

Newsletter

# NanoSky

From KING SKYFRONT to the world -NanoMedical Innovation

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The final issue

## Concept of “In-Body Hospitals” evolving toward the realization of a smart life care society

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# Connecting COINS' creation to the next generation

Center of Open Innovation Network for Smart Health (COINS) will end this year. Dr. KIMURA Hiromichi, Project Leader, Dr. KATAOKA Kazunori, Research Leader and Dr. MATSUDA Yuzuru, Visionary Leader COI STREAM Vision 1 "Secure sustainability as a country advanced in its aging population and declining birth rate: Smart Life Care, Ageless Society" look back at the beginning of the project, and evaluate the outcome. They discuss about future research and expectations for Innovation Center of NanoMedicine (iCONM).



## KATAOKA Kazunori

Vice Chairperson, KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION  
Director General, Innovation Center of NanoMedicine (iCONM)  
Research Leader, Center of Open Innovation Network for Smart Health (COINS)

Dr. Kazunori Kataoka is the Vice Chairperson of KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION (KIIP) and the Director-General of the Innovation Center of NanoMedicine (iCONM) at KIIP. He is also a Professor Emeritus, The University of Tokyo. Immediately after receiving his Ph.D. (1979) from The University of Tokyo, he started his academic career at the Institute of Biomedical Engineering, Tokyo Women's Medical College. He moved to the Department of Materials Engineering, Tokyo University of Science in 1989, and then moved to the Department of Materials Engineering, The University of Tokyo as a Full Professor in 1998. He was appointed joint-position of a Full Professor at the Center for Disease Biology and Integrative Medicine, The University of Tokyo Medical School in 2004. In 2016, he moved to his current position. He was appointed as Adjunct Professor at the Eshelman School of Pharmacy, University of North Carolina Chapel Hill in 2015.

## KIMURA Hiromichi

KAWASAKI INSTITUTE OF INDUSTRIAL PROMOTION  
Innovation Center of NanoMedicine  
COINS Project Leader

In 1979, he completed the doctoral course at the Graduate School of Pharmaceutical Sciences, The University of Tokyo. He is a doctor of pharmacy. After working at Kyowa Hakko and Morgan Bank, he served as President of Amersham Pharmacia Biotech Co., Ltd. and Monsanto Japan Co., Ltd. He is currently a specially appointed professor at the Institute for Future Initiatives, The University of Tokyo. A visiting professor of the Faculty of Pharmaceutical Sciences, The University of Tokyo. He also serves as President and Chief Executive Officer of Fast Track Initiative Inc.

## MATSUDA Yuzuru

Honorary Director, Kato Memorial Bioscience Foundation  
Visionary Leader, The Center of Innovation Program (COI) "Secure sustainability as a country advanced in its aging population and declining birth rate: Smart Life Care, Ageless Society"

In 1977, he completed the doctoral course at the Graduate School of Agriculture, The University of Tokyo. He is a doctor of agriculture. He joined Kyowa Hakko Kogyo Co., Ltd. and after working as a managing director, he served as President since 2003. In 2008, Kyowa Hakko Kogyo Co., Ltd. merged with Kirin Pharma Co., Ltd., thus he became President of Kyowa Hakko Kirin Co., Ltd. Currently, he serves as an honorary director of Kato Memorial Bioscience Foundation and an external board of director of Kubota Co., Ltd. and JSR Corporation.

## The Birth of the Term "In-Body Hospitals" shares Vision and Mission and promotes team unity.

### ■ What were your thoughts when you launched COINS 10 years ago?

**Kimura:** Around 2011, I heard that Kawasaki City was going to develop King SkyFront by narrowing the theme down to biotech and medicine, but when I came to visit, it was just a field with a few buildings. This is the former site of the Isuzu Motors' plant, with the oil plant visible from the highway. In a sense, this place is a symbol of the massive industries that have supported Japan, and I thought it would be a shame not to make use of this infrastructure. In the 1980s, I saw how the IT and biotech industries were gathering in Silicon Valley and the suburbs of Boston in the U.S. and how the cities were changing. There was no reason why we couldn't do the same in Japan, so I was glad that I could be involved in building a new mechanism for the world, and that I could do something that no one else was doing.

**Kataoka:** I was hopeful that we would be able to achieve what we had always wanted. When I became a professor at both the Graduate School of Engineering and the Graduate School of Medicine in 2004, I started Medical Nanotechnology Human Resources Training Unit to accelerate the medical-engineering collaboration that was progressing at The University of Tokyo. Next, I established a Center for NanoBio Integration within the university. With the help of Dr. Kimura, we have gathered scientists from the Faculty of Pharmaceutical Sciences and the Faculty of Science. We also ran the FIRST program "Development of Innovative Diagnostics and Therapeutic Systems Based on Nanobiotechnology." However, I felt that it should not be confined to universities and academia to develop this field further. That's when I heard about COI STREAM, learning that it would allow us to set a vision and conduct research in collaboration with the industry, academia, and government over a long period. Accordingly, I decided to apply for the COI STREAM program. At the time, nanotechnology compared to making the information in the National Diet Library the size of the palm of one's hand, with a science fiction' impression where medical nanotechnology makes medicine more accessible or turns hospitals smaller. I'm still amazed that this SF-like idea was adopted (laughs).

**Matsuda:** When I was asked to be a COI STREAM Visionary Leader (VL), I was initially reluctant, since I had been involved in government-led projects as a corporate scientist and manager and felt that the roles of corporations and academia were fixed and unattractive. However, I was persuaded by the then Director-General of the Ministry of Education, Culture, Sports, Science and Technology (MEXT), who explained that the project would be a long nine years, have a large budget, and would be conducted under one roof using backcasting so that only motivated companies would participate.

In vision 1, "Secure sustainability as a country advanced in its aging population and declining birth rate: Smart Life Care, Ageless Society" which I oversaw, seven sites were adopted. The difference between COINS and other centers is that COINS is supported by Kawasaki City, is not university-centered, and is a big challenge. Although COI



STREAM was supposed to be socially implemented in nine years, that was impossible for COINS. There was then a discussion about where to put the endpoints. As a VL, I was concerned that if we only aimed for social implementation in nine years, we would end up with a uniform proposal such as "use IT technology to collect health check-up data, analyze it, and return it to the community." I wanted to bring diversity to the project. In that sense, the SF-like COINS is unique, where we determined that the concept of creating a platform for innovation with social implementation, such as venture creation, would fit the purpose of COI STREAM.

### ■ How was the term "In-Body Hospitals" born?

**Kimura:** When we were thinking about the vision for COINS, everyone came up with the words "In-Body Hospitals" and "Smart Nanomachines." I don't remember who started them.

**Kataoka:** I probably think it was when we were writing the proposal. In the beginning, when we brought up the topic of "In-Body Hospitals", we were like, "What is the meaning of this topic?" However, as the meetings went on, everyone became more clear about this topic and started to think that "we could realize it!". While this concept alone is precisely science fiction, actual stage gates, such as the founding start-up companies, are set with Dr. Kimura at the helm. It was then essential for us to know what we should do now.

**Kimura:** In pharmacy and biology, what we don't know (the black box) is gradually revealed through research. On the other hand, in engineering, we are always aware of reality and gather logic and parts to assemble something new. While it's interesting that the ideas are reversed, it also comes with some difficulties. When people with such different ideas come together to achieve a single goal, there is power in creating your term to represent a concept and share it as a vision to solidify the team.

## An Innovation Ecosystem formed, Human Resources nurtured, and exchanges with citizens promoted

### ■ How do you evaluate the results of COINS?

**Kimura:** In my opinion, there are two results, one is the increased exchange with the citizens of Kawasaki, which is also the mission of COINS. Through tours, seminars, and symposiums, interest in science and technology by citizens has increased. While at the same time, scientists are now not only accountable for explaining their research due to using taxpayer money but also ready to make their research more understandable to the public. While many scientists may live in a world of isolation, saying, "They won't understand even if I talk to them anyways," scientists at COINS have realized that it is important for citizens to understand science and



technology and that this will benefit them. These exchanges have become an asset for both sides, with ones between citizens and scientists essential for a science-based country. The other result is that we were able to create the prototype of an innovation ecosystem. Research based on backcasting, the launch of venture companies, the use of venture capital, and intellectual property strategies have all taken shape over the past nine years, and we are now ready to hand over the baton to the next generation. We have reached the point where we can pass the baton to the next generation. This has been in line with the direction Kawasaki City is aiming for. The next phase is to expand overseas. For this purpose, we are making efforts to make English an official language in COINS while building incubation projects and other mechanisms.

**Kataoka:** To a certain extent, we achieved the three P's (platform, patent, and paper) that VL Matsuda had mentioned from the beginning, which is necessary for the creation of venture companies. Another significant P, people, has also been developed. We were able to teach young people how to think about R&D in terms of formulating and sharing a vision and mission, and how to think under one roof about innovative things in the long-range. The COI was an excellent opportunity for everyone to change their mindset. **Matsuda:** In a little more than eight years, we have published papers, created ventures, and raised funds from venture capitalists to build a solid foundation for the realization of an "In-Body Hospitals". I hope that the results of COINS will lead to the development of Kawasaki's industries.

#### ■ What are the key issues and breakthroughs in spreading "In-Body Hospitals"?

**Kimura:** There's the public acceptance of innovation. In a survey conducted in collaboration with the National Museum of Emerging Science and Innovation (Miraikan), we asked people if they would use "In-Body Hospitals" if it were built, and it felt that many Japanese people are skeptical about using new technologies. It's important to improve science and technology literacy and create a system to make people accept "In-Body Hospitals".

**Kataoka:** Under the pandemic situation, interest in science and technology is growing with high expectations, and thanks to the Internet, we all now have access to information. Scientists need to communicate how their research is helpful to society and what the risks are.

**Matsuda:** I hope everyone at COINS can stick to their goals and create the right environment to achieve them. That's the

significance of a long-term project led by the government, since if it can be done in two or three years, it'd be best to proceed without using taxpayer money.

#### ■ How do you see the impact of the COVID-19 pandemic on research at COINS and on society? What is important in a post-COVID era?

