohoku University concerned with this effort that collaborate on the Promotion of Medical Science Committee. In this body, they collect the seeds of potential development, identify the needs that exist on a university-wide basis, and promote effective development. We will also utilize the networks of industry, academia, government, and finance to improve the supporting framework that can realize the potential for practical application in the abundant seeds possessed by Tohoku University.
In August 2015, the Tohoku University Hospital was designated as a Clinical Research Core Hospital under the Medical Care Act, and became a medical center in Japan that promotes high-quality clinical research and clinical trials requisite for the development of innovative medicines, medical equipment and technologies originating in Japan.

CRIETO also serves as a center for implementation of the Translational Research Program: Strategic Promotion for practical application of Innovative medical Technology (TR-SPRINT) of the Japan Agency for Medical Research and Development (AMED). Along with 10 support centers located throughout Japan, it will eagerly aid seeds developed outside the center, strengthen industry-academia collaboration, and nurture the promising seeds of universities and other organizations. Currently, CRIETO is in the process of systemizing its transitional research support functions and Clinical Research Core Hospital functions, boosting its capabilities for gathering seeds, fostering the development of a diverse range of human resources, promoting clinical research through the creation of networks, and preparing a practical application program called the “Tohoku Translational Research Platform” (TRTP).

In addition to their quality, data about clinical research and trials such as number of hospitals, beds and so on are extremely important, and collaboration with regional medical institutions and counterparts overseas imperative. At CRIETO, as one aspect of the TRTP we make use of the “Tohoku Translational Network” (TTN) that we have built up centering on the Clinical Research Core Hospital functions of Tokyo University Hospital and seven universities in Tohoku. The TTN supports the practice of high-quality clinical research and trials that make the most of the local characteristics of the Tohoku region, and enthusiastically promotes domestic collaboration and international developments. It also creates developmental successful cases with international competitiveness, a benign cycle for the fostering of human resources, and by promoting the creation of innovative medicines and medical equipment originating in Tohoku it will form an R&D center that is renowned across the world.

In order to construct a system for the creation of innovative medicines and medical equipment originating in Japan, AMED took the Translational Research Support Promotion Program of MEXT in FY2007 and the Translational Research Acceleration Network Program also launched by MEXT in FY2012, starting the TR-SPRINT Program in FY2017. The TR-SPRINT Program aims to create continuously and in large quantities innovative medicines and medical equipment that can be effectively and efficiently provided to the Japanese public, and while using the infrastructure thus far developed, equip universities throughout the nation and other centers with the personnel and facilities essential in order that they can positively support industry-academia collaborations and the research issues of other external institutions. The program’s objectives also include making the function of nurturing seeds more robust, and the construction of an organization that will lead to the systematic practical application of the fruits of innovative basic research by academia and others across the whole of Japan. Tohoku University continues to be selected as the center for all these projects thus far carried out.

The Core Clinical Research Hospital under the Medical Care Act

The Core Clinical Research Hospitals are hospitals that have been accredited by the Minister of Health, Labor and Welfare (MHLW) under the Medical Care Act as medical institutions that play a central role in world-standard clinical research and investigator-initiated trials in order to maintain clinical research and investigator-initiated trials that meet the requisite quality for the development of innovative drugs and medical equipment within Japan.

The Tohoku University Hospital has thus far promoted the development of systems for the creation of next-generation medicine, principally through CRIETO, and pursued the construction of networks and improved clinical research in the Tohoku region. We will continue to seek further improvements to the system for implementing world-standard clinical research, seek to nurture human resources who can diffuse clinical research in Japan, and contribute to society as the clinical research center of Tohoku.
Introduction of research seeds supported by CRIETO

Development of innovative low-invasive angiogenic therapy using ultrasonic waves

Hiroyuki Shimokawa
Professor, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine

Ultrasonic waves at the same strength level as that used in diagnosis is found to enhance capillary development.

Ultrasonic imaging diagnostic devices have become widely popular in the world as a method for non-invasive test. At this time, we could identify that ultrasonic waves at the same strength level as that used in diagnosis leads to angiogenesis, and in response, we developed an ultrasonic neoangiogenesis device. For this study, an investigator-initiated clinical trial targeting cases in response, we developed an ultrasonic neoangiogenesis device.

