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ETTER

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Inquiry for research technology of CTC

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CHALLENGE



New approach through integrating medicine and engineering in a leap toward future cancer treatment

Meet new challenges by integrating all our knowledge

Consolidating the knowledge of the Tokyo University of Science - We have just begun our challenge in support of oncology

CTC goal



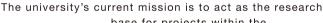
Advancements in cancer research. Even though a great deal of medical-engineering collaboration has already occurred, further advancements and progress areneeded. Leading-edge scientific technology plays an important and critical role in revolutionizing cancer research. Non-medical scientific technologies – science, engineering, pharmaceuticals, life science – these are the key to the future. Tokyo University of Science does not have a medical school and does not have many opportunities to become involved in clinical medicine. Yet the university is associated with the National Cancer Center (Hospital East), Japan's foremost cancer treatment institution, in an effort to move forward. Under the banner of "Cancer Medicine", the university has established a network for researchers to provide an extensive platform involving not only medicine, biology and pharmaceuticals but also mathematics, information science, applied biology,



engineering science, mechanical engineering, material engineering and biological engineering.

While applying the basic knowledge of technology to this

new collaboration, the university has a mission to develop and cultivate superior human resources – individuals who can contribute to future cancer research.





base for projects within the interdisciplinary researcher's network.

The university is moving forward

- its true value will be tested...

Energetic action, fruitful results

 $\hbox{Collision between medicine and academia-Information bang}$

Competition for higher objectives brings out unexpected "chemical" reactions creating something new "New" becomes the power to lead "Tomorrow's Medicine"

CTC activities

Realize visions and ideas and develop them.

Researchers from various fields in the university have started affiliating with the National Cancer Center (Hospital East). They have being meeting and sharing ideas on current problems and needs, and trying to determine how best to apply research results and technologies. They have also been discussing what they can do to contribute to cancer treatment and developing concrete ideas and solutions. Research results from this collaboration have been reported in seminars, lectures, workshops, etc. This supports effective public relations and enlightenment. The collaborative efforts are also aided by external evaluation and advisory committees that provide both suggestions and critiques. Additional efforts will be in such arenas as international symposiums.



Trinity collaboration

Intimate collaboration for a more challenging field

Medicine

[Clinical application]

National Cancer Center

Science, Engineering, Pharmaceuticals

[Manufacturing and Advanced Measurement Science Research] Tokyo University

okyo University of Science Biological Science

[Basic research (Biology, Chemistry, Information)]

Tokyo University of Science

Intimate collaboration provides an innovative platform for both new and novel ideas.

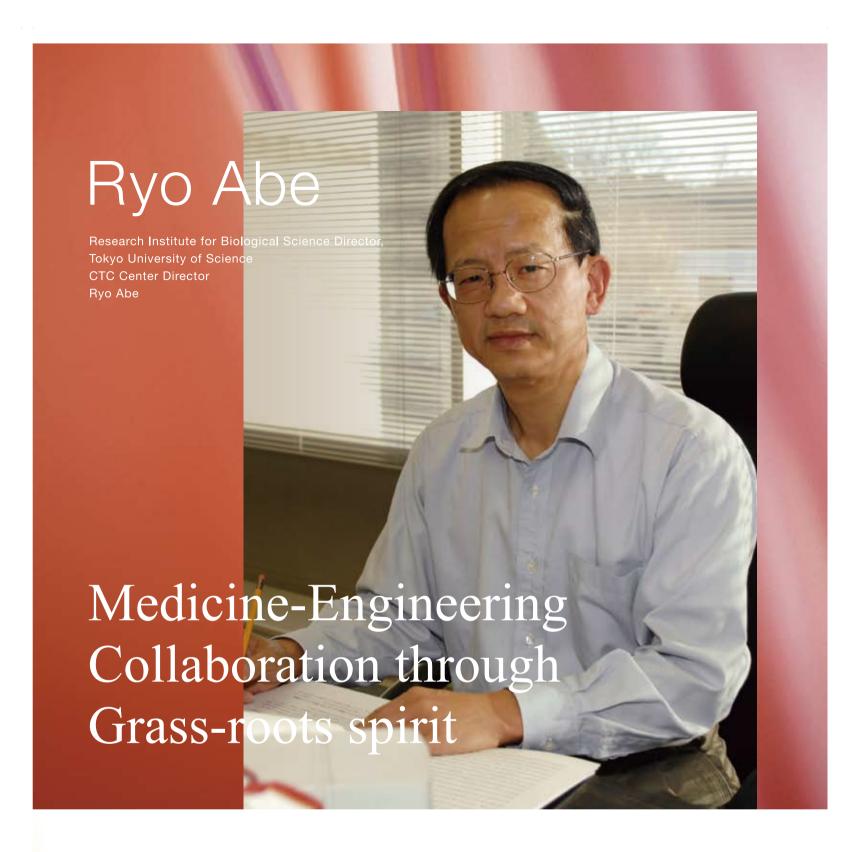
"Basic Research" that supports "Cancer Life Science" is based on biology, chemistry and information – this "trinity" brings forth wisdom...intelligence.