**Kataoka:** Going to the hospitals is recognized as a risk during the pandemic, reminding the importance of "In-Body Hospitals". My co-researcher, a doctor, told me that miniaturized diagnosis equipment integrated with AI bots and telemedicine would be delivered to people's homes in the future. While we need to amend the Medical Practitioners' Act requesting face-to-face medical care, I believe that this type of online diagnosis may become a reality in the future.

**Kimura:** Public acceptance of the "In-Body Hospitals" will drastically increase. As the world is not going back to the way it was, social models that fit the new normal will continue to expand. Competition may possibly become more intense in the field of medical nanotechnology, while there may still be some areas that can be characterized locally. This is a chance for COINS to rethink its approach.

**Matsuda:** In countries such as China and India, digital transformation (DX) in healthcare is progressing against a backdrop of poor access to healthcare. While it is true that Japan is lagging behind in DX, people will not be satisfied with DX that just improves access to medical care when a universal health insurance system exists with many areas having free access to local medical facilities. What we need is something revolutionary like the "In-Body Hospitals", which I believe is the right approach for the post-COVID era.

**Kimura:** In the future, we must create a new standard that brings social science and science and technology together alongside regulations, the latter of which Dr. Kataoka's group is working on.

**Kataoka:** Commissioned by the European Medicines Agency, we have been working with the Pharmaceuticals and Medical Devices Agency (PMDA) and the National Institute of Health Sciences (NIHS) to prepare a reflection paper for drug delivery systems (DDS) using polymeric micelles. This work is a provisional step in developing Guidelines for DDS using polymeric micelles. To popularize Japan's superior technology in the drug delivery field, taking global standards is essential. We need to work together with every expert from an early stage in advance to review and revise the regulations.



### Going Beyond COINS - Passing the Baton to the next generation of scientists and giving them a push

#### ■ Do you have any words of encouragement to the members of COINS and scientists in Japan?

**Kataoka:** I would tell them that diversity, in the end, is essential from having worked in a variety of settings, including research at the Faculty of Medicine after earning a Ph.D. in Engineering. While some people don't like interacting with people from different fields or positions, saying that it makes them "go off track," there is no track in essence. When you are in a new place, you realize the mistakes you made before and the narrowness of your perspective, but you also understand the weaknesses there. You can observe your knowledge and awareness objectively and see where you stand. University labs are just like "silos" where homogeneous people gather, and the mechanism for diversity is weak, so I would invite you to somewhat get into contact with the outside world.

**Matsuda:** I would probably say, "Take risks," where the word risk originally means "to try with courage." Scientists

#### ■ COINS R&D achievement displayed by 4 Ps

(Achievement until the end of September 2021)

#### Papers

Submitted papers: **464**

No. of citations  
Top 10% of papers **15%**

#### People

Human resource development

Human resources for interdisciplinary research  
Human resources for management

#### Products

Establishment of startup :

**7** companies

Braizon Therapeutics Inc. /AccuRna Inc./  
iXstream, inc./SONIRE THERAPEUTICS/  
iXflow, inc. /PrimRNA /  
Red Arrow Therapeutics Inc.

#### Patents

Patents no. of  
applications:

**222**

Includes 94 int'l  
applications

do not have a long time to do what they like. Although there seems to be a trend to not venture out while worrying about one's future post and livelihood, I would invite you to actively go abroad and work in top-notch places. Of course, the support of those around you is also important. In this way, iCONM can be said to be an international place where you can challenge yourself.

**Kimura:** It's essential in entrepreneurship to have the courage to do what others are not doing and to take the lead. Although Japan is said to be a vertically structured society, each of these vertically divided cylinders is packed with wisdom. Therefore, if you stick cross-sectional axes through them, innovation will spring forth, which is born when different ideas collide. I would invite you to have a bit of courage and curiosity to meet people who are different than those you are used to. With the COINS general meetings and other events, we've intended to provide opportunities to meet people.

#### ■ What are your future aspirations?

**Matsuda:** It has been a valuable experience for me to be involved in a project from a completely different national project through COI STREAM. As a special advisor for COI-NEXT, a program for supporting the formation of co-creation places, I'd like to produce results that will hopefully lead to research or industry.

**Kimura:** I'd like to continue to encourage young people who have the courage by creating an environment that makes it easier to take on the challenge of starting a business and further promoting the creation of a system that makes it easier to succeed.

**Kataoka:**

It's our role to support young scientists. I am relieved to have inherited the vision and mission of iCONM and COINS, which has developed human resources capable of managing. On the other hand, research is a serious business, with age-irrelevant. Since my research is not yet complete, I'd like to water and take care of the seed I have sown.

#### ■ If "In-Body Hospitals" were to become a reality, would you use it?

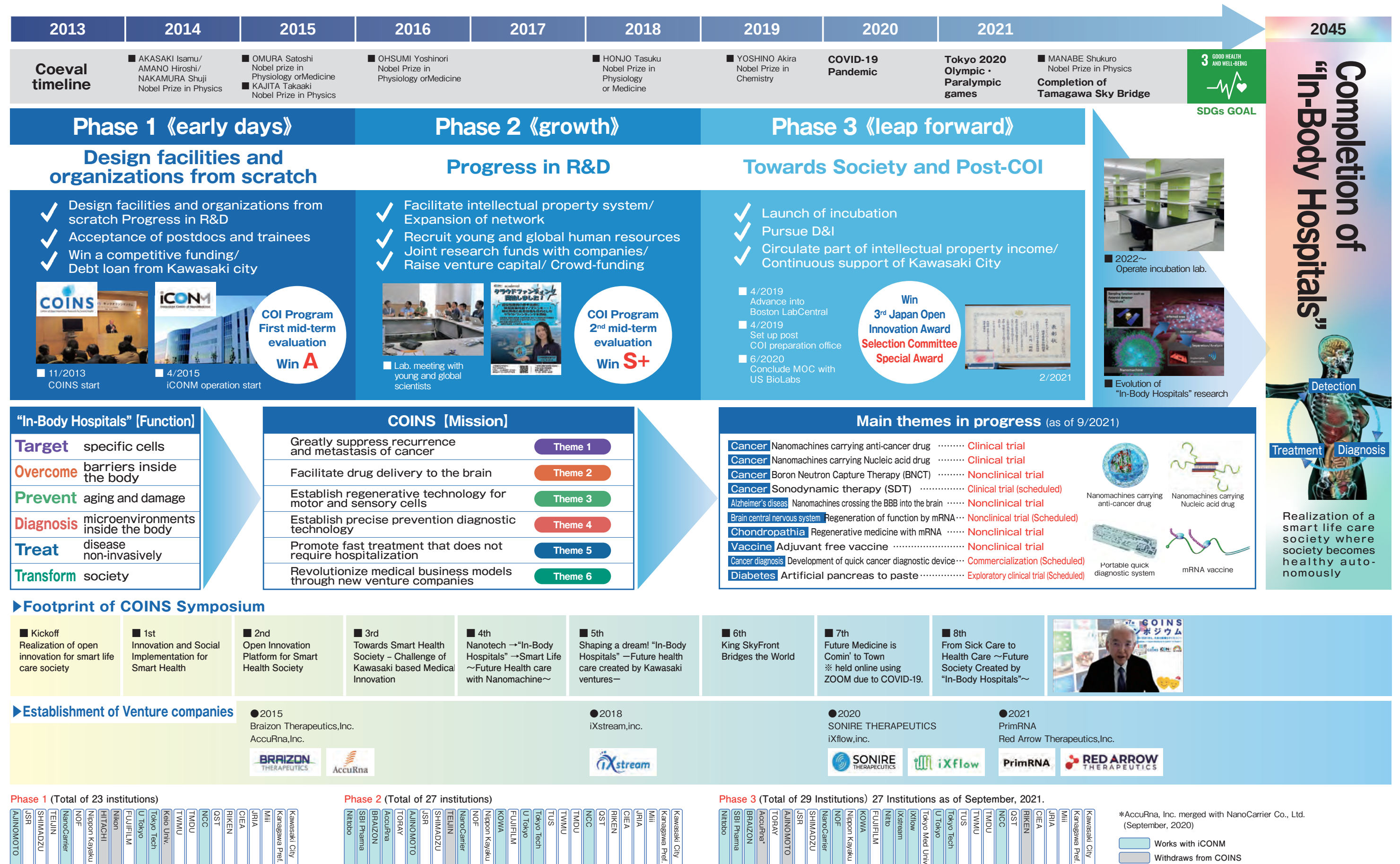
**Kataoka, Kimura, Matsuda:** Of course, we'll take the initiative to do so!

(Interviewer: Science Writer KOJIMA,Ayumi)

# Nine years history of COINS project

Under the background of building a new industry in the Keihin industrial area driven by the heavy chemical industry, Kawasaki City has decided to work on the formation of the world's top class R&D base in King SkyFront District (KSF) of Tonomachi Kawasaki, which was designated as an International Strategic Special Zone in 2011.

The Center of Open Innovation Network for Smart Health (COINS) started in 2013 in the Innovation Center of NanoMedicine as a core institution, with the vision of "In-Body Hospitals" that integrates nanotechnology such as "nanomachines" and "nanobio devices" for diagnosis and treatment, is aiming to realize a "smart life care society" where people can be free from illness and treatment, and are able to autonomously obtain health in their daily lives without having burden of the labor, cost, and access required for medical treatment.



\*AccuRNA, Inc. merged with NanoCarrier Co., Ltd. (September, 2020)

Works with iCONM  
Withdraws from COINS



I have been involved in the development of King SkyFront since my previous job as Deputy Mayor of Kawasaki City.

MIURA Atsushi

Chairperson,  
Kawasaki Institute of Industrial Promotion

## World class approach from Kawasaki City

The COINS project has reached its final year. Since I was involved in the development of King SkyFront as a Kawasaki City employee at the time when it started, it was a long way. Globalization, that started with the fall of the Berlin Wall in 1989, had a serious impact on Japan as well, with the collapse of the bubble economy and long-term stagnation, Kawasaki City was also urged to shift from heavy industry. Isuzu Motors Ltd. in Tonomachi also moved to somewhere else, and in 2001, half of the site was sold to UR Urban Organization. In 2003, the government issued a policy for re-expansion and internationalization of Haneda Airport and the other half of the site of Isuzu was sold to Yodobashi Camera. This was the beginning of the

development of King SkyFront.