Professor, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine

Consequently, no anesthesia and analgesics are needed for complications. This is an epoch-making discovery. Diagnosis and treatment can be performed with one probe, and the market and spread of this discovery is considered to be large.

Novel dental therapy system using hydroxyapatite thick film formation: development and clinical applications

Keiichi Sasaki
Professor, Advanced Prosthetic Dentistry, Tohoku University Graduate School of Dentistry

Applying advanced engineering technologies to dental therapy
Effective for both cosmetic and preventive dentistry

Powder jet deposition (PJD) for dental applications involves the spraying of fine particles of hydroxyapatite (HA), the main constituent of bones and teeth, so that the particles collide with the dentine surface to form a strong artificial enamel made of HA. This PJD method has potential for use to prevent or treat dental caries, suppress hypersensitivity, and as a cosmetic coating for discolored teeth (whitening). To treat dental caries, the decayed part of the tooth is removed and a film of HA is created to rebuild the enamel through remineralization. The interface between the tooth enamel and the HA film is gapless (see photo on the right) and integrated, because the HA film strongly adheres directly on the dentine without the need for a glue layer. The HA film exhibits superior acid resistance and superior temperature cycling resistance and is reliable even in mouths undergoing sudden changes in temperature or acidity because it is made from the same materials as the dentine. We expect this system to provide a novel dental therapy.

Development of novel antioxidative intraocular perfusate using reactive sulfur species

Toru Nakazawa
Professor, Ophthalmology, Department of Neuroscience and Sensory Organs, Tohoku University Graduate School of Medicine

Clinical development aimed at reducing complications from intraocular surgery

The number of intraocular surgical procedures has been on the rise in line with population aging, as Japan develops into a super-aged society. Such procedures are increasingly expected to be safe and produce positive outcomes, but complications do occur in a certain percentage of cases due to the invasive nature of the surgery. Even if the number of cases where complications occur amount to only a small percentage of the total, Prof. Nakazawa and his team consider it a problem that such complications still affect several thousand individuals nationwide. The research has focused on the intraocular perfusate used to preserve the eye tissues during intraocular surgery. The team started joint research with Prof. Takaaki Aoki (of the Department of Environmental Medicine and Molecular Toxicology at Tohoku University Graduate School of Medicine) after they came across his research into the antioxidant properties of reactive sulfur species. Using samples, Prof. Nakazawa’s team proved that reactive sulfur species with multiple sulfur molecules exist within the human eye and that they function as an antioxidative self-defense system. After confirming that manufacturing processes for reactive sulfur species have already been established and stable supplies are possible, the team began to develop a novel intraocular perfusate. Preparations are currently underway to obtain non-clinical proof-of-concept. There has been no new R&D into perfusates for many years, so Prof. Nakazawa and his team expect their work to be applied in other areas, as well as intraocular surgery.

Development of new pharmacotherapy for autism spectrum disorder

Toshio Miyata
Professor, Molecular Medicine and Therapy, Tohoku University Graduate School of Medicine

R&D into schizophrenia medications
Further potential for pyridoxamine

Antipsychotic medications are currently the mainstay treatment for autism spectrum disorder (ASD), but side effects like extrapyramidal symptoms mean we need to develop treatments with a better safety profile for pediatric patients. Prof. Miyata and his team have developed a hypothesis that pyridoxamine, a drug under development by his laboratory for the treatment of schizophrenia and that has yet to be approved, might also be effective in the treatment of ASD. This research team has therefore started a multi-center, investigator-initiated clinical trial on pyridoxamine.

Although ASD is different from schizophrenia, both clinical pathologies involve the action of y-aminobutyric acid (GABA) and other monoamines in the brain. Prof. Miyata and his team hypothesized that pyridoxamine might also be effective in the treatment of ASD because pyridoxamine is involved in the metabolism and biosynthesis of brain monoamines, such as serotonin and GABA, and both schizophrenia and ASD share the symptoms of excitability and aggression.

Pyridoxamine is a form of vitamin B6 that occurs naturally in the body. Pyridoxamine is expected to have a better safety profile than conventional treatments and has potential as a pediatric treatment for autism spectrum disorder.
The Academic Science Unit (ASU) is Japan’s first bedside solution program aimed at developing and commercializing new medical equipment and services. There are many instances in which something we have given up in the medical field turns out, after all, to be technically feasible according to engineers; conversely, technology available but buried in the medical field happens to meet needs in other fields. In this program, we open up our medical site to researchers from corporations and other fields and, by enabling them to understand medical needs on the spot, bring about new innovation. Based on the three conceptual pillars of “clinical imagination,” “brainstorming” and “networking,” we seek win-win partners that have a global perspective and promote medical equipment development and clinical research.