Following the "workmanship" philosophy, "Leading-Edge Science Technology" (mechanics, electronics, materials – realizing the vision) provides the tools and systems in

which knowledge is applied and acts as the hands and feet of the research and development efforts.

The National Cancer Center has been utilizing knowledge from this collaborative effort in its clinical applications – functioning as a new action for cancer research. That in itself is a challenge for CTC and is the reason for the existence of CTC From daily activities, opinions and reactions are carefully chosen, professionally reviewed by those in every specialized field and the feedback is returned to every activity. This means higher reliability and more

opportunities to find new possibilities. This process means an increase in human resources with an expanded vision.



Integrate leading-edge knowledge For unexpected synergy

Of cancer patients, half are cured and half of the remainder, that is, one-fourth of cancer patients, could have been cured if they had been diagnosed earlier. Current medicine, however, does not have the knowledge to cure cancer for the remainder.

Profile

Research Institute for Biological Science Director. Doctor of Medical Science.

After working at the US National Institutes of Health (NIH), National Cancer Institute (NCI) (researcher) and Uniformed Services University of the Health Science (assistant professor), Dr. Abe took a position at the Tokyo University of Science in 1995.

Council of Japanese Society for Immunology. Kyoto T-cell Convention Steering Committee.

Research fields: Immunology, Tumor immunology, Allergy/autoimmune disease

Why was collaboration created? What kind of progress has been made so far?

Q. For which concept was the activity initiated?

Abe. The Tokyo University of Science has a variety of human resources in addition to its students. If we could link these resources to medicine and the renowned National Cancer Center in particular, which would be a rare and unique collaboration, this mutual joint effort could be established because each would complement the other.

When the National Cancer Center visited the university to see all those researches, there was surprise at the high level of the research. When the university visited the National Cancer Center , we understood that our research could be of help to advance leading-edge medicine. This of course has led to strong motivation from both parties.

Through collaboration between the National Cancer Center and industry, we are able to validate the effectiveness of the results coming from these efforts. If we can advance the collaboration further, the results may be a more effective form of organization.



Difference between viewpoints in clinical and scientific research Benefit of merging different research results.

Q. How do clinical research and scientific research differ?

Abe. The way of looking at a problem and the way of thinking about it are quite different. For example, in a hospital, there are patients who are there to get better. This is result-oriented. In a laboratory, we first establish a theory and then gone on to try and prove every aspect. We make gains in research with some expectations of results. The results are, of course, important but we also evaluate the process very carefully.

In a hospital setting, there are always more unexpected incidents. However, those incidents that are puzzling in a hospital setting can be explained in a research situation. Some technologies that are used rather off-handedly can be quite effective in solving difficult problems.

Those different ways of looking at things means there are a large variety of approaches to cancer treatment. There will be more opportunities to develop more technologies.

This collaboration also brings another benefit. For example, in education and human resource development, if you are a student of engineering or chemistry, when you realize that your field can be applied to medicine your motivation may become increase. You might even be able to think of a career in medicine.

An engineering student can apply skills in a leading-edge medical specialty such as endoscope technology or radiology instead of industrial machinery or robotics. If the skill cannot be applied to medicine it can still be expanded. In this process, the

student can recognize wider possibilities or opportunities that can lead to involvement in "Life". It is wonderful to expand the view to the world.