In 2008, Kawasaki City started discussions with related parties and decided on a policy of aiming to integrate cutting-edge technologies and R&D functions in fields such as the environment, health, welfare, and medical care. Around that time, I heard from one of the companies located in the coastal area that they were conducting joint research with Dr. KATAOKA Kazunori, a professor of The University of Tokyo. I met him and Dr. KIMURA Hiromichi after that. We confirmed that we would make a world-class initiative in Kawasaki. This was the beginning of the establishment of Innovation Center of NanoMedicine (iCONM). In 2011, the Great East Japan Earthquake occurred.

In the same year, the Central Institute for Experimental Animals, the first facility of King SkyFront, started operation and was designated as a National Strategic Special Zone. In 2013, with the support of the government and the city, iCONM construction has progressed, and we applied for "COI STREAM" to obtain research funds. In applying, academia concerned had discussed through the night, then Dr. ANZAI Tomohiro summarized. It was successfully adopted in October of the same year and in April 2015, iCONM started operation with the vision of "In-Body Hospitals". I would like to express my sincere gratitude to all of you who supported us for your efforts and cooperation.

SAKURAI Toru

Administration Manager  
Innovation Center of NanoMedicine

## Tumultuous decade since preparation for opening of iCONM

Let us just have your name. It is ok to help us only a little." This is what Kawasaki City asked me, but I am still here although it supposed to be only a little. Construction of "Center of Monozukuri Medical Innovation (Initial name) =photo, and opening of research center was like a change of job for me. While responding to construction work, everything such as applying for research institution, going through e-RAD procedure, making rule, making real estate transaction, etc. was for the first time. We had trouble opening the phone and the Internet, and among the members of the preparation room, we were often anxious about we couldn't make it in time for the opening, however, it was finally opened just the day before and I

remember we were relieved.

The foundation specialized to support small and medium-sized enterprises could successfully establish iCONM because of advice and support from the Ministry of Education, Culture, Sports, Science and Technology-Japan, JST, Kawasaki City, Collaborative University, National Cancer Center Japan, KISTEC, and Central Institute for Experimental Animals. We would like to take this opportunity to thank everyone who supported us. For tumultuous decade, as a core base of the COINS project, iCONM has become a world class nanomedical research institute in Japan, and a symbol of King SkyFront.

I am proud of being involved in this project. I don't



I am involved in the iCONM management and operation from the day one preparation for the opening of the Innovation Center of NanoMedicine.

know how long I will be able to stay, but I look forward to the day when I can witness the historic moment of the realization of an "In-Body Hospitals" without waiting for 2045.



Center of Monozukuri Medical Innovation (Initial name) =photo Construction scene

MATSUMURA Yasuhiro

Visiting Scientist, Division of Developmental Therapeutics, EPOC, National Cancer Center Research Institute  
Director of Research, RIN Institute Inc.  
Principal Research Scientist/Laboratory Head, Innovation Center of NanoMedicine

## Aiming for integration of materials engineering and materials biology

When I heard about this project, I felt that, unlike normal research, it was too grand and beyond my own control. Nevertheless, I had been doing joint research with Dr. KATAOKA Kazunori since 1995 and had the chance to think about the contribution I could make as a member of the National Cancer Center Japan (NCC). I also had to decide what to do with my theme. Prior to this project, I had been working together with NanoCarrier and Nippon Kayaku in charge as well as Dr. HAMAGUCHI Tetsuya, a current professor at Saitama Medical University, on clinical trials of micelles encapsulating anti-cancer drugs.

I felt it was my responsibility to take over that line of work. As for my own theme, the starting point was research on the effects of EPR over 35 years ago, I had shown that high molecular weight proteins, especially IgG, naturally collect in cancer, and tumor vascular hyperpermeability, which is essential for EPR effect, is based on the production of vascular hyperpermeability factor as a by-product of blood coagulation by cancer. From such this backdrop, we came up with the idea of selecting a tissue factor (TF) antibody, which is a trigger molecule for exogenous coagulation that we established, and adding it to the micelle surface to serve as a pilot

molecule for micelle. In collaboration with NanoCarrier, we have successfully produced anti-TF, antibody-added micellar nanoparticles with Dr. TAKASHIMA Hiroki (Leader of Division of Developmental Therapeutics, EPOC, NCC) as the lead along with the support of Dr. YASUNAGA Masahiro (Director of Division of Developmental Therapeutics, EPOC, NCC) and Dr. KOGA Yoshikatsu (Chief of Department of Strategic Programs, EPOC, NCC). We hope that this drug will be used as a prototype for the creation of more advanced complexes in the future.



I am engaged in research aiming establishment of antibodies focusing on cancer specificity and clinical application.



I work on social implementation of research results under Theme 6 at COINS and disseminate seeds from academia to the world as my life work.

ANZAI Tomohiro

Principal Research Scientist, Innovation Center of NanoMedicine  
COINS Theme 6 Leader

## The day when the "In-Body Hospitals" was born

I was in 2010 that I first visited the King SkyFront in Tonomachi. Only the Central Institute for Experimental Animals, which is scheduled to open next year, was there, and the other lots were completely vacant. I still remember that the sky looked very wide. It's been 11 years since then. Many companies and research institutions are gathering together here, and a community is steadily being formed. Now that the Tama River Sky Bridge, which was our fervent wish, is about to be completed. I feel the time just flies by. It was in the winter of 2012 that we started preparations with Dr. Kataoka and Dr. Kimura to propose the establishment of a new inter-

disciplinary research center in this area. In order to create a proposal led by Professor Kataoka, it is essential to have discussions that continue until midnight to solidify the concept. Also, not only faculties from The University of Tokyo but also faculties from other universities and local governments participate in a wide range of discussions in the cross-sector and sharpen the content of the proposal. Our vision is shared with everyone involved and a sense of unity is fostered through this process. The word "In-Body Hospitals," which is our goal, is a word that suddenly came down from the discussions that inquired into the concept. Keeping the passion we had at the time of our

establishment, where we talked about the future health care, we shall continue to work on the realization of "In-Body Hospitals" and the construction of an innovation ecosystem.



Overlook Haneda Airport, where iCONM is located (photographed in 3/2013)



MIYATA Kanjiro

Professor, Department of Materials Engineering  
Graduate School of Engineering, The University of Tokyo  
COINS Theme 1 Leader

Involved in the research and development of nanomachines that "target" cancer, I am particularly focused on the research of nanomachines for gene/nucleic acid delivery.

## Bringing "Panacea on the desk" to Reality

I started my research on nucleic acid delivery in April 2000. As I learned more about nucleic acids in medicine, I realized the appeal and excellent potential they have to become a panacea. Since the most important issue was said to be "delivery technology," I felt the importance of my own research and began focusing on it. On the other hand, the practical application of nucleic acid drugs had not progressed in spite of the huge R&D cost, which, around 2010, made me feel that it was just a panacea on the desk. However, this situation has changed drastically in the past few years, with new nucleic acid drugs being approved every year. This can be attributed

to the progress in delivery technology as well as the integrated development of nucleic acid chemistry, cell biology, and evaluation technology.

As such, the R&D of nanomachines equipped with nucleic acid medicine from COINS has progressed, and the start of clinical trials for cancer treatment became a big step in my research life. I think that this progress was possible due to COINS' promotion of integrated research as well as its open innovation projects with companies. This achievement has not only been a big step but also a first step. Although there are still many issues to be solved in nucleic acid delivery, we will continue to work together

with our lab members on further research to realize a true panacea.



Members from Miyata Lab.  
Department of Materials Engineering, UTokyo

ANRAKU Yasutaka

Project Associate Professor, Department of Bioengineering  
Graduate School of Engineering, The University of Tokyo  
COINS Theme 2 Leader

## A Brighter future seen beyond the Blood-Brain Barrier

In Theme 2, we have been developing innovative therapeutic technologies for neurological diseases with the keyword "go beyond" when it comes to nanomachines for realizing the "In-Body Hospitals". The brain is protected by a highly developed barrier (Blood-Brain Barrier: BBB), which makes it difficult to deliver bioactive substances to the brain. As a result, the prevalence of neurological diseases is high in the aging society while no effective therapeutic approach has been found. In the midst of this, our research group has developed a "BBB-crossing nanomachine," a nanomachine that "goes beyond" the BBB and is composed of a precisely designed polymer that

is safe in vivo and has glucose molecules on its surface layer. This nanomachine is localized in the cerebral vascular endothelial cells that construct the BBB, appropriately recognizes glucose transporter 1 whose localization changes according to the blood glucose concentration, and passes through the BBB according to the change in blood glucose concentration. Using this BBB-crossing nanomachine as a platform, we have succeeded in delivering a wide variety of modalities into the brain. For example, we succeeded in efficiently suppressing the expression of a target protein by delivering a nucleic acid drug into the brain, and for an antibody drug that can control the post-translational process, we succeeded in

achieving the same therapeutic effect with 1/10 of the dosage of the antibody administered alone by using the BBB-crossing nanomachine in an Alzheimer's disease model mouse. In addition to this research, I have also participated in many outreach activities. One of my most memorable moments was a talk session held at the National Museum of Emerging Science and Innovation, where I had a chance to hear directly from people who are interested in cutting-edge science and technology about their high expectations and concerns about our nanomachines. The comments we received there have been a great motivation for us to continue our research activities.



Our goal is to develop smart nano-machines using precisely designed and synthesized macromolecules as building blocks, which will be applied to innovative diagnostic and therapeutic technologies for neurological diseases.

ITAKA Keiji

Professor, Department of Biofunction Research  
Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University  
Laboratory Head/Principal Research Scientist, Innovation Center of NanoMedicine  
COINS Theme 3 Leader

## Believing in the Future of mRNA Medicine and Vaccines

As you all may know, Dr. Kataoka and his team have worked on major projects such as Center for NanoBio Integration and First program prior to COINS, so old members such as myself are probably less aware of when COINS started.

