World Premier International Research Center Initiative (WPI)
FY 2023 WPI Project Progress Report (The center selected in and before FY2020)

Host Institution	Kanazawa University	Host Institution Head	Takashi Wada
Research Center	Nano Life Science Institute (NanoLSI)		
Center Director	Takeshi Fukuma	Administrative Director	Masafumi Iwami

Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2024) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.
➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

Summary of State of WPI Center Project Progress (write within **2 pages**)

1. Research Progress

At NanoLSI, we have been working on three major projects: (1) the development of novel nanoprobe technologies especially for live-cell imaging, (2) nano-level understanding of basic cellular functions and cancer, and (3) the establishment of a new research field "Nanoprobe Life Science" (Fig. 1).

(1) Development of novel nanoprobe technologies

Imaging at surfaces and inside of living cells: While improving the performance of the newly developed techniques, we explored various biological applications and narrowed our efforts down to the most promising ones that can provide insights otherwise inaccessible with existing methods. For in-cell imaging, **Fukuma** succeeded in visualizing elasticity distribution changes of focal adhesions during their growth and disassembling and they measured the cell-cycle dependence of nuclear elasticity. For cell-surface imaging, **Watanabe** imaged structural and elasticity changes of filopodium, lamellipodia, and microvilli-like structures of breast tumor cells during their migration using high-speed SICM.

Nanoendoscopic analysis and manipulation: We have devoted continuous effort to develop fundamental technologies relating to nanoendoscopic analysis and manipulation. **Takahashi** established a technique for injecting reagents such as inositol lipids into cells for controlling organelle functions and a technology for organelle collection with sub-microscale positional accuracy. **Arai** expanded the availability of quantitative fluorescence lifetime imaging (FLIM)-based biosensors capable of detecting intracellular signaling molecules such as ATP. **Akine, Ogoshi, Maeda,** and **MacLachlan** developed new cyclic or helical compounds that could be used as molecular sensors and machines.

Modeling & simulation for nano life science: To provide a theoretical understanding of the AFM data, several mathematical models have been developed for multiscale structures such as proteins, cell membranes, chromosomes, and cell populations. **Foster** applied simulations to explore nanoscale interfaces, organic materials, biominerals, and surface properties (***Nat Chem* 2023a, b, *Phys Chem Chem Phys* 2023, *J Phys Chem Lett* 2023**). **Sumikama** analyzed HS-AFM movies to elucidate biological function of biomolecules such as a Na^+ channel (***PNAS* 2023a, *Sci Adv* 2023b, *Nat Commun* 2023b, c**). **Flechsig** developed new data assimilation methods (***Front Mol Biosci* 2023, *Algorithms* 2024**) to advance integrative modelling for the atomistic understanding of biomolecular HS-AFM observations (***ACS Nano* 2023a, *Sci Adv* 2023b, *Nano Lett* 2023a, *Nat Commun* 2024, *Int J Mol Sci* 2024**). **Okuda** proposed new mathematical models that describe the dynamics of three-dimensional multicellular dynamics (***EPJE* 2023, *Acta Biomater* 2023, *Sci Rep* 2023, *Plos ONE* 2024**).

(2) Nano-level understanding of cellular functions and cancer

Basic cell functions: Using HS-AFM and protein engineering technology, **Matsumoto** developed high-performance MET-activating proteins using IgG-Fc and ubiquitin as scaffolds (***Nat Biomed Eng* 2023, *Angew Chem Int Edit* 2023h**). They also discovered that MET is crucial for antiviral innate immunity (***PNAS* 2023b**). **Wong** highlighted the significance of NPCs in transport in glioblastoma (GBM) (***Cell Rep* 2023**). They used HS-AFM to analyze the structural dynamics of the SARS-CoV-2 ORF6 protein (***J Phys Chem Lett* 2023**). They also investigated microtubules in a bio-SPM study **(*Nat Phys* 2023)**. **Wong, Hanayama** and **Ando** investigated the molecular properties of anti-spike neutralizing antibodies (S Nab) and their interactions with SARS-CoV-2 spike proteins (***Nano Letters* 2023b**). **Hanayama** conducted a study in which they produced extracellular vesicles (EVs) that simultaneously expressed an anti-spike neutralizing nanobody (***Pharm Res* 2023a**). Their current

focus is on actively developing disigner EVs specifically designed to enhance immune responses against tumors (***bioRxiv* 2023b**). **Toda** and **Kodera** initiated a joint effort to visualize the nanoscale dynamics of the Wnt-Afamin complex. **Miyanari** achieved the simultaneous visualization of chromatin accessibility and epigenetic changes (***Methods Mol Bio* 2023**) and created a low-input MNase-seq technique to accurately characterize nucleosome occupancy (***Gens & Dev* 2023**).

Cancer research: **Oshima** discovered the molecular process of cancer cell cluster movement by an imaging study of tumor-derived organoids (***Cancer Res* 2024)**. **Nakajima** discovered that cancer cell-derived EVs isolated using different approaches have distinct responses to the activation of inflammatory cytokines in macrophages (***Pharm Res* 2023b**). **Hirao** identified the molecular pathways behind treatment resistance in lung cancer, which is mediated by the mitochondria-shaping protein Opa1 (***Cell Death Disease* 2023**). They also emphasized the importance of NAD+ metabolism in malignancies (***Nat Comm* 2023d**). **Yano** devised a treatment strategy for lung cancer by inducing a rearrangement of ROS1 (***Cancer Med* 2023**). **Sato** emphasized the revelation of the spatial and temporal coordination of molecular interactions that underlie gene expression (***Nat Rev Genet* 2024**).

(3) Establishment of the novel research field "Nanoprobe Life Science"

Extending capabilities of various Bio-SPM techniques: To maintain our current world-leading position in Nanoprobe Life Science, we have been improving the performance and functionality of our cutting-edge bio-SPM techniques. For high-speed AFM (HS-AFM) techniques, **Ando** developed a mass-controller for the cantilever to achieve higher resonant frequency using photothermal excitation. Faster and low-invasiveness HS-AFM imaging combining the previously developed OTI mode and dynamic PID mode revealed a new intermediate state of F_1-ATPase, a rotational molecular motor protein. **Kodera** improved the optical system for measuring the deflection of an ultra-small cantilever accurately. For SICM techniques, **Watanabe** developed a low capacitance nanopipette probe with high S/N ratio, thus facilitating high-speed SICM scanning, and **Takahashi** developed an organelle biopsy technology that automatically collects cells and organelles using nanopipettes. For FM/3D-AFM techniques, **Fukuma** enhanced the scanning speed of 2D and 3D FM-AFM without losing atomic-resolution-imaging capability, allowing analysis of the dynamic properties of water and ions on various materials including biological systems.

Nanoprobe studies on various life phenomena: To lead the development of the Nanoprobe Life Science field, we worked on various transdisciplinary collaborations among the four major disciplines: nanometrology, life science, supramolecular chemistry and computational science. The published examples include bio-SPM studies of HGF receptor agonist (***Nat Biomed Eng* 2023**), CaMKII holoenzymes (***Sci Adv* 2023b**), peptide self-assembly (***ACS Nano* 2023b, *Small* 2024**), root hair surface structures (***Plant Cell* 2023**), on-surface synthesis of a covalent organic framework (***Nat Chem* 2023a**), mechanical properties of metastatic intestinal organoids (***Small* 2023a**), SARS-CoV-2 protein sensing (***Nat Commun* 2023d**), and helicity inversion control of peptides (***Nat Commun* 2023a**).