"Find small, treat gently" What is the latest research status?

Q. Tell us the current situation

Abe. Abe: We are now looking for technology that will "find it small, treat it gently".

"Find it small" means to find cancer at the very early stages. Currently, many cancers cannot be found unless they are 1cm. We are searching for a technology that will allow us to find very small cancers in very early stages and also allow us to find cancer during a surgery.

"Treat gently" refers to lowering the cost. Instead of a biopsy, which is the most widely used method – sticking a needle in the body – we may be able to find cancer from a blood test, just like other diseases. We might be able to detect a very small cancer cell in the blood and, in a safe and secure manner, determine the characteristics of the cancer and treatment effect. This type of research has already started.

The researchers from related fields joined to work in three groups according to the approach on a particular type of cancer. One of these groups is termed "Visualization/Recognition Engineering" (VRG). This group is studying technology that will allow us to find a cancer or the spread of cancer without the use of a microscope during surgery.

"Pharmaceutical / DDS Science" group (PDG) allow us to find cancer cells in the blood and develop a system to check the nature of the cancer and the effectiveness of a particular drug.

"Mathematical Information" group (MIG) is doing research on how to categorize cancer from the biological point of view, and also taking a look at the predisposition and malignancy. Doctors from the Cancer Center are participating and vigorous research is ongoing.

To reach bigger goals Synergy of active activities

Q. What are the issues and visions for the future?

Abe. The highest priority is to yield results. We need to apply our basic technologies at the National Cancer Center to develop new products and applications. Important issues include insufficient research funds, technologies and equipment, etc. Our organization is not that large but we have to integrate our abilities to establish closer collaboration. We want to move forward to attack the problems with a "Grass-roots" spirit. This is because we have many "potential" human resources. We can get surprising results after stimulating each other, by competing with each other but also by complementing each other.

We, who want to understand life – and what a complex thing it is – are trying to find out what it is by using various methods and tools. We are living in a rather suffocating environment but have to bear in mind that the responsibility of a university is to send promising people out into the world.

Respecting the group's individuality and organically connect the groups.

Collaboration of three groups

CTC is a center between Japanese science, engineering,

pharmaceuticals and cancer medicine elites.

Each applies its unique skill to each collaboration to develop unprecedented results.

Each actively participates to this center.

Satisfying real needs in the front line, making more improvements, bringing

forth new discoveries.

Delivery of illuminant to

Pharmaceutical DDS(Drug Delivery System) an electron microscop



Visualization Recognition Group

Under the goal of detecting cancer early and development of a diagnostic system, the group supports the research from the technology aspect to develop a system that can visualize the illuminant particles by linking the research results to the development efforts.

The group is also researching various imaging processing technologies required by other groups.

Kohei Soga (Industrial Science and Technology, Materials) Masami Ando (Research Institute for Science and Technology) Noriaki Yanaka (Pharmaceutical Sciences) Naoyuki Aikawa (Industrial Science and Technology, Applied Electronics)

Hidehiro Kishimoto

Hirofumi Fujii National Cancer Center - Higashi Hospital)

Kazuhiro Kaneko Kiyotsugu Kojima (Olympus Corporation) Hideo Yokota (Riken) Hirotada Akiyama (ndustrial Science and Technology, Biological Science and Technology)

Hiroshi Hvodo HEMMER EVA

(Research Institute for Science and Technology

Mathematics

Information



Pharmaceutical DDS (Drug Delivery System) Group

Aiming to develop the cancer drugs with target specificity, the teams are doing research on various chemical compounds. Parts that are chemically bound before actual production must be

searched; after this occurs, MIG can support the project by providing the virtual screening technology.