If you look back at the materials of the first General Meeting in 2013, other than already having the word mRNA in it, you can also see a diagram of animal experiments via pDNA next to it, which makes you realize how long COINS has been as a program. As Moderna was founded in 2010, mRNA drug discovery is still a young field, in which I am very happy to have been involved in terms of mRNA and

coincides with our achievements at COINS. At COINS, I have been working on motor-sensory organ regeneration for Theme 3, and coincidentally, a project for articular cartilage therapy was launched this spring, which aims for the practical application of Japan's first mRNA medicine. Of course, this is a first for all of us and many twists and turns to be expected, however, the experience and network cultivated at COINS will be another great asset for us. The R&D for vaccines and their application to many diseases is just beginning, and we hope to move forward step by step in collaboration with many scientists and companies.



With Dr. Kariko Katalin(who is much talk about) in front of Head office of BioNTech



With lab. members of Dr. Kariko (March, 2015)

IWASAKI Hirokazu

Vice Director, Innovation Center of NanoMedicine  
I supported PL and RL as a COINS Research Promotion Leader.  
I have been a Vice Director since iCONM started.

## Build a unique innovation platform

When COINS started, we were working hard just to meet the challenges that were required one after another, but when iCONM started its operation in April 2015, "Under one roof" and "Back casting approach from the vision" provided a tangible foundation to function.

When we launched, we had a very busy period, however, we thought it would be good to design iCONM suitable for the core of COINS, therefore we thought that while advancing COINS which aims to realize "In-Body Hospitals" and backcasting from the vision of aiming for the most innovative research center in the world, we should be able to create an innovation platform. To build the organization, human resources, management, etc. were challenges from a scratch. However, with

new members with a proven track record in private companies, the cycle of "R&D⇒intellectual property strategy ⇒ paper publication ⇒ public relations strategy ⇒ commercialization opportunity" began to rotate. I am proud to say that we could build a unique innovation platform that sets us apart from existing universities and research institutions. Particularly, I am proud of the relationship of trust with the COINS participating institutions and members, and also the collaboration between the Research Promotion office and the Kawasaki Institution of Industrial Promotion Foundation team who made this possible. The surrounding environment is changing. As we respond to new challenges, I am sure that this experience, we will continue to have the resilience to adapt to change.



With Ms. Mayuko Suzuki of the COINS Research Promotion office, who holds the Japan Open Innovation Award.



AKINAGA Shiro

Managing Director of R&D Division & CSO  
NanoCarrier Co. Ltd.

My lifework is to create new medicine, focusing on translational research from the drug discovery stage to obtaining clinical POC in human. I have extensive experience to cross the "death valley" in drug discovery towards human clinical trials.

## A unique drug discovery procedure by small venture company that cannot be achieved by major pharmaceutical companies

After retiring from a domestic pharmaceutical company in 2017, I joined AccuRna and participated in collaborative research and development of nucleic acid drugs with iCONM. We had little knowledge the new field of mRNA drug discovery, which was still rare in Japan, but we managed to start research activity. However, on the way, we invited and collected our colleagues from the previous company to the research team and managed to build a structure to catch up the cutting-edge research. While human beings face an unprecedented crisis of a COVID-19 pandemic, the mRNA vaccine for the virus has been approved at an astonishing speed of less than one year of development. As a result, mRNA therapeutics has

flowered as a new modality, then the interest in mRNA drugs has been increasing in Japan as well. When I was thinking about the strategy of the company, as the CEO of AccuRna, I received an M&A offer from Mr.Matsuyama, the CEO of NanoCarrier. The company was merged by absorption and I have become the CSO for NanoCarrier again in September 2020. It has been four and a half years since I entered into the venture industry world. We have not "created" anything as medicine, but I am in the midst of "creating" new corporate values of the new NanoCarrier after a replacement of the president. From now, the major focus will be on how far we can advance mRNA drug candidates in-house and

when we can hand them over to pharmaceutical companies to create a medicine. As an individual scientist, after receiving the mRNA vaccine, I can imagine that mRNA activates our immunity in the body like a SF movie "Fantastic Voyage".



New and old members create core values together.

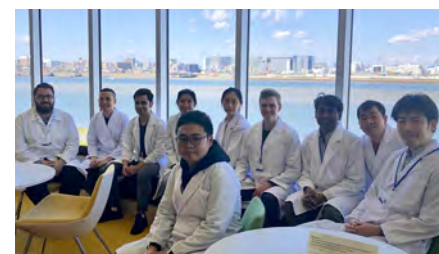
QUADER Sabina

Senior Research Scientist  
Kataoka • Kinoh Laboratory, Innovation Center of NanoMedicine

## Witnessing iCONM becoming a global research hub

April 2015, Kinoh-sensei, Mochida-san, Liusan, Wu-san, and me, from Kataoka-lab at the Material Engineering Department of the University of Tokyo, came to iCONM to continue our nanomedicine research. We had so many unopened boxes to open, so many machines to install, and so many laboratories to set up. It took six months to start my first experiment at iCONM; since then, our COINS research project relentlessly escalated to reach the top. I have seen many world-renowned academics and researchers visiting our center; I have witnessed their appreciation and acknowledgment towards our world-class research facilities and cutting-edge scientific research. Many research

trainees from all over the world came to iCONM to experience doing innovative research. Worth mentioning here that the strength of our COINS innovative research lies in its multidisciplinary nature, contributed by researchers with diverse academic and geographical backgrounds. Today, I feel satisfied; our mission to make iCONM a prominent global research hub has been achieved. The next goal is to make iCONM one of the leading research centers in the world.



Our research strength – diversity • equality • inclusion



Nanomedicine for the treatment of Brain Cancer

TOSU Mariko

Founder & Chairperson  
Braizon Therapeutics, Inc.

## Aiming for Intel in the field of therapeutic agents for central nervous system diseases

Braizon Therapeutics, Inc. was founded in 2015 by FTI, led by Professor Kimura, as a recipient of the social implementation of COINS research results. We challenge social implementation of "drug delivery technology that efficiently delivers drugs to the brain" that solves key issues in the development of therapeutic agents for the treatment of central nervous system diseases. It was one person company when I took over the management in 2017. Initially, I had no research ability systematically, thus I was going back and forth alone with the great cooperation of Dr. Kataoka, Dr. Anraku, Mr. Iwasaki, and Dr. Fukushima. However, from 2018, colleagues

and scientists who share our ambitions to innovate on this social issue have increased, and it has become possible to proceed with in-house research along with the discussions with Professor Kataoka and Professor Anraku. In 2019, we opened our own laboratory in both iCONM and in Boston. I feel that all the members are working together to accelerate research and play a role to connect the results of COINS to the hopes of society. We would like to become such a company that Braizon's technology is always fully utilized in the therapeutic drugs for central nervous system diseases of the brain marketed by pharmaceutical companies all over the world.



All of us are working together to open a new door to the development of therapeutic agents for patients who suffer from intractable brain diseases around the world. We cause a paradigm shift in the treatment of central nervous system diseases.



We conduct research even during COVID-19 pandemic.



Launching member of iCONM. In the COINS project, I have been mainly involved in accounting.

YOKOYAMA Miyako

Account Department / Secretary  
Management office, Innovation Center of Nanomedicine (iCONM)  
COINS Research promotion office

## Starting from scratch-Rewarding to create from there

I became a member of COINS in 2014. Construction of iCONM was completed in 2015 and COINS research and promotion office moved its base from The University of Tokyo. I was involved as one of the launching members, and now we have reached the final year of the COINS project. iCONM that has just established had nothing in the beginning and started from scratch, thus I was extremely busy with moving, organizing a new office and a regular work. I was assigned to work as an accountant. Firstly, I had to learn the rules of the core organization Kawasaki Institute of Industrial Promotion and to create a business flow of iCONM. In addition, there was no online purchase system

so that a large number of accounting slips were not converted into data, budget execution management was extremely inefficient, and creating an accurate accounting report was difficult. I explained the foundation about the difficult situation and proposed systematization. We discussed about systematization that can collectively manage orders, deliveries, payments, and budget management and after exchanging opinions between the headquarter of Kawasaki Institute of Industrial Promotion and iCONM, the long-awaited online purchasing system went into full-scale operation in 2020. I was pleased to know that this has made it possible for our scientists to check the status of orders for

reagents, etc., and to create COINS accounting reports accurately and quickly. I would like to connect our work to the years to come as a result of our efforts.



Accounting ladies taking care of research funds

Listen to  
COINS'  
Members

# Draw in the future



Conducting R&D for new diagnostic equipment and measurement technologies that hold the key to preventive medicine

ICHIKI Takanori

Professor, Department of Materials Engineering  
Graduate School of Engineering, The University of Tokyo  
Laboratory head/Principal Research Scientist, Innovation Center of NanoMedicine  
COINS Theme 4 Leader

## Beyond COINS: From Sick Care to Health Care

**F**uture medical care "In-Body Hospitals" that COINS aims for. The novel idea of a medical team boarding a miniaturized submarine and treating patients from inside their bodies was depicted in the 1960s science fiction film *Fantastic Voyage*, and now, 50 years later, that worldview is getting closer to reality thanks to the nanomedical technology that COINS is promoting in R&D. Nanomachines for cancer treatment are one step closer to practical application, and the R&D of nanodiagnostic devices that can detect cancer with a single drop of blood is also underway. On the other hand, futurist Ray Kurzweil, who advocates the arrival of a singularity in which artificial intelligence (AI) will surpass human

intelligence, predicts that the fusion of AI and nanomachines will lead to the realization of tiny molecular machines that can enter the body to treat diseases, repair genes, and manage health in the 2030s.

The nanomachines and nano diagnostic devices developed at COINS will be linked to AI and data science in the future and will function with dramatic intelligence. They are expected to bring about a major change in consciousness, that is, a health care transformation, from "sick care to health care" in 10 years' time. The origin of the word "health" comes from the word "heal" with "-th" added to it, in other words, to heal. That is to say health care does not just mean maintaining

physical and mental health but also includes the act of finding the seeds of abnormalities that occur daily in the body and returning to an original state. I believe that the nanomedical technology developed at COINS has the potential to realize not only sick care but also advanced health care that enables so-called preventive medicine.