2. Generating Fused Disciplines

Both the top-down and bottom-up Transdisciplinary Research Promotion (TDRP) Grants were continuously provided for the promotion of fused disciplines. The new top-down research themes were set up and will be executed from FY2024.

3. Realizing an International Research Environment

The total number of papers by NanoLSI researchers in 2017-2023 was 1,014, of which 426 (42.0%) were internationally co-authored papers. Various measures have been executed for internationalization, such as outreach programs for external researchers, support for young overseas researchers to acquire research funds, and promoting mobility of and career path for young researchers.

4. Making Organizational Reforms

The successful reforms of NanoLSI have been continuously executed, such as research professorships for concentrating on research, a rigorous evaluation-based salary system, the tenure-track junior PI program, and English-based administration. Gender balance among NanoLSI researchers has been steadily improved.

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

Roadmaps on 6 nanotechnology and 7 life sciences have been updated. The total amount of external funds acquired in FY2023 by NanoLSI researchers was approximately 1,301 million yen.

6. Others

Thirty-one press releases of research outcomes were issued, of which 21 were also issued in English. Outreach activities for students of Super Science High Schools have been executed.

* Describe clearly and concisely the progress being made by the WPI center project from the viewpoints below.
- In addressing the below-listed 1-6 viewpoints, place emphasis on the following:
  (1) Whether research is being carried out at a top world-level (including whether research advances are being made by fusing disciplines).
  (2) Whether a proactive effort continues to be made to establish itself as a "truly" world premier international research center.
  (3) Whether a steadfast effort is being made to secure the center's future development over the mid- to long-term.

1. Advancing Research of the Highest Global Level

* Among the research results achieved by the center, concretely describe those that are at the world's highest level. In Appendix 1, list the center's research papers published in 2023.
* Regarding the criteria used when evaluating the world level of center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

Outline

Continuing from the last year, we worked on the three projects shown in Fig. 1.

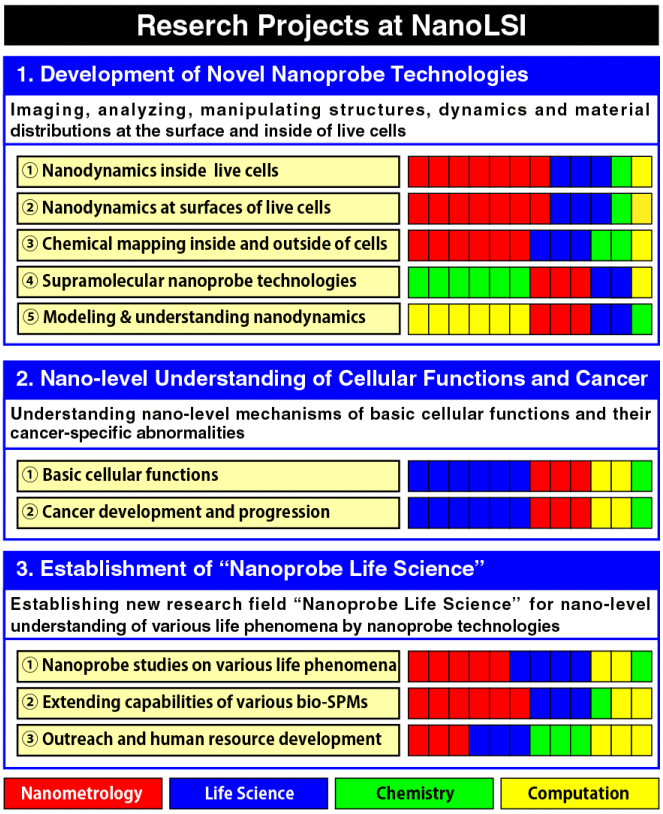

Fig. 1: Research projects at NanoLSI and contributions from the four major disciplines to each project.

(1) We have been developing bio-SPM technologies for visualizing the structures, dynamics and chemical distribution inside and at the surfaces of living cells. By the last year, we had largely completed proof of principle of the newly developed techniques and explored their biological applications. This year, while continuing to improve the performance and functionality of the methods, we narrowed down the promising applications that may provide new insights that cannot be obtained by other existing methods. Examples include a nuclear envelopathy study by Nanoendoscopy AFM and database construction by high-throughput cell characterization by SICM. Although the development of the chemical mapping technique is slightly behind schedule, it has finally entered the stage where it can be used to explore biological applications.

(2) We have been investigating nanoscale mechanisms of cellular functions and cancer using bio-SPM techniques. Life science research with our world-leading bio-SPM technologies (e.g., HS-AFM, 3D-AFM and bio-SICM) continued to produce impactful publications. Examples include HS-AFM analyses of HGF agonist (***Nat Biomed Eng* 2023**) and CaMKII (***Sci Adv* 2023a**), FM-AFM analyses of peptide self-assembly (***ACS Nano* 2023b**, ***Small* 2024**), and nanopipette sensing of SARS-CoV-2 proteins (***Nat Commun* 2023d**). Meanwhile, we have actively explored applications of the newly developed live-cell imaging techniques to different life science disciplines. In some of these projects, we started to seriously explore their medical applications. Examples include immunotherapy by designer exosomes and diagnosis by supramolecular sensors for 1-MNA.

(3) We aim to establish the "Nanoprobe Life Science" field by creating a world-leading center for bio-SPM collaborations. Continuing from the last year, we organized various symposiums, seminars and a summer school, through which many researchers visited NanoLSI from all over the world and worked on Bio-SPM Collaborative Research. In particular, we hosted the largest number of participants (32) for the summer school since we started this program in 2012, highlighting the enhanced visibility of our institute. To continue to lead the bio-SPM research community, we have been working on extending the capabilities of our world-leading bio-SPM techniques. This year, major improvements were made in the speed of these techniques. Examples include 70 fps imaging of actin fibers by HS-AFM, 20 fps atomic-resolution imaging of mica by FM-AFM, and 1 fps subnanoscale imaging of calcite hydration structure by 3D-AFM.

Achievements in FY2023 are summarized as follows.
- Papers: 193 (41.5 % internationally co-authored; 65 with an IF > 10; 88 with an IF > 7),
- Invited talks in int'l meetings: 63,
- Funding: 1,300,949,912 yen overall (30 grants > 10,000,000 yen).

These achievements are of the highest global level for an institute with 87 researchers (as of March 2024).

(1) Development of techniques for measuring nanodynamics on the cell surface and interior

(Development of nano-imaging techniques)

·Measurement of nanodynamics on cell surfaces:

Various subcellular structures, such as filopodia lamellipodia, and microvilli, which are associated with cytoskeletal motion and appear on the cell surface, are more commonly found in cancer cells than in normal cells. However, the detailed movements of these structures at nanoscale resolution and their connection to cell migration remain unexplored. Watanabe *et al.* investigated the subcellular structural dynamics of breast tumor cells using high-speed SICM. They visualized and analyzed changes in the shapes of filopodia lamellipodia, and microvilli-like structures. Their research revealed that these subcellular structures exhibit both continuous and intermittent movements, characterized by phases of progression and pause, during cell migration. Furthermore, they evaluated how local cell elasticity and movements of subcellular structures collectively relate to the mechanisms of cell migration, providing insight into cell migration by linking the movements of subcellular structures and local mechanical properties of cells. This link could deepen our understanding of cancer metastasis.