Shin Aoki (Pharmaceutical Sciences, Medicinal and Life Science) Susumu Kobayashi reutical Sciences Medicinal and Life Science)

Fumio Sugawara (Science and Technology, Applied biological Scince) Takeo Konakahara

cience and Technology, Pure and Applied Chemistry) Makoto Yuasa (Science and Technology, Pure and Applied Chemistry)

Kengo Sakaguchi ch Institute for Science and Technology) Isamu Shiina (Science, Applied Chemistry)

Keiko Inami

Masanori Kitamura

Shinya Ariyasu (Research Institute for Science and Technology)

Masanori Hayase (Science and Technology, Mechanical Engineering) Hidenori Otsuka

(Science, Applied Chemistry) Takashi Ishiguro (Industrial Science and Technology, Materials)

Hiroshi Takemura (Science and Engineering, Mechanical Engineering) (Science and Technology, Industrial Chemical)

Mitsutoshi Tsukimoto

Structuring a chemical compound database, software development for drug design

Powerful collaboration transforms itself into a force to move forward

as a shared goal,

one's own field,

Using skill in

Mathematics Information Group

Nothing can start unless the Bio Material Team delivers the materials. If the research data from the groups is accumulated, it can be processed - information process.

This group is the focal point for finalizing the collaboration.

Biomaterials Team

Ryo Abe (Research Institute for Biological Science) Ryo Goitsuka (Research Institute for Biological Science) Takachika Azuma (Research Institute for Biological Science) Fumio Fukai (Pharmaceutical Sciences, Medicinal and Life Science) Joe Chiba (Industrial Science and Technology, Biological Science and Technology) Naoko Nakano (Research Institute for Biological Science) Rvushin Mizuta (Research Institute for Biological Science) Tetsuya Nakatsura (National Cancer Center – Higashi Hospital) Masaaki Ito (National Cancer Center - Higashi Hospital) Shuhei Ogawa (Research Institute for Biological Science) Toshihiro Suzuki (Research Institute for Biological Science) Moyuru Hayashi (Science, Chemistry) Kazutaka Horie (Research Institute for Science and Technology)

Akihito Murakami (Research Institute for Science and Technology)

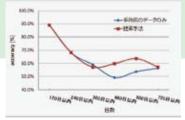
Mathematics / Bioinformatics Team

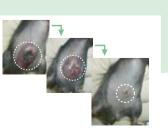
 Hayato Ohwada (Science and Technology, Industrial Administration) (Science and Technology, Industrial Administration)

Hirohito Kojima (Science and Technology, Civil Engineering)

(Science and Technology, Information Sciences)

Hiroyuki Nishiyama ence and Technology, Industrial Administration)





Technologies against okyo University of Science

Diverse researches are divided into three groups for cancer treatment types

Features and visions of those three research groups



Detecting cancer /

Diagnostic System

is to "See" and "Recognize"

The most critical mission

Developing

the cancer.

PDG

Pharmaceutical DDS (Drug Delivery System) Group

Discovery of cancer drug with high target specificity

Three pillars – "Drug Discovery / Diagnostics", "Screening", "Activity Assessment"

Drug Discovery Team

The team designs and synthesizes anticancer drugs based on a new acting mechanism. It researches chemical compounds that enable both cancer cell imaging and treatment. Each member brings chemical compounds and develops a chemical compound library. Using the university's characteristics, the team is trying to discover innovative anticancer drugs. Currently, the most promising drug is SQAG (Anticancer antibiotic) – functional analysis and clinical application.

Since the blood concentration of acetaldehyde (metabolized by alcohol intake) is high, the carcinogenic rate becomes high. The team is also trying to determine the quantity and to develop a new diagnostic method using the difference in a cancer cell's pH.

●Bio-device Team activities

The team is heavily involved in developing a device to detect CTC (Circulating Tumor Cell) in the blood. (Collaboration Project). The device traps cells in a section where the antibodies has been modified after being separated from normal tissue by a "micro-flow path" based on the Deterministic Lateral Replacement Method (existing technology) and thus concentrating cancer cells. This is a trial to release the cells using the "Optical Cutting Linker" developed by Prof. Aoki, group leader of the Drug Discovery Team. There are many tasks - adjusting/modifying the CTC capture chip. observing the antibody modification, culturing spheroids, etc. The team is also developing a tactile sensor as an approach to cancer treatment. Using a small sensor attached to an endoscope, data is collected, for example, on the hardness of the gastric wall. New types of data can be collected such as the level of cancer cell invasion. When a cancer cell multiplies or proliferates, the enzyme level in the blood changes, so the team is focusing on a method to measure the enzyme concentration in the blood.