The participation (participatory) of many citizens is said to be essential for the development of health care technology. By deepening partnerships with local governments and local communities and preparing a grassroots R&D environment, I would like to expand the circle for the creation of new health care technologies and health/medical industries.

NISHIYAMA Nobuhiro

Professor, Institute of Innovative Research, Tokyo Institute of Technology  
Laboratory head/Principal Research Scientist, Innovation Center of NanoMedicine  
COINS Theme 5 Leader

## 2045 – For the Realization of “In-Body Hospitals”

**T**he COINS project, which has been running for about 10 years with the grand concept of "In-Body Hospitals", has finally reached its final year. As a leader of Theme 5, I have been involved in R&D on "the Integration of Nanomachines and Medical Devices," achieving research results that had a social impact such as pathological diagnosis by imaging (NatNanotech, 2016) and cancer treatment by liquid glue (SciAdv, 2020). We were able to advance the research of boron neutron capture therapy (BNCT) and sonodynamic therapy (SDT) toward social implementation. As the Theme leader, I would like to express my gratitude once again to all

the people involved in Theme 5 for their efforts. While COINS is coming to an end soon, "In-Body Hospitals" is aiming for realization in 2045, and we will continue to run at full speed for another 24 years. 24 years ago, I was a graduate student in the laboratory led by iCONM Director General, Prof. Kazunori Kataoka, where I received my Ph.D. for research on micelles encapsulating anticancer drugs.

One of our results is the NC-6004, which is currently in phase 2 clinical trials at NanoCarrier Co.,

Social implementation is a dream I have had for many years, and I feel that it is my responsibility to fulfill it as a scientist. In the past 24 years

in the field of medicine, regenerative medicine, gene therapy, nucleic acid medicine, and more have been put to practical use, with various technological innovations such as wearable devices and AI-based diagnostic support, which have brought great changes to our lives. In the next 24 years, we would like to steadily implement nanomachine-based diagnosis and treatment in our society, step by step, and realize "In-Body Hospitals". "Nothing is impossible." "No dream, no success." In this milestone of the end of COINS, I would like to renew my mind and strive toward our great dream with my colleagues who share the same aspirations as me.



We are conducting R&D for imaging-based pathological diagnosis and non-cutting surgery via the integration of nanomachines and medical devices in hopes to realize day-case treatment that does not require hospitalization.

SENGOKU Shintaro

Professor, School of Environment and Society  
Tokyo Institute of Technology

## Promote an innovation process based on citizen participation in Kawasaki

**F**or expanding preventive medical care, which will be the key to a healthy society in the future, it is indispensable that in addition to technological development to realize the iCONM's concept "In-Body Hospitals", the local government, which is responsible for health and welfare administration, will directly play a principal role in the citizens and process to implement and verify together.

Not only building narrowly defined "In-Body Hospitals", but also it is necessary to develop a social system for providing the technology and products created by COINS as a healthcare service by making dialogues with government and regulatory agencies and communicating with

citizens at the same time.

Specifically, it is urged that we will set up a system for utilizing health data such as public health checkup and receipt data, develop intervention measures based on technologies such as machine learning and nudge, implement, evaluate and verify trials through social experiments in the demonstration field, and proceed system design and development to initiate the program as a part of citizen's life and city administration.

In addition, as it has become apparent due to the recent spread of COVID-19 that establishing a so-called new normal lifestyle that contributes to health measures and prevention of spread has become a new issue such as the construction of a medical

care provision system that is different from the past, the mental health care of the frailty of the elderly due to stay at home, and the younger generation. We need to set a goal for a resilient society that protects and develops the health of citizens even in an emergency. From now on, through awareness of these issues and a series of measures, we shall pursue SDGs such as "Good Health and Well-Being"(contributing to the achievement of universal health coverage) and "Quality Education"(fostering a health care mindset and improving science and medical literacy through public awareness activities and outreach activities) and contribute to the realization of a wellness and health society from Kawasaki.



I am engaged in research and education on technology and innovation management at the Tokyo Institute of Technology. I have participated in COINS in 2014 and am engaged in R&D management research.

TANABE Shihori

Senior Researcher, Division of Risk Assessment  
Center for Biological Safety and Research, National Institute of Health Sciences (NIHS)

## Promote a development of medical health research with broad view in international collaboration

**I** think it was at the King SkyFront New Year's party that was held when NIHS moved here at Tonomachi end of 2017 to 2018 that I encountered iCONM. The joint research with Dr. QUADER Sabina of iCONM was the trigger to the valuable opportunity to participate in the 150th anniversary ceremony of diplomatic relations with Spain at the AMED Japan-Spain International Joint Research Project Start Commemorative Symposium in Madrid, Spain. Afterwards, this led to the publication of co-authored papers at Nanomedicine, discussions at cancer and stem cell-related conferences, and publication of papers.

When overseas scientists visited iCONM

and NIHS, we were able to get a deeper understanding of the actual research site by introducing each other's research. I am grateful for Prof. Kataoka, Director General of iCONM and iCONM members for introducing the latest nanomedicine trend when I visited iCONM for COINS seminar or lab. Tour. Due to the impact of the COVID-19 after 2020, the importance of problem-solving on a global scale from an international perspective is increasing. I hope we will be able to develop problem-solving by taking advantage of diversity.



Spanish and Japanese researchers, Dr. Suematsu, AMED First Director (at that point) and other scientists at the Spanish Ministry of Science, Innovation and Universities (photographed in November 2018)



**SATAKE Mami**

Kawasaki Institute of Industrial Promotion  
Research Coordinator, COINS Research Promotion Support  
Office

I joined COINS three years ago. In addition to administrative duties related to the project within the research promotion support office, I worked to set up and run events and carry out public relations activities.

## I want to say! “In-Body Hospitals”

It is essential to foster a public understanding and acceptance for realization of "In-Body Hospitals". We have externally disseminated information through symposiums and seminars, and at the same time, we held the first iCONM Public Lecture in March 2021. The lecture plan was finalized by the scientists, the research promotion support office, and the iCONM management office in order for general publics who did not have a knowledge on "In-Body Hospitals" to readily understand the concept. I am pleased to say that the participants were very satisfied, and it was a great success!

It is also important to communicate not only with society but also with everyone involved in COINS.

It has become difficult to meet face to face due to COVID-19, however we could manage holding various workshops and general meetings online. Utilization of online has some problems, but I think it has become easier for people to participate than face to face event in the difficult circumstances. The goal of "In-Body Hospitals" is to realize by 2045.

I would like to continue working and keep increasing our fans and enhance the sense of unity of the team now and even after 2045. I will do my best to improve public acceptance and to ensure that everyone involved in COINS can go forward toward the vision of "In-Body Hospitals" to the full extent.



Recently, I have started a column to introduce nanomachines with illustrations so that it can be easily understood by more people.



**DATE Yusuke**

Science Communicator  
Japan Science and Technology Agency  
The National Museum of Emerging Science and Innovation(Miraikan)

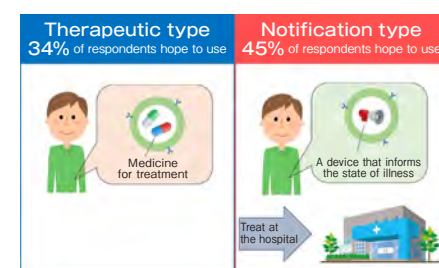
## Future “normal” which is created with citizens

Miraikan and iCONM have created opportunities for dialogue to interact with citizens about "In-Body Hospitals". In the survey of "In-Body Hospitals" conducted in 2020, we asked if they would like to use, the nanomachine "therapeutic type" that consistently performs treatment from disease detection, or the "notification type" that detects and notifies diseases and performs treatment at medical institutions (right figure). As a result, 79% answered that they would like to use nanomachines, however, looking at the breakdown, 45% of the respondents chose "notification type" compared to 34% of "therapeutic type". This is the result that shows the gap between the future image of the concept

of "In-Body Hospitals" that comprehensively performs the treatment, which is the final goal and the values of the citizens who would like to decide whether to treat or not. The actual future will change depending on efforts. I would like iCONM to continue to set up a place for dialogue with citizens, and to practice incorporating the place itself into the research and development process. Future options have now increased because of the progress of science and technology. I believe that recognizing the gap between the creator and the user of the new technology, updating the future image is what we say, "create together."

As a pioneer, I hope iCONM will pave the way

to the "Normal" of future medical care for all the citizens.



※ 21% of respondents answered "I don't want to use either."  
※ Number of valid respondents were 375  
Result of survey regarding "In-Body Hospitals"

**ATSUMI Hiroshi**

Innovation Center of NanoMedicine  
Office for post COINS, Business Strategy Manager



We are working on the formation of an ecosystem, notably the launch of the incubation business.

## Shape our own future with our own hands

One day, I brought perilla (shiso) seedlings grown in a field to my apartment in Tokyo. I planted them in a pot and found they did not grow well because of spider mites. In nature (my hometown), there are insects that eat pests and the moderate humidity enables plants to grow, which are needed to grow well. It seems difficult to grow plants in urban balconies because of a lack of "the helps". It is said that an appropriate environment called the innovation ecosystem, is necessary to foster start-ups and continuously happens innovation. Especially, biotech companies require highly unique and diverse supports for growing their business, such as up-to-date equipments, huge investment, and

exceptional scientists. However, it is not easy for one organization to provide these supports. Even in Boston, the central of biotech, the various supports are always provided by diverse ecosystem members. The incubation for start-ups that I am currently involved will be a member of the ecosystem, because appropriate wet-labs help biotech start-ups to be able to concentrate on their research and business. As mentioned above, the ecosystem could not be built all by myself, and Tonomachi still has lot of work to do ahead. However, I dream many startups are growing and being successful here. Today, I see the ecosystem in Tonomachi grow gradually. When

I was in Boston, people involved in startups looked very vibrant and energetic. The energy is transferred to others (energy transfer!) and finally will shake our society. That is exactly what I want to do and will help to shape our own future.