Ichikawa *et al.* worked on the development of a method to label specific molecules using DNA origami using AFM. They designed several DNA origamis and tested if they could be observed in AFM. They found that a multi-layered triangle-shaped DNA origami works well. In order to label c-Met receptors with the fabricated DNA origami, they inserted the SNAP-tag gene into the C-terminal region of the c-Met gene. In the future, they will add benzyl guanine, which binds to the SNAP-tag, to the DNA origami and establish the method to observe the single c-Met dynamics in living cells using AFM imaging. They have also developed a new method to bind a FRET biosensor molecule to the tip of the cantilever in order to detect local functional molecules using AFM. As a result of examining various methods, they confirmed that it is possible to bind FRET biosensor molecules only to the tip of the probe by using Celltak, which is an adhesive molecule used to stop cell migration. They are now examining the simultaneous imaging of AFM and fluorescence and developing a new method of super-resolution imaging for local functional molecules in the cell using AFM.

·Visualization of intracellular nanodynamics (nano-endoscopic observation):

(i) Nanoendoscopy AFM: So far, Fukuma *et al.* have developed Nanoendoscopy AFM (NE-AFM), which allows insertion of a needle probe into a live cell and visualization of intracellular nanodynamics and mechanics (***Sci Adv*** **2021,** ***STAR Protocols*** **2023**). Last year, they reported direct imaging of focal adhesion (FA) growth dynamics in a live cell. This year, they further visualized elasticity changes and found that FAs are stiffened during their growth and softened while disassembling. They also measured the cell-cycle dependence of the nuclear elasticity, and the preliminary results suggest significant stiffening during the S-phase. This method is useful for the studies on various diseases called nuclear envelopathies. To explore this possibility, Shimi, an expert in such studies, joined NanoLSI and started investigating various diseases such as cardiomyopathy. Meanwhile, other researchers in NanoLSI started to use NE-AFM. Kodera *et al.* combined NE-AFM with HS-AFM and successfully visualized actin fiber dynamics in a live cell. Okuda *et al.* started to apply NE-AFM to understand synaptic interactions between neurons. Observing each neuron's 3D intracellular structure and stiffness, they are now exploring its dynamics and roles in neuronal communication and plasticity. Meanwhile, Fukuma *et al.* continued their efforts to improve the NE-AFM technologies. Examples include developments of anti-fouling probe functionalization, home-built NE-AFM with FM detection combined with a confocal fluorescent microscope, a temperature-sensing technique with a nanodiamond functionalized probe, analysis software to derive mechanical properties from 3D-NE-AFM data, and optically controlled nanomanipulator probes for local pulling or collection of intra-cellular structures.

(ii) Deroofed cells: Franz (Jr. PI) is developing cell-deroofing tools for opening the cell interior for SPM exploration, while maintaining the functionality of the exposed intracellular protein complexes. For instance, microsonication-based cell de-roofing was used in combination with complementary fluorescence microscopy to visualize a novel localization of the small Ca^{2+}-binding protein S100A11 to actin stress fibers and focal adhesion

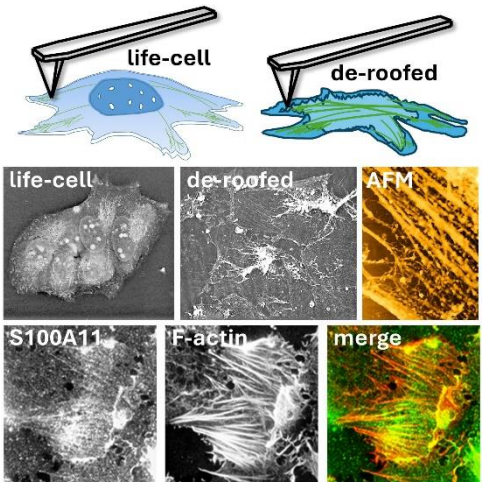

Fig. 2: Verification of Ca^{2+}-dependent S100A11 localization to actin stress fibers and focal adhesions in de-roofed cells.

complexes (***J Cell Sci* 2024**), identifying a new role of S100A11 in promoting adhesion site turnover. Moreover, a mechanical single-cell de-roofing method was employed to expose the cytoplasmic side of native cell membranes for investigating the structure and function of the ion and lipid channel TMEM16F by HS-AFM imaging and AFM-based single-molecule force spectroscopy (SMFS) (***Nat Commun* 2024**). This approach revealed a structural and functional heterogeneity of the TMEM16F channel which had escaped previous cryo-EM studies. While mechanical deroofing methods are suitable for exposing relatively stable intracellular components like actin stress fibers, more delicate intracellular protein assemblies and organelles require non-mechanical methods for minimally invasive cell deroofing. To address this challenge, the Franz group is currently developing an electroporation-based approach to create precise membrane incisions for nanoscale imaging inside living cells. (Fig. 2)

(Development of nano-endoscopic analysis and manipulation techniques)

·Injection and sampling of substances using a nanopipette

The nanopipette of SICM enables direct injection of various substances into cells. Takahashi performed injections of inositol lipids, which are closely associated with organelle functions but for which caged compounds have not been established, in order to control organelle functions. Together with Professor Shimizu of Tokyo Medical and Dental University, injections using PI4P nanopipettes were conducted to study Golgi membrane-associated degradation (GOMED), a protein degradation mechanism similar to autophagy of the Golgi apparatus. In GOMED, the dissociation of trans and medial Golgi was observed, but introducing PI4P into the Golgi apparatus was found to inhibit this dissociation. Additionally, by introducing organic electrolytes into the nanopipette and applying voltage, control of nanopipette interfacial tension was achieved. This phenomenon enables control of sample collection volumes at the atto-liter level using nanopipettes. The combination of SICM and this collection technology allows for organelle collection with sub-microscale positional accuracy. Through collaborative research with Associate Professor Hirabayashi of the University of Tokyo, mitochondria present in axons and dendrites were collected, and upon confirming the expression state of mtDNA, it was found that mitochondria in axons lack mtDNA (***bioRxiv* 2024**). Furthermore, Takahashi is collaborating with Arai to develop fusion technology between FLIM and SICM, with plans to investigate the relationship between concentrations of ATP and GTP and gene expression. (Fig. 3)

·Analysis of nano-distribution of physical properties using a molecular sensor

Arai *et al*. expanded the availability of quantitative fluorescence lifetime imaging (FLIM)-based biosensors capable of the detection of intracellular signaling molecules. Notably, the collaboration study with Oshima exemplified the utility of FLIM-ATP biosensors in discerning cancer cells at different metastatic stages, leveraging cytoplasmic ATP level as a distinguishing factor (***bioRxiv* 2023a**) (Fig. 3). This progress sets the stage for broadening the analytical capabilities available for examination of genes of interest alongside nanopipette technology with Takahashi. Such integration facilitates spatial-temporal metabolomics and transcriptomics in various applications.

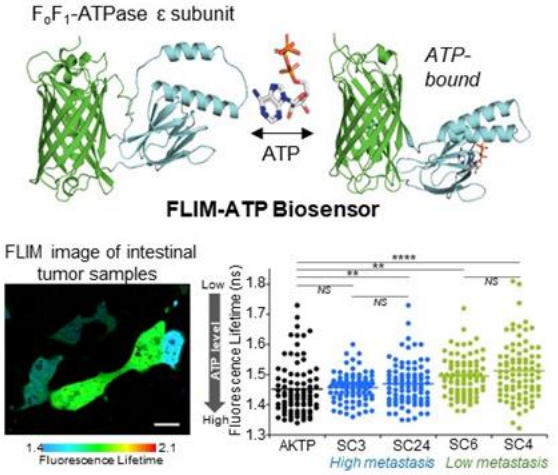

Fig. 3: FLIM-based biosensors to quantify ATP in cancer cells with different metastasis states.