The team's primary research is "Imaging and Recognition Technology - Targeting Cancer".

Prof.Soga, the group leader, is researching the "Illuminator" used in optic fiber communication, using the 1-2 micron wavelength band. (The wavelength band allows permeation of "biological object" that is termed the "window of biological body". This can be a universal solution for such current problems as discoloration in fluorescent observation. in a biological body, self-fluorescence, biotoxicity, light scattering. The "near-infrared fluorescent bioimaging" is developed using ceramics nanoparticles containing rare-earth compounds. The optic fiber wavelength region, used by Prof. Soga in the past, is 1.5 microns wavelength band and the optical component used in the optical fiber communication can be used as is. As a result, the "Cancer detection method = Visualization" project - the innovative method - has started. As an application concept, the doctor's "user demand" is emphasized to develop further "effective" and "usable" technology. A near-infrared in-vivo fluorescent bio-imaging device has been developed. That is one of the first such devices in the world. They have already developed three units. For treating colorectal cancer, current endoscopes can mark the affected area with near-infrared fluorescence to define the exact location; it can be removed precisely with the abdominoscope. The team is researching system development.

In the area of recognition technology, a more effective interface must be developed that will enable physicians to find cancer using more sophisticated methods from diverse/many diagnostic images (CT, MRI, SECT, etc.).

"Finding small = Early detection" — This is a universal issue for physicians. In this case, "Marker" is critical. The team is actively developing markers that react only to cancer cells. The team is also researching on new cancer detection methods

Prevention Diagnose Treatment

<Prevention><Diagnostics><Treatment> : Critical elements in Cancer Medicine

The research area can be further categorized into the following:

- Prevention: [MIG] Genome analysis
- Diagnostics: [VRG]
- Treatment: [PGD:

Actual research effort transcends those walls – Each group contributes to research in Prevention, Diagnostics and Treatment.

MIG

Mathematics Information Group

Mathematical Information Science Team, Biological Materials Tear

Cancer differentiation, Malignancy, Metastasis – Mechanism Study

Simulation programs and information strategy Platform for whole center

● Mathematics / Bioinformatics Team - Activities

The involvement with the medicine started when Prof. Owada, the group leader, developed a "glaucoma diagnostic system" when researching artificial intelligence. The system (i.e., computer), not the physician, asks the patient such critical questions as age, sex. eye pressure and automatically diagnoses for glaucoma. Currently, the team is involved in "predictions of liver cancer recidivation". Liver cancer has high recidivation rate. The test data can be input in the computer, and the computer can calculate the conditions for recidivation – probability and time. The data mining method is used in this project. This is now a universal way to search for regularity in massive amounts of data. In the future, the team will be involved in many projects such as matching data with genetic data, the relationship between protein and disease, system biology - combining the networks among cells called "pathways". These projects require sophisticated analysis that investigates the relationship between the data and clinical data from many directions.

Biological MaterialsTeam - Activities

Staff mainly from the Life Science Research Center is trying to develop new cancer drug technology with high target specificity. The team analyzes the CTC (Circulating Tumor Cells), designs and selects the antibody particles that specifically identify the cancer cells. This field is different from that of the Mathematical/Information group, but the combination of the beginning point (providing various materials) and the ending point (final analysis of the data) can enhance cancer treatment strategic point of view.

New vision focusing on specialized fields

The research results of each group, based on results from individual researchers, will be applied to cancer treatment, and under CTC's framework needs and benefits are combined into an innovative approach to cancer research.

Members of CTC research group

PDG

Drug discovery Team



Research project! Cancer diagnosis with high target specificity, Development of treatment method, Implementation of compound library that is proprietary of Tokyo University of Science

Listen for "voices" from the medical front and apply the original research in the latrochemistry.