Our students are stimulated by visiting the research institutions every year.

**FUKAZAWA Yukiko**

School teacher  
Kawasaki City High School for  
Science and Technology

## To the future from Kawasaki

At Kawasaki Municipal Kawasaki General Science High School, Science Department, the students aim to enter a topnotch university by deepens systematic understanding through the process of exploring phenomena such as basic concepts, principles, and rules in science and mathematics, and at the same time enhances general education, and goes to scientific topnotch university. There are many students who aspire to research positions at universities and research institutes in the future, and they are working hard toward their dreams. In the influence of environment, students of the department of science visit research institutes at various research facilities on the King

SkyFront every year. The students see the adults (scientists) who realize their dreams in front of them in Kawasaki, conduct cutting-edge research and achieve results, and talk about the future like a child just before a summer holidays. This 'real' experience makes them motivated more than anything else. In general, high school students are in the process of heading toward self-actualization with little by little facing themselves, assessing their abilities and aptitudes and it is not too much to say that many children have great anxiety about the future. However, when I saw the students who were enjoying the lab. tour

and lecture, I could feel their spirit that they are spreading their wings from where they are. All in all, it became a very precious day for me. Thank you very much for having us.



35 students and 4 teachers visited.

9.17.2020 [Award] Dr. GONZALEZ Daniel Carter, iCONM research scientist, won the second prize in the poster presentation at an academic conference held online at the University of British Columbia, Canada.

9.25.2020 [Activity] COINS workshop (ONLINE)2020 was held.  
Theme: Post COVID-19 era

9.27.2020 [Coverage] iCONM Nanomachines was introduced on BS Fuji "Think what if...Naruhodo! Nattoku-juku".  
Name of the program: BS Fuji "Think what if ...Naruhodo! Nattoku-juku"  
Title: If we could go to a micro world?

9.28.2020 [Press release] COINS exhibited at "Innovation Japan 2020 -University Trade Shows Online". An article on this matter was published in Pharmaceutical News Agency.

10.1.2020 [Activity] iCONM has set October as "Compliance Promotion Month" and carried out various activities to ensure compliance.

10.12.2020 [Coverage] COINS member Prof. OCHIYA Takahiro of Tokyo Medical University announced that industry-academia collaboration has identified a new predictor of aggravation of COVID-19. Articles on this matter have been published in a number of media.  
Articles on this matter have been published in a number of media  
Discriminate the corona aggravation by protein in blood. Professors of Tokyo Medical University and colleagues | Nikkei Inc.  
Predict the corona aggravation by blood Identify candidate substances. Tokyo Medical University | The Okinawa Times | KYODO NEWS | The Chunichi Shimbun | KAHOKU SHIMPO PUBLISHING  
Predict the corona aggravation | Nishinippon Shimbun | Niigata Nippou Jigyousya | Kanagawa Shimbun Ltd.

10.16.2020 [Activity] Dr. UCHIDA Satoshi, Deputy Principal Research Scientist Kyoto Prefectural University, (iCONM Principal research scientist) gave a lecture at the Webinar organized by the Embassy of India in Tokyo. Title was "Stable delivery of mRNA to affected areas using nanomicelles and gene therapy for rare diseases". He explained the features of nanomicelles, such as comparison with delivery methods using viruses, and suggested the possibility of treatment of rare genetic diseases in future medical treatment.

10.21.2020[Activity]Dr. ATSUMI Hiroshi from iCONM took the stage on the online event "[Accelerate research!]" Demonstration experiment to create a future society" at the National Museum of Emerging Science and Innovation.

11.4.2020 [Coverage] An interview article with Dr. UCHIDA Satoshi, Deputy Principal Research Scientist Kyoto Prefectural University, (iCONM Principal research scientist), entitled "Corona Vaccine with Partial Double-stranded mRNA" was covered by Chemical Daily. "Future medicine care is right there – iCONM's challenge" [The Chemical Daily

11.6.2020 [Activity] #53 COINS Seminar was held ONLINE.  
Speaker: Dr. ANRAKU Yasutaka / Project Associate Prof. Dept. of Bioengineering, Graduate School of Engineering, The University of Tokyo (Leader, Theme 2).  
Title: "New Route to Innovative Treatment of Central Nervous System Disease with Nanomachines" Contents of the seminar was published on the media. [Nikkei Beyond Health

11.9.2020 [Coverage] An interview article "Cancer care, information sharing issues" with Dr. MURAGAKI Yoshihiro, Professor, Tokyo Women's Medical University, and NODA Mayumi, Vice President, Sasaeau-Kai q (a NPO for Cancer Patient Advocacy) was covered by Chemical Daily.

11.9.2020 [Activity] An exchange event was held in zoom between foreign research scientist working at iCONM and Japanese administrative staff. It was the first attempt of a joint project by the iCONM management office and the COINS research promotion office aiming activating inner communication.

11.19.2020 [Activity] Dr. KATAOKA Kazunori, iCONM Director General iCONM appeared live on TV Asahi "Hatori Shinichi Morning Show" and explained not only about new corona vaccine but also about cancer treatment and Alzheimer's disease using mRNA and applied research of smart nanomachines for cartilage regenerative medicine in easy-to-understand manner. Articles on program appearances is covered in a number of media.  
JCASTTV Watch, Rakuten Infoseek News, JCC\_1, JCC\_2

11.20.2020 [Activity] Dr. UCHIDA Satoshi, Deputy Principal Research Scientist, Kyoto Prefectural University, (iCONM Principal research scientist), appeared live on Fuji TV's "Tokudane!" and explained the development of a new corona vaccine using mRNA.1  
Another TV programs  
TV Asahi "Sunday Live" – Sunday, November 22 at 6:00  
Fuji TV "Sunday coverage THE PRIME" on Sunday, November 29 at 7:30.  
A few media introduced the Dr. Uchida's appearance program. livedoor NEWS, excite, News JCC

11.20.2020 [Activity] #54 COINS Seminar was held ONLINE.  
Speaker: Prof. ICHIKI Takanori / Professor, Department of Materials Engineering, Graduate School of Engineering, The University of Tokyo/Ichiki Lab, iCONM  
Title: "Application of nanobio device technology to medicine and drug discovery"

11.20.2020 [Coverage] An article by Toru Sakurai, Manager of iCONM was published in the Shizuoka Shimbun under the title of "Kawasaki Model also in Shimizu".

11.20.2020 [Coverage] An article about the interview with Professor ITAKA Keiji (Leader, COINS Theme 3) Tokyo Medical and Dental University, entitled "Why is Japan's vaccine development delayed?" was published.

11.24.2020 [Coverage] An article of the interview with Dr. KARIYA Yuko (iCONM research support specialist) and Dr. ATSUMI Hiroshi (COINS business strategy manager) entitled "Strengthening the support system for the realization of "In-Body Hospitals" was posted in The Chemical Daily. "Future medical care is right there – iCONM'S challenge" ③ | The Chemical Daily

11.24.2020 [Activity] Dr. UCHIDA Satoshi, Deputy Principal Research Scientist, Kyoto Prefectural University, (iCONM Principal research scientist), appeared on multiple TV programs from November 20th to November 24th, and explained the development of a new corona vaccine using mRNA.  
Appearance program  
Friday, November 20, 8:00 - Fuji TV "Tokudane!"  
Saturday, November 21, 5:30 - TBS "Marutto! Saturday"  
Sunday, November 22, 5:55 - TV Asahi "Sunday Live!"  
Tuesday, November 24, 7:00 - TBS "Asa chan!"

11.25.2020 [Activity] Project COINS opened a new website. The contents were exhibited at "Innovation JAPAN2020", that was an online matching event between Academia and Industry, organized by JST (Japan Science and Technology Agency). A new site that summarizes COINS's vision on one page in an easy-to-understand manner. Introducing an "In-Body Hospitals" aiming for realization in 2045.

11.25.2020 [Award] Dr. ANZAI Tomohiro, Senior Research Scientist, iCONM Kimura Lab, ranked second in the 2021 edition of "Japan's MIDAS LIST" published by Forbes Japan.

11.26.2020 [Coverage] An interview article of Prof. ITAKA Keiji, Tokyo Medical and Dental University (Leader, COINS Theme 3) under the title "mRNA vaccine, using genetic information, developing quickly" in Nikkei electronic version.

11.30.2020 [Coverage] In collaboration with the Department of Bioengineering, Graduate School of Engineering, The University of Tokyo, iCONM has developed a high-molecular-weight nanomicelle that uses the acidity in the target tumor tissue to selectively release antineoplastic agents and we had a press meeting. There were articles about this research.  
Treatment of malignant brain cancer| Nikkan Kogyo Shimbun  
Release drug inside brain tumor| Nikkei Sangyo Shimbun  
Shoot malignant cancer cells with "super molecular nanomachines" |Nikkei Beyond Health  
Release of anti-cancer drug as a function of pH pH| The Chemical Daily  
Kawasaki City Coastal Area New letter "i-newsletter"  
This research result was published in Biomaterials.  
Title: Supramolecularly enabled pH- triggered drug action at tumor microenvironment potentiates nanomedicine efficacy against glioblastoma

12.1.2020 [Activity] Dr. UCHIDA Satoshi, Deputy Principal Research Scientist, Kyoto Prefectural University, (iCONM Principal research scientist), appeared on multiple TV programs from November 28th to November 30th, and explained the development of a new corona vaccine using mRNA.  
Appearance program  
Saturday, November 28, 9:30 - ABC "Oshiete News Live ~ Seiginomikata"  
Sunday, November 29, 7:30 - Fuji TV "THE PRIME"  
Monday, November 30, 20:59 - BS11 "Press Live Inside Out"

12.2.2020 [Coverage] The article of the lecture given by Prof. ITAKA Keiji, Tokyo Medical and Dental University (Principal Research Scientist, Leader, Theme 3), on mRNA in Chiba City was published in The Chemical Daily.

12.2.2020 [Award] Prof. KATAOKA Kazunori, Director General of iCONM, won the KOSÉ Cosmetology Encouragement Award.