Maeda and Zhang *et al*. successfully demonstrated that SICM glass-pipettes filled with the polymer gel bearing the carboxylate-modified pillar[6]arene-based sensor as the pendants can specifically detect the oncometabolite 1-MNA (1-methylnicotinamide) with a very high-sensitivity based on changes in the ion current passing through the pipette. They also developed new stimuli-responsive helical polymers, which can be potentially applied for a highly sensitive chirality sensing system toward various chiral compounds (***Chem Commun* 2023, *JACS* 2023a, *Angew Chem Int Edit* 2023a**). MacLachlan *et al*. developed cellulose nanocrystals (CNCs) that are functionalized with metal organic framework (MOF) crystals. When porphyrins within the structure were metallated, these polymer-coated CNCs could be used for catalytic reactions. As CNCs have the potential to be used as tips for nanoprobes, this work illustrates a new way to functionalize the tips for various applications and sensing (***Angew Chem Int Edit* 2023b**). MacLachlan *et al*. also studied supramolecular polymer structures that may be useful for catalysis and sensing. They discovered that trimetallic complexes with a benzenetris(amide) core self-assembled into nearly monodisperse 1-D fibres with excellent

length control (***ACS Appl Nano Mater* 2023**). Ogoshi *et al*. have achieved pillar[n]arene-based chiral supramolecular assemblies (***Angew Chem Int Edit* 2023c, d *JACS* 2023b, c**), water-transportation channels (***Angew Chem Int Edit* 2023e**), functionalization of pillar[n]arenes (***Angew Chem Int Edit* 2024a, *JACS* 2023d, *JACS* 2024**), and capture of fluorocarbon gases by pillar[5]quinone crystals (***Adv Funct Mater* 2024**).

·Nano-manipulation using molecular machines

Arai *et al*. established a near-infrared (NIR) light-operated molecular machinery, comprising nano-sized vesicles, enabling the manipulation of local concentration of neurotransmitter within targeted areas. To validate the effectiveness of this molecular machinery, they created an imaging platform using *Drosophila* brain to visualize neural activities, which is an important milestone (***JACS* 2023e**). That could be extended in future applications using such molecular machines.

Akine *et al*. developed a new molecular machinery system in which the triple-helical molecular chirality can be inverted upon stimulation with alkali metal ions. The inversion speeds can be both accelerated and decelerated by selecting suitable alkali metal ions (***Sci Adv* 2023a**). Akine and MacLachlan *et al*. also successfully controlled the molecular chirality inversion speeds using a different strategy. They introduced one or two stapling groups into α-helical peptides to slow down the helix inversion and found that double stapling can practically stop the helix inversion (***Nat Commun* 2023**). MacLachlan *et al*. developed a different type of molecular machinery like a flytrap that can bind and release ions. Based on a dimeric structure with Pt---Pt bonds, these molecules are capable of binding to alkali metal cations, and can subsequently release them upon exposure to light (***Angew Chem Int Edit* 2023f**). Maeda *et al*. succeeded in developing useful methods of synthesis for linear and cyclic helical poly(diphenylacetylene)s with high molecular weights having functional groups. This will contribute to the development of molecular machines for nano-manipulation since helical poly(diphenylacetylene)s bearing functional pendants can show spring-like elongation and contraction in response to external stimuli (***Angew Chem Int Edit* 2023g, *Macromolecules* 2023a**).

(Understanding measurement principles of newly-developed nano-probe techniques and life phenomena by means of mathematical/computational sciences)

·Surface and interfaces at the nanoscale (Foster)

The Adam S. Foster Laboratory uses a range of simulation methodologies (including machine learning, molecular dynamics and quantum simulations) to investigate various problems at nanoscale interfaces. Recent work has focused on simulating Scanning Probe Microscopy in the characterization of designer organic materials (***Nat Chem* 2023a**) and understanding the role of molecular adsorption in the structure of biominerals (***Phys Chem Chem Phys* 2023, *J Phys Chem Lett* 2023**). They have also studied how the wetting properties of surfaces can be tuned by the adsorption of self-assembled organic layers (Fig. 4, ***Nat Chem* 2023b**).

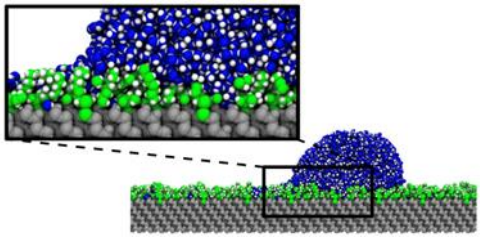

Fig. 4: Molecular dynamics simulations of the interface between a water droplet and a self-assembled organic layer.

·Analyses of HS-AFM movies to elucidate the functions of biomolecules (Sumikama)

Sumikama *et al.* published papers, in which HS-AFM movies were analyzed using statistical mechanics to reveal the functions of biomolecules. The free energy landscapes were estimated for TRPV1 channel motions (***PNAS* 2023a**), and the collective rotational motions of CaMKII were clarified (***Sci Adv* 2023b**). HS-AFM revealed that the voltage sensor domains (VSDs) in a Na^+ channel dissociate from the pore domains, and dissociated VSDs form a dimer via inter-channel interactions. A novel gating mechanism was proposed by calculating possibilities of network formation via inter-channel connection (Fig. 5, ***Nat Commun* 2023b**). Molecular dynamics simulations combined with AFM simulator helped to validate HS-AFM measurements. The group also published a paper about Na^+ ion permeation and the selectivity mechanism

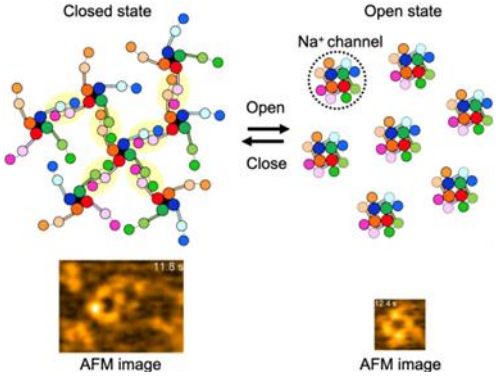

Fig. 5: A proposed gating mechanism of a Na^+ channel by formation of inter-channel network (left) and its disconnection (right).

through a Na^+ channel (***Nat Commun* 2023c**) and a review about computation of AFM images of biomolecules (***Biophys Rev* 2023**).

·Data assimilation for atomistic understanding of HS-AFM observations (Flechsig)

The Flechsig group has developed a physical model and computational method to explain biomolecular placement on AFM substrates and dynamic stability under tip-probed HS-AFM imaging based on electrostatic interactions (***Front Mol Biosci* 2023**). As an important step for automatized interpretation of scanning probe observations, they developed GPU-based computation of simulation AFM (***Algorithms* 2024**), which allows efficient construction of big-data training sets for planned applications of machine learning to HS-AFM data.

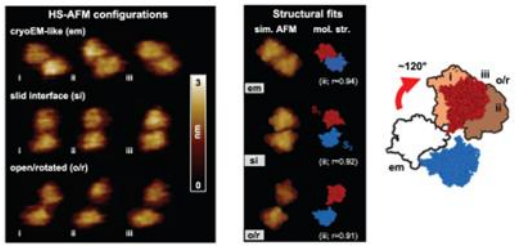

Fig. 6: Data assimilation methods to infer atomistic dynamics from HS-AFM measurements.