ASU program flow

Clinical immersion

We explore end-user-focused medical needs based on our own clinical experiences.

Brainstorming

We provide a forum where medical professionals and developers may engage in discussion from their point of view perspectives.

Networking

We speed up development by exploiting multiple networks and expanding perspectives.

3 components

Clinical immersion

Brainstorming

Networking

Clinical Immersion: Needs Validation

Brainstorming: Concept Generation

Networking: Business Planning

Clinical Learning: Needs Selection

Business Planning: Appointment

Strategic Focus: Instruction / Training

Would you like to join us at CRIETO in developing advanced medicine?

For inquiry about ASU, please contact
Department for Bedside Solution Program, CRIETO
Tel: 022-274-3501 Fax: 022-717-7104 E-mail: asu@crieto.hosp.tohoku.ac.jp
About CRIETO

“CRIETO” is read as “Ku-Ri-Ei-To.”

It is the acronym coined for the Clinical Research, Innovation and Education Center, Tohoku University Hospital. Pronounced in the same way as “create” in Japanese, CRIETO embodies the meaning of this word and is emblematic of what this center does: creates new medical technologies.

Concept of the Logo Mark

Two “C” s are shown in succession. The thin, elastic curve demonstrates CRIETO’s all-round approach of being able to adapt flexibly to a range of challenges. The six lines on the left side of the logo exemplify the mutual breakthroughs made between CRIETO and its partner Tohoku universities and medical institutions.

The Department of Development Promotion serves as the contact point with regard to seeds at any and all stages of development.

There are a variety of phases of research seeds projects, ranging from the idea phase through to the pre-clinical application phase. CRIETO accepts all inquiries irrespective of the development phase of the project, and regardless of whether the researcher is or is not from Tohoku University. The Department of Development Promotion will serve as the contact point for all consultations and will explore a development support plan that is appropriate for each and every research seeds project. On this basis, the Department of Development Promotion will offer support in partnership and coordination with all the departments of CRIETO.

Access

**Tohoku University Seiryo Campus**

**Access**

Department of Development Promotion
review@crieto.hosp.tohoku.ac.jp
TEL. 022-717-7136
FAX. 022-274-2522

**CRIETO Tokyo site**

NIHONBASHI Life Science Building #607,909
2-3-11 Nihonbashi Honmachi, Chuo-ku, Tokyo Japan
TEL: 03-3273-3601

- 3 min. walk from Exit A6 of Mitsukoshimae Sta. (Tokyo Metro Ginza Line or Hanzomon Line)
- 2 min. walk from Exit 5 of Shin-Nihonbashi Sta. (JR Sobu Line)
- 11 min. walk from South Exit of Kanda Sta.; 13 min. walk from Nihonbashi Exit of Tokyo Sta. (JR Yamanote Line, Keihan Tohoku Line, Chuo Line Rapid)

**Bus Stop**

[Sendai City Bus]

From JR Sendai Sta. West Exit Bus Pool No. 13, 15-1, 15-2. Get on a bus for “Tohoku Daigaku Byoin Keiyu” or bus stop No.60 “Kotsukyoku Tohoku Daigaku Byoin Mae.” Get off the bus at “Tohoku Daigaku Byoin Mae.”

(About 20 min., ¥180)

**Subway Station**

[Sendai City Subway]

From Sendai Sta. Take a Nanboku Line subway for “Bunri Chuu,” and get off the subway at “Kitayobancho” Sta.

(About 5 min., ¥200)

From North 2 Exit, 15 min. walk towards Yamagata.

- 3 min. walk from Exit A6 of Mitsukoshimae Sta. (Tokyo Metro Ginza Line or Hanzomon Line)
- 2 min. walk from Exit 5 of Shin-Nihonbashi Sta. (JR Sobu Line)
- 11 min. walk from South Exit of Kanda Sta.; 13 min. walk from Nihonbashi Exit of Tokyo Sta. (JR Yamanote Line, Keihan Tohoku Line, Chuo Line Rapid)