12.2.2020 [Award] Prof. KATAOKA Kazunori, Director General of iCONM and Dr. OCHIYA Takahiro, Professor, Tokyo Medical and Dental University / COINS' member, were selected as a Highly Cited Researcher.

12.3.2020 [Coverage]: An interview article with Dr. UCHIDA Satoshi, Deputy Principal Research Scientist, Kyoto Prefectural University, (iCONM Principal research scientist), on the approval of the new coronavirus vaccine by Pfizer Inc. US was published in Jiji.com. The articles on this matter have been published in various media.  
"Utilizing genetic information, first practical application, shorten development period-mRNA vaccine"|jiji.COM | Jiji Medical | livedoor NEWS | BIGLOBE News | YAHOO! News | msn News | mixi News | au WEB Portal domestic News | Rakuten Infoseek News

12.4.2020 [Activity] The 7th COINS Symposium was held ONLINE.  
Theme: "Future Medicine is Comin' to Town". An article on this subject was published in Kanagawa Shimbun.

12.14.2020 [Activity] The 2nd iCONM x COINS Internal Communication Event was held ONLINE. Dr. TOCKARY Theofilus A. (Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced orangutans, which is a famous of Indonesia in English. After Dr. TOCKARY's talk, questions and impressions were exchanged in both Japanese and English. It was a short event but fun.

12.16.2020 [Activity] #55 COINS Seminar was held ONLINE.  
Speaker: Dr. MATSUMURA Yasuhiro / Visiting Scientist of National Cancer Center Research / Matsumura Lab, iCONM  
Title: "Looking back on my DDS research"  
Article about this seminar was published in Iyaku-Tsushinsha.

12.17.2020 [Activity] Newsletter "NanoSky Vol.8 COINS' Innovation Platform that leads to Future Health Care" was published. An article related to NanoSky Vol.8 was posted in Iyaku Tsushinsha.

1.8.2021 [Coverage] An article about the COINS venture company iXstream,Inc. was published in The Chemical Daily.

1.19.2021 [Activity] The 3rd iCONM x COINS Internal Communication Event was held ONLINE. Dr. QUADER Sabina (Senior Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced Mangoes, which is a famous of Bangladesh in English. After Dr. QUADER's talk, questions and impressions were exchanged in both Japanese and English. It was a short event but fun.

1.19.2021 [Coverage] The iCONM developed an ultra-small nanomedicines called Unit Polyion Complex (uPIC) in collaboration with a group led by Prof. MIYATA Kanjiro in Department of Material Engineering, Graduate School of Engineering, The University of Tokyo. The contents of this press release have been published in multiple media.  
news-medical.net | headlinesmania.com | Yakuiji Nippo [The Science News  
This research result was published in "Journal of Controlled Release"  
Title: Structural tuning of oligonucleotides for enhanced blood circulation properties of unit polyion complexes prepared from two-branched poly (ethylene glycol)-block-poly(l-lysine)

1.22.2021 [Activity] The 15th COINS General Meeting was held ONLINE.

1.22.2021 [Activity] Dr. ABBASI Saed, a foreign research scientist at iCONM, gave a class on mRNA medicine etc. at Tama Senior High School.

1.29.2021 [Coverage] COINS member National Institutes for Quantum and Radiological Science and Technology announced to develop new quantum sensor that allows detection of "oxidative stress". This research result was published in "Analytical Chemistry"  
Title: Quantum Sensors to Track Total Redox-Status and Oxidative Stress in Cells and Tissues Using Electron-Paramagnetic Resonance, Magnetic Resonance Imaging, and Optical Imaging

2.3.2021 [Coverage] Universitat Internacional de Catalunya (Spain) and iCONM, a virtual Bilateral Meeting was successfully held ONLINE and agreed to continue and expand Spain-Japan joint project "CONCORD"

2.10.2021 [Coverage] KAWASAKI coastal area PR video has been released by Kawasaki city. In this video, iCONM is highlighted as the core institution of King SkyFront.  
An article on this subject was published in the media. TOWNNEWS

2.18.2021 [Coverage] iCONM developed functional nano-micelles with optimal drug release depending on the c-Myc expression level. This was collaborative research with Dept. of Otolaryngology and Head and Neck Surgery, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo (Prof. YAMASOBA Tatsuya) Research group of Dr. MATSUMOTO and Dept. of Bioengineering, Graduate School of Engineering, The University of Tokyo (Head: MIYAKE Ryo) Research group of Dr. CABRAL Horacio A press conference was held. Articles related to this matter have been published in ACS Nano.  
Title: Efficacy of pH-Sensitive Nanomedicines in Tumors with Different c-MYC Expression Depends on the Intratumoral Activation Profile

2.22.2021 [Activity] An exchange event (Administrative staff x foreign research scientists, Japanese x English) was held in zoom between foreign research scientist working at iCONM and Japanese administrative staff. Dr. van GUYSE Joachim (Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced to delicious Belgian foods such as potatoes, which is a famous of Belgium

2.22.2021 [Activity] COINS Seminar #56 was held at web.  
Speaker: ANZAI Tomohiro / Principal Research Scientist, iCONM  
Title: "Evolving Bio Startup Ecosystem" COINS. Articles related to this matter have been published Iyaku Tsushinsha.

3.1.2021 [Coverage] iCONM made a video about iCONM's major research theme nanomedicine that mainly targets junior and senior high school students. Article related this was published in Iyaku Tsushinsha [Town News CONM Kids movie "Challenge to the world".

3.2.2021 [Coverage] A research group consisting of Prof. KONDO Yutaka, TASAKI Yoshihiko, Graduate student (Division of Cancer Biology, Nagoya University Graduate School of Medicine) made a new therapeutic drug that the targeting of TUG1 by anti-TUG1 coupled with our new cancer-specific drug delivery system (TUG1-DDS). This was collaborative research with Nagoya City University, The University of Tokyo, Innovation Center of NanoMedicine, Japanese Foundation for Cancer Research. Articles about this press release have been published in multiple media. Nikkei Biotechnology | The Chemical Daily | QLifePro  
This research result was published in "Cancer Research"  
Paper title: Cancer-specific targeting of taurine upregulated gene 1 enhances the effects of chemotherapy in pancreatic cancer  
Title: Cancer-specific targeting of taurine upregulated gene 1 enhances the effects of chemotherapy in pancreatic cancer

3.4.2021 [Award] COINS received the Japan Open Innovation Prize (JOIP) Selection Committee Special Award. An article on this subject was published in the Iyaku tsushinsha.

3.8.2021 [Activity] An exchange event (Administrative staff x foreign research scientists, Japanese x English) was held in zoom between foreign research scientist working at iCONM and Japanese administrative staff. Dr. PARAISO West (Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced to Philippine folktales "The Monkey and the Turtle", which is a famous of Philippine in English.

3.10.2021 [Coverage] Dr. UCHIDA Satoshi, Deputy Principal Research Scientist, Kyoto Prefectural University, (iCONM Principal research scientist) reported that optimized nano-micelles can induce efficient genome editing in the mouse brain. A press seminar was held. An article about this matter was published in the media research-er.jp | Iyaku tsushinsha | crisp bio | Drug TARGET REVIEW | News Medical life Sciences | Bio World | Nikkei Biotechnology & Business | THE NIKKAN KOGYO SHIMBUN, LTD. | new switch | AZO LIFE SCIENCES. | TriLink BYOTECHNOLOGIES  
This research result was published in Journal of Controlled Release. Title: Co-encapsulation of Cas9 mRNA and guide RNA in polyplex micelles enables genome editing in mouse brain

3.14.2021 [Activity] Prof. KATAOKA Kazunori, Director General of iCONM (COINS research leader) has appeared as the world's top doctor in the special program "The latest medicine for 120 years of life-Toward an era where cancer and diabetes are cured" commemorating the 20th anniversary of the opening of BS Asahi.

3.15.2021 [Activity] At Kawasaki FM "Kawasaki Hot ☆ Studio", Ms. SATAKE Mami, COINS Research Promotion Coordinator of the COINS research promotion office acted as a navigator with a TV announcer for a live broadcast of iCONM and made a tour inside the building.

3.18.2021 [Activity] Dr. SHIMAZAKI Makoto, COINS Communication Officer and Post COI Preparation Office Officer, who is in charge of public relations, appeared in Kawasaki FM "Kawasaki Hot ☆ Studio" and introduced the highlights of the public lecture scheduled to be held on March 27.

3.25.2021 [Activity] #57 COINS Seminar was held ONLINE.  
Speaker: Dr. ITAKA Keiji, Prof. Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University / Itaka Lab, iCONM  
Title: "mRNA therapeutics: from vaccine to regenerative medicine"

3.26.2021 [Activity] Prof. KATAOKA Kazunori, Director General of iCONM (COINS research leader) gave a lecture at the symposium of NanoTech in Thailand.

4.12.2021 [Activity] The 6th exchange event of foreign research scientists and administrative staff was held online in zoom. Dr. LIU Xueying, a research scientist from Kataoka/Kinoh lab. introduced her home town's dumplings in China, along with a video of how she actually cooks.