Applications of their previously developed methods for data assimilation and integrative modelling with HS-AFM observations allowed detailed understanding of functional biomolecular dynamics for 1) Cas9-RNA-DNA endonuclease (***ACS Nano* 2023a**), 2) CaMKII protein complex (***Sci Adv* 2023b**), 3) E6AP ligase (***Nano Lett* 2023a**), 4) TMEM16 membrane transporters (Fig. 6, ***Nat Commun* 2024**), 5) Laminin proteins (***Int J Mol Sci* 2024**), 6) EML4-ALK protein complex ((cancer research) (***under revision***), and 7) MET receptors (cancer research). Combining modelling and HS-AFM experiments of the myosin V motor, they proposed a paradigm changing model for energy transduction in molecular motors (***under revision***). Making leading contributions to the field, they published invited topical reviews (***Curr Opin Struct Biol* 2023, *Annu Rev Biophys* 2024**).

·Modeling multiscale cell dynamics from cytoskeletal to multicellular systems (Okuda)

The Satoru Okuda Laboratory proposed new mathematical models that describe the 3D multicellular dynamics. To calculate long-term multicellular dynamics during cell proliferation, they proposed a cell proliferation model for nonconservative fluid membrane (***EPJE* 2023**). Moreover, by combining the particle-based model with biological experiments, they revealed the mechanism of cell detachment from the 3D-structured dish surface (***Acta Biomater* 2023**). In this model, they simplified 3D multicellular structures to be particles and their topological connection network (Fig. 7). Furthermore, they proposed estimation methods of spatial gene expressions and mechanical stress within tissues (***Sci Rep* 2023, *Plos ONE* 2024**), bridging the gap between microscopic molecular dynamics and macroscopic cell and tissue dynamics.

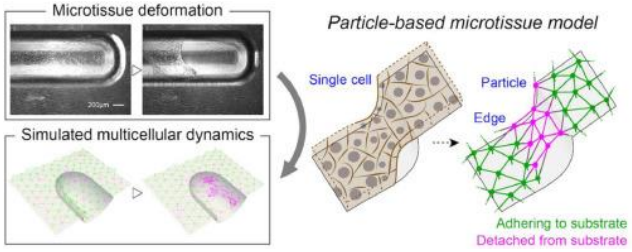

Fig. 7: A computational method to simulate multicellular dynamics on scaffolds, addressing cell detachments.

(2) Nano-level understanding of basic cellular functions and cancer-specific abnormalities

·Cell membrane receptor engineering and dynamics (Matsumoto)

The Matsumoto group has been investigating 1) dynamics of growth factor receptor (MET) activation and 2) creation and AFM proving of growth factor receptor agonists capable of activating MET/HGF receptor, using molecular engineering and cyclic peptides. In FY2023, MET-agonists were created, using IgG-Fc and ubiquitin proteins as scaffolds into which MET-binding peptides are incorporated (Fig. 8, ***Nat Biomed Eng* 2023; *Angew Chem Int Edit* 2023h**). The HS-AFM analysis proved that the MET-agonist induces MET dimer formation, an essential molecular event for its activation. They also revealed that MET is essential for anti-viral innate immunity (***PNAS* 2023b**).

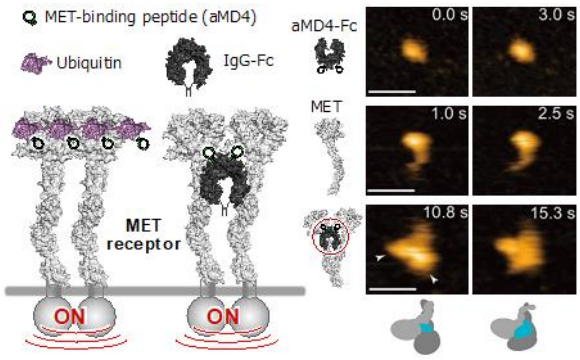

Fig. 8: MET receptor activation by newly created designer receptor agonist (aMD4-Fc).

·Intracellular trafficking (Wong)

The control of intracellular trafficing is critical for cell growth and differentiation. Nuclear pore complexes (NPCs) are multi-protein turnstiles that regulate nucleocytoplasmic trafficing. Recently, Wong *et al*. reported genomic amplification of NUP107, a component of NPCs, in glioblastoma (GBM) and showed that nuclear pore protein NUP107 is overexpressed simultaneously with MDM2, a critical E3 ligase that mediates p53 degradation. Depletion of NUP107 inhibited the growth of GBM cell lines through p53 protein stabilization. Their findings established roles of NPCs in transport surveillance and provide insights into p53 inactivation in GBM (***Cell Rep* 2023**). In an interdisciplinary project with the Hanayama and Ando groups, using HS-AFM, they elucidated the molecular property of an anti-spike neutralizing antibody (S Nab) and its interaction with spike proteins of SARS-CoV-2. The dynamic S Nab–spike protein interaction at the receptor-binding domain (RBD) induces neither RBD opening nor S1 subunit shedding. These findings indicated that the S Nab could have a negligible risk of antibody-dependent enhancement (Fig. 9, ***Nano Letters* 2023b**). They also investigated the structural dynamics of ORF6 protein of SARS-CoV-2. ORF6 oligomers were ellipsoidal and readily assembled into ORF6 protofilaments in either a circular or a linear pattern hijacking nuclear pore proteins. ORF6 self-assembly could be necessary to sequester host factors and causes collateral damage to cells via amyloid aggregates (***J Phys Chem Lett* 2023**). In a bio-SPM project, collaborating with Austrian researchers, Wong *et al*. also elucidated how the flexibility, density and chirality of the active filaments affect their collective behavior. Their findings shed light on the fundamental properties of active chiral matter and explain how treadmilling FtsZ filaments organize during bacterial cell division (***Nat Phys* 2023**).

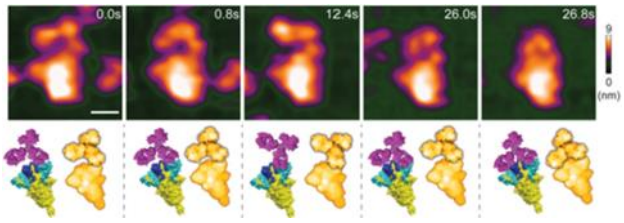

Fig. 9: HS-AFM visualization of dynamic anti-spike neutralizing antibodies (S Nab) and Spike (S) protein interactions. A representative set of HS-AFM image sequence illustrating the real-time binding of S Nab to the receptor-binding domain (RBD) of recombinant S protein.

·Cell communications via extracellular vesicles (Hanayama)

The Hanayama group has pioneered a methodology enabling the targeted expression of proteins on extracellular vesicles (EVs) through genetic modification techniques. EVs bearing the SARS-CoV-2 spike protein on their membrane surface were engineered, leading to a collaborative investigation with the Wong group to elucidate the mechanism of action of anti-spike neutralizing antibodies using high-speed AFM (***Nano Lett* 2023b**). Additionally, they have engineered EVs concurrently expressing anti-spike neutralizing nanobody and the antiviral growth factor interferon-beta, demonstrating their potential as therapeutic agents capable of concomitantly inhibiting viral infection and replication (***Pharm Res* 2023a**). Through the application of these methodologies, they are actively pursuing the development of designer EVs tailored to augment anti-tumor immune responses (***bioRxiv* 2023b**), with the aim of developing EV formulations.