Susumu Kobayashi

Faculty of Pharmaceutical Sciences
Department of Medicinal and Life Science

[Research project] Drug-discovery technology

Fumio Sugawara

Professor
Faculty of Science and Technology
Applied Biological Science

[Research project]
Search technology for in vivo target of medicinally-active small molecule

Takeo Konakahara

Faculty of Science and Technology

[Research project]
Drug-discovery technology

Makoto Yuasa

Faculty of Science and Technology Pure and Applied Chemistry

[Research project] Drug-discovery technology

Kengo Sakaguchi

Research Institute for Science and Technology

VRG

[Research project] Medical application of the next generation imaging using near infrared fluorescence

Don't think Do it

Masami Ando

Noriaki Ynaka

Faculty of Pharmaceutical Sciences
Department of Pharmacy

[Research project] Medical diagnosis of cancer image

Naoyuki Aikawa

[Research project] Medical diagnosis of cancer image

Hidehiro Kishimoto

[Research project] Study on malignant cancer and

Hirofumi Fujii National Cancer Center -Higashi Hospital

Professor Research Institute for Science and Technology

Bio-device Team



Isamu Shiina

Keiko Inami

Junior Associate Professor Faculty of Pharmaceutical Sciences Department of Pharmacy

Masanori Kitamura

Takahiro Suzuki

Reiko Ikeda

Assistant Lecturer Faculty of Science and Technology Pure and Applied Chemistry

PD Research Institute for Science and Technology

Masanori Hayase

[Research project]
Development of the device for

Starting from the far-end of cancer. Unconver

Takashi Ishiguro

Faculty of Industrial Science and
Technology Material Science and Technology

[Research project]
Analysis of biological structure by electron microscope

Hidenori Otsuka

Associate Professor Faculty of Science, Division 1 Applied Chemistry

[Research project] Surface design of the cell target material, development of mini-tissue array

Shinya Ariyasu Hiroshi Takemura

Junior Associate Professor Faculty of Science and Technology Mechanical Engineering

[Research project]
Development of organ simple model

Kenichi Sakai

Mitsutoshi Tsukimoto

Assistant Lecturer Faculty of Pharmaceutical Sciences Department of Pharmacy

Kazuhiro Kaneko

[Research project] Cancer diagnosis by endoscope and treatment

Kiyotsugu Kojima

Kiyotsugu Kojima Olympus Corporation

[Research project] Medical diagnosis of cancer image

Hideo Yokota

Hirotada Akivama

Hiroshi Hyodo

Assistant Lecturer Faculty of Industrial Science and Technology Material Science and Technology

HEMMER EVA

PD Research Institute for Science and Technology

Bio-material Team

Mathematical Science/ Information Analysis Team

Ryushin Mizuta

[Research project] Canceration and inflammation

Chief

[Research project] T-cell antigen recognition and activation mechanism, development of antigen-specific immunotherapy

We can consolidate our effort to create an epoch-making opportunity for revolutionary "Medicine".

Ryo Goitsuka

Research Institute for Biological Sciences

Tetsuya Nakatsura

National Cancer Center -Higashi Hospital

Masaaki Ito

National Cancer Center -

[Research project]
Cancer diagnosis and treatment

Hayato Ohwada

[Research project] Developing the prediction system

Developing IT technology for cancer medicine for the world.

Shunsuke Mori

Faculty of Science and Technology

Hirohito Koiima

Keiko Sato

Froressor
Faculty of Science and Technology
Civil Engineering

[Research project]
Development of image processing technology

Junior Associate Professor Faculty of Science and Technology

Takachika Azuma

[Research project]
Antibody molecule design and selection

Fumio Fukai Professor Faculty of Pharmaceutical Sciences Department of Medicinal and Life Science

[Research project] Search for new anticancer molecule

targeted drug

Joe Chiba

[Research project] Search for new anticancer molecule targeted drug

Naoko Nakano

[Research project] Measure anticancer effect using mouse model

Shuhei Ogawa

Assistant Lecturer Research Institute for Biological

Toshihiro Suzuki

stant Lecturer earch Institute for Biological nces Division of Immunobiol

Moyuru Hayashi

Kazutaka Horie

Akihito Murakami

Research Institute for Science and Technology

Hiroyuki Nishiyama

[Research project] Research on cancer mutation

Junior Associate Professor
Faculty of Science and Technology

[Research project]
Study on development of computation algorithm

Nobuyuki Ota

[Research project] Study on development of computation algorithm