4.20.2021 [Coverage] The research group of Dr. TANIGUCHI Hiroaki, Project Associate Professor, Keio University School of Medicine Clinical Research Promotion Center, (Visiting Associate Professor, Division of Advanced Medicine Promotion, The Institute of Medical Sciences, The University of Tokyo), jointly researched with Kanagawa Cancer Center, iCONM, and Hokkaido University, have succeeded in developing nucleic acid drug consisting of a chimeric siRNA with high sequence specificity targeting the PRDM14 gene, which is a transcription factor whose expression is upregulated in breast cancer and pancreatic cancer, and a Y-shaped block co-polymer (YBC) that delivers nucleic acid to lesions.  
This research result was published in the "International Journal of Cancer".  
Title: Treatment of primary and metastatic breast and pancreatic tumors upon intravenous delivery of a PRDM14-specific chimeric siRNA/nanocarrier complex  
※Articles on this subject have been published in multiple media. Nihon no Kenkyu.com | QLife Pro | Nikkei Biotechnology and Business | Care Net [The Chemical Daily | The Science News

5.10.2021 [Activity] #58 COINS Seminar was held ONLINE.  
Speaker: MIYATA Kanjiro / Associate Professor / Department of Materials Engineering, Graduate School of Engineering The University of Tokyo / Kataoka・Kinoh Lab, iCONM  
Title: "Nanomedicines for oligonucleotide delivery"

5.18.2021 [Coverage] A research group led by Associate Prof. MIYATA Kanjiro (COINS Theme 1 Leader), Graduate School of Engineering, The University of Tokyo, succeeded in significantly improving lung tissue retention of antisense nucleic acids administered intrabronchially by nanomicell technology. This study is expected to lead to the creation of inhalants for the treatment of lung cancer in the future. An article about this subject was published in the media. Iyaku Tsushinsha | Nikkei Biotechnology and Business  
This research result was published in "Advanced Therapeutics".  
Title: "A 50-nm-Sized Micellar Assembly of Thermoresponsive Polymer Antisense Oligonucleotide Conjugates for Enhanced Gene Knockdown in Lung Cancer by Intratracheal Administration", Advanced Therapeutics, 3, 1900123 (2020);

5.31.2021 [Activity] The 7th iCONM x COINS Internal Communication Event was held ONLINE. Dr.Junjie Li from Kataoka・Kinoh6.4.202 Lab. introduced his home country China in English.

6.4.2021 [Coverage] COINS' research activity was introduced in JST news June issue.

6.14.2021 [Activity] The 16th COINS General Meeting was held.

6.21.2021 [Activity] The 8th iCONMxCOINS Internal Communication Event was held ONLINE. Dr. Anjaneyulu Dirisala (Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced about "Cultural similarities between India and Japan" in English.

6.25.2021 [Activity] iCONM was introduced in TVK "NewsLink" and TVK "LOVE Kawasaki".

7.2.2021 [Coverage] An article in JST NEWS June issue was posted on Chinese website "Kyakkann Nihon".

7.4.2021 [Coverage] An article related to King SkyFront where iCONM is located was published in page 22 of Yomiuri Shimbun morning edition.

7.15.2021 [Activity] An article about the press release on "Treatment of primary and metastatic breast and pancreatic tumors upon intravenous delivery of a PRDM14-specific chimeric siRNA/nanocarrier complex" was published in Science Japan.

7.26.2021 [Activity] The 9th iCONMxCOINS exchange event (Administrative staff x foreign research scientists, Japanese x English) was held in zoom between foreign research scientist working at iCONM and Japanese administrative staff. Dr. YANG Tao (Research Scientist, Kataoka & Kinoh Lab, iCONM) introduced about City of Suzhou, China in English.

7.26.2021 [Activity] Dr. ANRAKU Yasutaka (Project Associate Prof, Dept. of Bioengineering, Graduate School of Engineering, The University of Tokyo) was appeared NHK World "Medical Frontiers" and explained nanomachines with the ability to deliver drug into the brain.

8.3.2021 [Coverage] iCONM and the International University of Catalunya jointly announced that Polymeric Nanomicelles Improve Internalization of Lipid Metabolism Modulators in Brain Cells. This research result was published in "Biomaterials Science"  
Title:"Poly-ion complex micelle effectively delivers CoA-conjugated CPT1A inhibitors to modulate lipid metabolism in brain cells"

8.4.2021 [Coverage] An Article of JST NEWS (published on June) was published in Science Japan website.

8.10.2021 [Coverage] Introduction of iCONM video (6/26 TV program LOVE Kawasaki) was introduced on COI website and COI Drive.

8.11.2021 [Coverage] An article about our research "Nano-micelle Packaging CRISPR/Cas9 Components Enables Brain Genome Editing" was posted on TriLink BYOTECHNOLOGIES.

8.14.2021 [Activity] Prof. KATAOKA Kazunori, Director General of iCONM (COINS research leader) appeared on Ten minutes TV. "Development of corona vaccine / What is the role of venture company?"

8.26.2021 [Activity] Dr. ICHIKI Takanori, Prof. Graduate School of engineering, The University of Tokyo (Leader COINS Theme 4) was appeared on Kawasaki FM "Kawasaki Hot Studio".

9.2.2021 [Activity] COINS joined "Innovation Japan 2021 – University trade fair ONLINE" and exhibited.

9.2.2021 [Activity] First Industry-Academia Co-creation Seminar was held.  
Speaker:Prof. INADA Toshifumi, Division of RNA and Gene Regulation, The Institute of Medical Science, The University of Tokyo  
Title: Physiological function of sensing and elimination mechanism of abnormal translation

9.3.2021 [Coverage] An article on "Development of nanomachines that deliver drugs that regulate lipid metabolism into brain parenchymal cells", which was released on August 3, was published in AZO NANO.

9.10.2021 [Coverage] An article about Prof. ICHIKI Takanori (Graduate School of Engineering, The University of Tokyo / Leader, Theme 4) research was posted in page 4 Chemical Daily.

9.10.2021 [Activity] Challenge forefront of prevention and treatment of Alzheimer's disease and dementia! that Prof. KATAOKA Kazunori, Director General of iCONM (COINS research leader) appeared was released on YouTube Galileo channel [Galileo x#175] .

9.17.2021 [Coverage] A special feature on preventive medicine is published in the Japanese version Newsweek. Prof. KATAOKA Kazunori, Director General of iCONM (COINS Research Leader) and Prof. ICHIKI Takanori, Graduate School of Engineering, The University of Tokyo (Leader, Theme 4), introduced "Advanced medical technology for early detection and early diagnosis of diseases".

9.24.2021 [Activity] #59 COINS Seminar was held ONLINE.  
Speaker: AOKI Ichio, PhD. / Institute for Quantum Medical Science, National Institutes for Quantum and Radiological Science and Technology (QST)  
Title: "In vivo MR Imaging for nano-machine and theragnostic"

9.26.2021 [Coverage] An article about research of iCONM was published in the Koumei Shimbun. Nano size Capsule Research / Disease Detection, Diagnosis, Treatment

9.28.2021 [Coverage] An interview article about round-table discussion which Director General, KATAOKA Kazunori joined was published in the Monthly Keidanren Sep. 2021 issue.  
Round-table discussion:Accelerate the social implementation of innovation

## COINS Seminar Report - Global communication using online -

We organized a series of COINS seminars with COINS scientists who are active on the front lines as a part of outreach activities, using an entrenched online meeting system due to COVID-19 pandemic outbreak. (From November 2020, seven times #53 - #59. Please refer the topic for details).

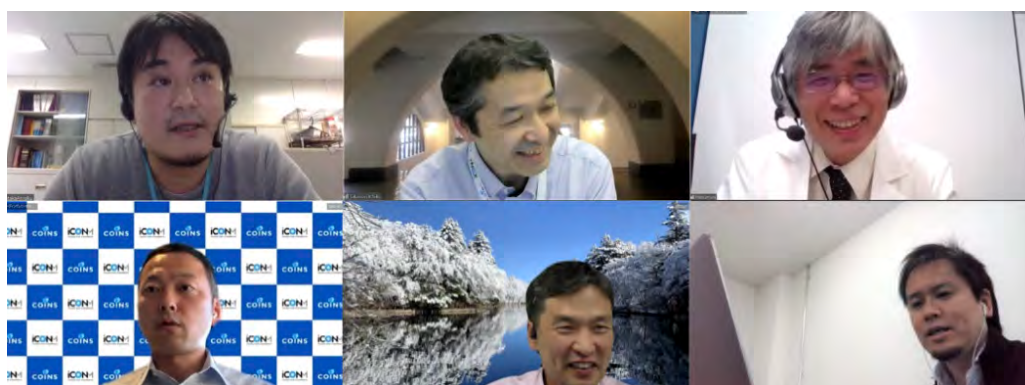
We had a large number of participants in every seminar, mainly those from universities and companies, and the lecturer gave an easy-to-understand presentation of the latest research results and trends in the field, followed by lively discussions. This series covers topics from science and technology such as nanobiotechnology, nucleic acid medicine, mRNA, DDS, and imaging to social sciences such as the venture ecosystem, and very well received by the participants.

Also, on October 7, 2021, the 60th COINS Seminar "Targeting Neurons: More Brain than Brawn to Solve Obesity" was held with an invited lecturer Dr. RODRIGUEZ-RODRIGUEZ Rosalia, Associate Professor, Department of Basic Sciences, Catalunya International University (UIC-Barcelona). This seminar was held as a first global online seminar, and there were many participants from overseas, and the discussions across borders were very exciting.



Lecturer Dr. AOKI Ichio from GST (above) and a chair, Dr. KATAOKA Kazunori, RL (below) 59th Seminar

Lecturer Dr. RODRIGUEZ-RODRIGUEZ Rosalia (above) and a chair, Dr. QUADER Sabina, iCONM Senior Research Scientist (below) 60th seminar



Lecturers: From the above left – Dr. ANRAKU Yasutaka (UTokyo), Dr. ICHIKI Takanori (UTokyo), Dr. MATSUMURA Yasuhiro (National Cancer Center)  
From the bottom left Dr. ANZAI Tomohiro (iCONM), Dr. ITAKA Keiji (Tokyo Medical and Dental University), Dr. MIYATA Kanjiro (UTokyo)

## Editorial Note:

We are pleased to publish NanoSky #9, the final issue of the COINS Newsletter.

The diversity in COINS that has expanded over the last nine years has activated the organization and gave various ideas, which brought novel technology and science and raised talented people. For example, in oncology field, it has become possible to selectively deliver (nano-DDS) anti-cancer drugs that were hardly used due to their severe adverse effects even though they work very effectively. Even for intractable cancers that are hard to protect themselves and resist to anticancer drugs, some nanomachines that break through the shield of cancers to work are currently studied in clinical trials.

Also, nano-DDS has contributed to the more practical use of "Chemical Surgery (surgery that does not cut)", which has become a hot topic in a popular TV drama. For the next step, we are working towards building a future where we can manage our health at home by downsizing of clinical devices for examination and diagnostics and blood tests that do not require painful blood sampling.

The research outcome and platforms that came with practice at COINS will surely be inherited toward the realization of "In-Body Hospitals" in 2045.

Chief Editor SHIMAZAKI Makoto