·Morphogenesis - a bottom up and mechanical approach (Toda)

Toda *et al.* have been working on the mechanisms of how interacting cells organize tissue morphologies. In FY2023, they have engineered synthetic reaction diffusion circuits between mammalian cell lines to explore minimal programs for spontaneous pattern formation. They found that a combination of membrane-tethered activator and soluble inhibitor can generate reaction diffusion patterns, and that coupling reaction diffusion with cell adhesion reduced pattern fluctuations. In addition, to understand how the diffusion of signaling proteins is regulated, they have started a collaboration with the Kodera group using HS-AFM to visualize the nano-level dynamics of Wnt-Afamin complex and to study how Afamin and lipid-modified Wnt form a stable and soluble complex.

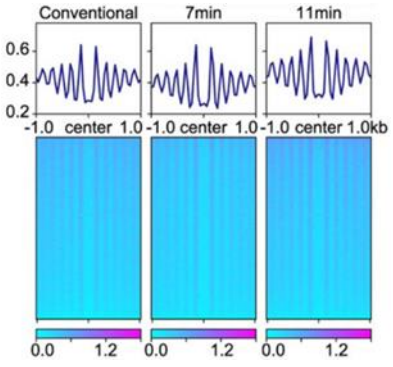

Fig. 10: Low-input MNase-seq profiling of mouse embryos.

·Transcriptional regulation and epigenetics (Miyanari)

Miyanari *et al*. have been studying roles for chromatin dynamics in transcriptional regulation, which is crucial for cell lineage allocation in mammalian development. They have succeeded in simultaneously visualizing chromatin accessibility and epigenetic modifications; both are key chromatin

signatures in the regulation of transcription (***Methods Mol Bio* 2023**). They also studied nuclear structure of mouse early embryos, especially focusing on H3.3, a histone variant. They developed a low-input MNase-seq to profile nucleosome occupancy during embryo development and found that Yy1, a transcription factor, plays a major role in remodelling nuclear-organization in the development process (Fig. 10, ***Gens & Dev* 2023**).

·Oncogenes and Cancer Cell Dynamics (Oshima)

Oshima *et al*. have identified the biological mechanism of cancer cell cluster migration by imaging analysis using tumor-derived organoids (***Cancer Res* 2024**). A novel concept of polyclonal metastasis has been proposed, in which cancer cell clusters migrate from the primary site towards distant organs. Their study confirmed the concept using the *in vitro* organoid modeling system for the first time. Treatment with TGF-β family cytokine caused drastic morphological changes of organoid tumors with multiple protrusion formation (Fig. 11). Such protrusions are thought to be prior step for cluster migrations. Importantly, p53 gain-of-function mutation is a basic requirement for TGF-β-induced cluster migration. These results significantly expanded our knowledge about the process of cancer metastasis.

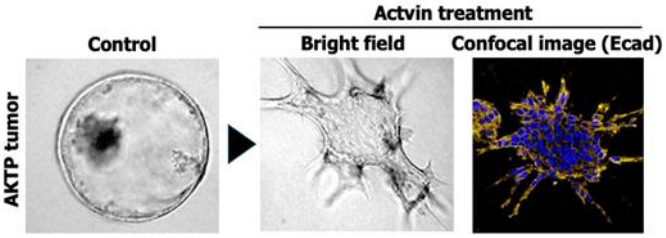

Fig. 11: TGF-β family cytokine Activin treatment induced morphological changes of the intestinal tumor-derived organoid tumor (AKTP) with multiple protrusions. Confocal image of immunochemistry with E-cadherin antibody confirmed partial EMT.

·Development of DNA aptamers as anti-cancer molecules (Nakajima)

Nakajima *et al.* have successfully developed DNA aptamer molecules targeting ADAR, an enzyme catalyzing RNA editing, the abnormal expression of which is relevant to cancer development. By collaboration with the Kodera group, they clarified the molecular dynamics of the binding of DNA aptamer to ADAR dimers by HS-AFM. Furthermore, they have developed an aptamer-based PROTAC (Proteolysis Targeting Chimera), which can knockdown ADAR in the cancer cells. Interestingly, the aptamer-based PROTAC significantly suppressed the proliferation of cancer cells. By collaboration with the Fukuma group, they clarified by AFM that cell elasticity was decreased by the knockdown of ADAR, supporting the involvement of ADAR in cancer malignancy. In addition, they found with the Hanayama group that cancer cells-derived EVs prepared by different isolation methods show dissimilar responses for the induction of inflammatory cytokines in macrophages (***Pharm Res* 2023b**).

·Development of cancer therapeutic technology (Hirao)

Hirao *et al*. have recently elucidated the molecular mechanisms underlying drug resistance in lung cancer, mediated by the mitochondria-shaping protein Opa1 (***Cell Death Disease* 2023**). Their research revealed that cells resistant to anti-cancer therapy exhibited elongated mitochondria with narrower cristae (Fig. 12), attributed to the up-regulation of Opa1. Genetic or pharmacological inhibition of Opa1 reversed the mitochondrial morphology changes and sensitized the cells to therapy. Additionally, they highlighted the critical role of NAD+ metabolism in the malignant properties of cancers (***Nat Comm* 2023d**). In their efforts to advance innovative imaging technology, they evaluated the performance of a novel sensor for detecting a niacin metabolite in human samples. The sensor exhibited notable advantages in diagnosing cancer-associated metabolic disorders. These discoveries are expected to propel the development of nano-pipette imaging technology, thereby deepening our understanding of the mechanisms governing malignant traits in cancer cells.

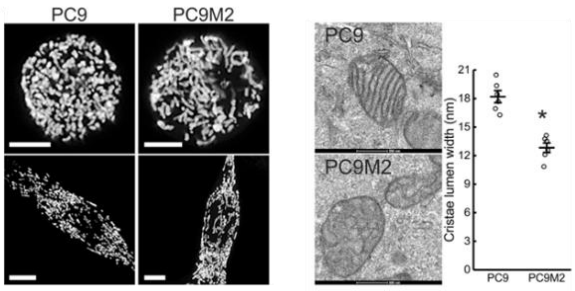

Fig. 12: Abnormalities of mitochondrial morphology in cells exhibiting drug resistance. Left: Elongation of mitochondria; Right: Narrow cristae lumen observed in the resistant cells (PC9M2) compared to parental cells (PC9).

·Development of therapeutic approach to lung cancer (Yano)

Yano *et al.* developed a therapeutic approach to lung cancer with *ROS1*- rearrangement targeting a microenvironment derived growth factor, hepatocyte growth factor (HGF) (***Cancer Med* 2023**). They found that fibroblasts in the tumor microenvironment could produce HGF and induced resistance to ROS1 kinase inhibitor. HGF-induced ROS1 tyrosine kinase inhibitor (TKI) resistance was reserved by the active-HGF-specific macrocyclic peptide HiP-8 or the MET-TKI (Fig. 13). These findings suggest a new therapeutic approach consisting of ROS1 inhibitor and HGF/MET-inhibiting compounds.

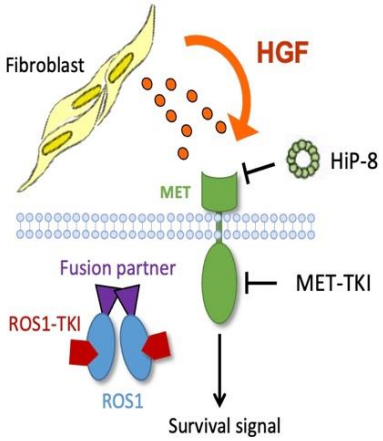

Fig. 13: HGF/MET inhibitors reverse resistance to ROS1 inhibitor induced by fibroblast-derived HGF in ROS1-rearranged lung cancer.

·RNA Therapeutics for nonsense-associated Genetic Disorders & Development of Single-molecule imaging application (Sato)

Nonsense mutations give rise to numerous human genetic disorders. One clinical treatment strategy for nonsense mutations is nonsense suppression therapy, which aims to restore functional proteins by introducing nonsense suppression at the mutation site within disease-causing transcripts. However, a significant limitation in the recovery of disease-causing nonsense genes is the marked reduction of mRNA abundance caused by nonsense-mediated mRNA decay (NMD).

Sato *et al.* have been developing a novel RNA therapeutics approach targeting nonsense-associated mRNA and NMD using a unique single-cell NMD reporter. They have also pioneered a cutting-edge single-molecule imaging approach to detect dynamic mRNA decay processes in real-time. Advances in single-molecule fluorescence imaging have facilitated the real-time observation of individual gene regulatory components in living cells and organisms. They also underscore how these cutting-edge imaging technologies have unveiled the spatiotemporal coordination of molecular interactions underlying gene expression (***Nat Rev Genet* 2024**).

(3) Establishment of a new research field: nanoprobe life science (Further improvement of Bio-SPM technologies)

·HS-AFM technology

To expand the range of biological samples and dynamic phenomena that can be studied with HS-AFM, the HS-AFM team has been trying to further increase the imaging rate since 2017. Ando and Fukuda have already developed the Only Trace Imaging (OTI) mode, which eliminates retrace imaging during backward X-scanning. They have confirmed that the combination of OTI and dynamic PID control is effective in reducing tip perturbation of the sample. They also developed the mass control method for cantilever by using photothermal excitation, which can increase the cantilever resonant frequency from 1.2 MHz to 2.3 MHz. As a result, actin filaments and microtubules could be imaged at 70–100 fps. Using F_1-ATPase, they have confirmed that faster imaging can capture short-lived intermediate states, allowing new discoveries. In addition, improvements on the various devices (Z-scanner, amplitude-detector, cantilever, and so on) in the HS-AFM system have been made. This year, continuing from last year, Kodera and his colleagues worked on the improvement of the optical beam deflection system to obtain an accurate deflection signal of the ultra-small cantilever. Consequently, the lengths of the major and minor axes of an elliptical laser spot shape became ~1.1 μm and ~0.8 μm, respectively. The area of laser spot on a cantilever could be reduced to ~10% of that of a conventional system, allowing them to use a smaller cantilever with a higher resonant frequency. In addition, by employing the radio-frequency modulation method, the deflection of an ultra-small cantilever can be detected with a higher signal-to-noise ratio in the optical feedback noise-free manner. Collaboration with a cantilever manufacturer is also progressing. This collaboration will soon produce smaller cantilevers with resonant frequencies of 3–4 MHz in water, while keeping the spring constant small at 0.1–0.2 N/m. Thus, exceeding 100 fps seems to be a realistic goal.

·Scanning ion conductance microscopy (SICM)

Watanabe *et al.* developed a nanopipette probe with low capacitance, which enhances the signal-to-noise ratio, thus facilitating high-speed scanning in SICM. In this probe, a tube encases the nanopipette tip with glue. This configuration effectively traps air bubbles around the tip, significantly

reducing the capacitance that arises at the interface between the liquid and the pipette surface. They have successfully reduced the capacitance to approximately 0.5 pF or less without sacrificing the quality of SICM imaging, regardless of the depth at which the nanopipette is immersed in the liquid.
Comprehensively understanding the distribution of subcellular-level and fractionated biomolecules is crucial for analyzing biomolecules other than genes that cannot be amplified. By utilizing machine learning, it becomes possible to obtain positional information of cells and organelles from images captured by inverted microscopes. Leveraging this positional information, Takahashi *et al.* are developing organelle biopsy technology that automatically collects cells and organelles using nanopipettes. Already, they have established techniques for collecting organelles using nanopipettes based on specific structures such as the leading edge of cells, organelle identification, and utilizing voltage or pressure (Fig. 14).

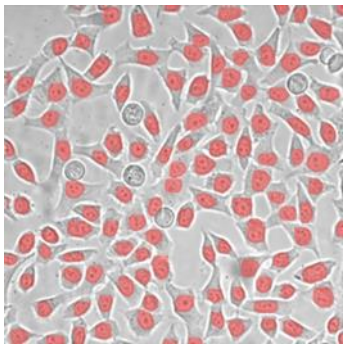

Fig. 14: Automated identification of cell nuclei using machine learning.

·Improvement of FM/3D-AFM imaging speed

So far, Fukuma *et al.* developed in-liquid frequency modulation AFM (FM-AFM) and 3D-AFM, making it possible to image atomic-scale surface structures and 3D hydration structures at solid-liquid interfaces. Since then, they have been making efforts to enhance the speed without losing atomic-resolution-imaging capability. This year, they succeeded in 20 fps atomic-resolution 2D FM-AFM imaging of mica in PBS solution, revealing the line-shaped irregularity in water or ion adsorption. In addition, they succeeded in 1 fps 3D-AFM imaging of calcite in water. These capabilities should allow analyses of the dynamic properties of water and ions on various materials including biological systems.

(Nanoprobe studies on various life phenomena)

i) Creation of high-performance artificial growth factor applicable for the treatment of intractable diseases (*Nat Biomed Eng* 2023, Sakai, Imamura, Shibata, Matsumoto, IF: 28.1**)**

By incorporating cyclic peptide sequences that bind to the MET transmembrane receptor for hepatocyte growth factor (HGF) into scaffold protein (IgG-Fc), high-performance artificial growth factors were created that have the same activity as the natural growth factor but are highly stable in blood for a long time or can pass into the brain. High-speed AFM revealed that these agonists dimerized the MET receptors, suggesting the induction of biological responses similar to those induced by the natural ligand. These results may allow for designer protein therapeutics with enhanced stability and pharmacokinetics. (Fig. 15)

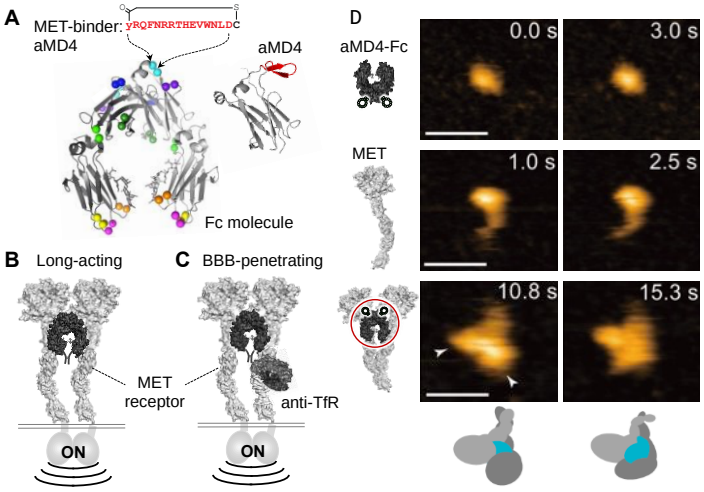

Fig. 15: MET receptor activation by newly created designer receptor agonist (aMD4-Fc).

ii) Imaging single CaMKII holoenzymes at work by highspeed atomic force microscopy (*Sci Adv* 2023b, Sumino, Sumikama, Flechsig, Puppulin, Kakuta, Ogoshi, Umeda, Kodera, Shibata, IF: 13.6**)**

Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) has long been central in synaptic plasticity research. CaMKII is a dodecameric serine/threonine kinase that has been essentially conserved across metazoans for over a million years. While the mechanisms of CaMKII activation have been extensively studied, its detailed behavior at the molecular level has not been clarified. Here, high-speed atomic force microscopy was used to visualize the activity-dependent structural dynamics of rat/hydra/*C. elegans* CaMKII in various states at nanometer resolution. Among the species, rat CaMKII underwent internal kinase domain aggregation in an activity-dependent manner and showed a higher tolerance to dephosphorylation by phosphatase. Our findings suggest that mammalian CaMKII has evolutionarily acquired a new structural form and a tolerance to phosphatase to maintain robust CaMKII activity for proper neuronal function. (Fig. 16)

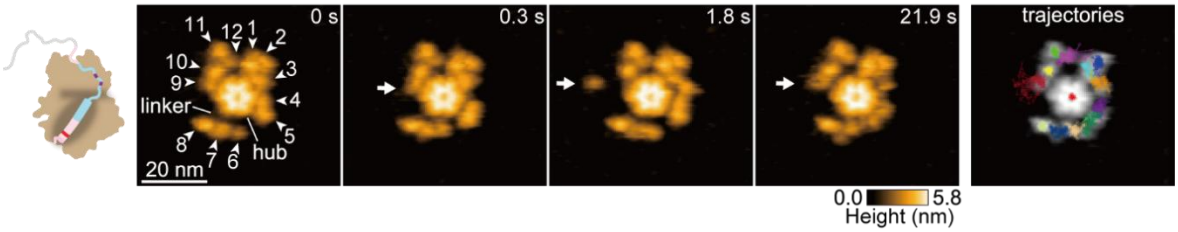

Fig. 16: Sequential HS-AFM images of rat CaMKIIα. White arrowheads indicates kinase domains with arbitrary numbers. White arrows indicate the kinase domains in motion Frame rate, 3.3 frames/s.

iii) Molecular scale structure and kinetics of layer-by-layer peptide self-organization at atomically flat solid surfaces (*ACS Nano* 2023b, Yurtsever, Sun, Fukuma, Watanabe, IF:17.1**; *Small* 2024, Yurtsever, Miyazawa, Miyata, Sun, Maeda, Fukuma,** IF:13.3**)**

Understanding the mechanisms of self-organization of short peptides into two- and three-dimensional architectures is of great interest in the formation of crystalline biomolecular systems and their practical applications. In this study, they used a graphite-binding dodecapeptide, GrBP5, and recorded the self-organization process of its first two layers on a HOPG surface in an aqueous solution using FM-AFM *in situ*. Their observations suggest that the first layer forms homogeneously, generating self-organized crystals with a lattice structure in contact with the underlying graphite. The formation of the second layer is mostly heterogeneous, triggered by the crystalline defects on the first layer, growing row-by-row to establish nominally diverse biomolecular self-organized structures with transient crystalline phases (Fig. 17). Self-assembled peptide crystals are composed of either singlets or doublets, establishing *P1* and *P2* oblique lattices, respectively, each commensurate with the underlying graphite lattice with chiral crystal relations. This work offers fundamental guidance in designing organized molecular-scale genetically coded and controlled nanostructures for use in hybrid surface technologies, such as protein and peptide arrays, bioelectronics, and biomolecular logic devices.

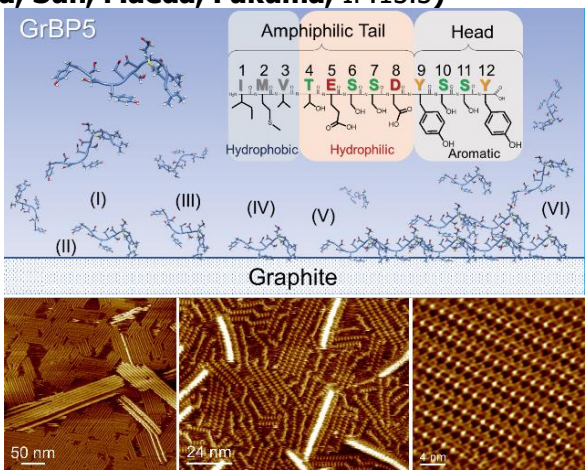

Fig. 17: The amino acid sequence of the dodecapeptide and schematic representation of the possible surface phenomena. Molecular resolution AFM images of self-assembled peptide nanostructures, acquired in water.

iv) The SYP123–VAMP727 SNARE complex delivers secondary cell wall components for root hair shank hardening in *Arabidopsis* (*Plant Cell* 2023, Watanabe-Nakayama, Konno, IF: 11.6**)**

Root hair formation involves tip growth and the concomitant hardening of the shank by producing a secondary cell wall layer to form an elongated tubular structure. However, little is known about the secretion of secondary cell wall materials in the root hair shank. They observed increased localization of SYP123 at the plasma membrane (PM) of the subapical and shank zones compared with the tip region in elongating root hairs. The syp123 and vamp727 mutants exhibited reduced shank cell wall stiffness due to impaired secondary cell wall component deposition (Fig. 18a, b). Inhibition of PtdIns(3,5)P_2 production impaired SYP123 localization in the PM and SYP123-mediated root hair shank hardening, and root hair elongation in syp123 mutant is insensitive to the PtdIns(3,5)P_2 synthesis inhibitor. SYP123 interacts

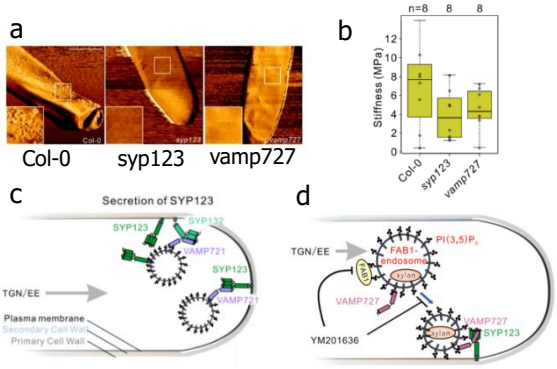

Fig. 18: Root hair surface structure as observed using AFM (a). Cell wall stiffness of root hair shank (b). The models of the secretion of primary cell wall (c) and secondary cell wall (d) components via SYP123 and VAMP727 on FAB1 endosomes.

with both VAMP721 and VAMP727 (Fig. 18c, d). In conclusion, the SYP123/VAMP727-dependent secretion system delivers secondary cell wall components for hardening the subapical zone and shank of *Arabidopsis* root hairs (Fig. 18c, d).

v) On-surface synthesis of disilabenzene-bridged covalent organic frameworks (*Nat Chem* 2023a, Foster, IF: 21.8**)**

Substituting carbon atoms with silicon atoms in organic molecules/materials has long attracted attention as a way of modifying the aromatic and electronic properties of molecules/materials. While graphene analogues, such as graphene nanoribbons and doped-graphene, have been reported to exhibit exotic properties, syntheses of two-dimensionally conjugated porous graphene with atomically precise Si-substitution remain a major challenge. In this work, syntheses are presented of two-dimensional and linear covalent organic framework (COF) substructures linked with 1,4-disilabenzene (C_4Si_2). A combination of high-resolution scanning probe microscopy, photoelectron spectroscopy and density functional theory calculations reveals the detailed structures of the Si-incorporated COF as well as its chemical properties. These results demonstrate the high-generality of the C-Si on-surface coupling, further extending the possibilities for syntheses of various low-dimensional nanostructures with designed elemental combinations. (Fig. 19)

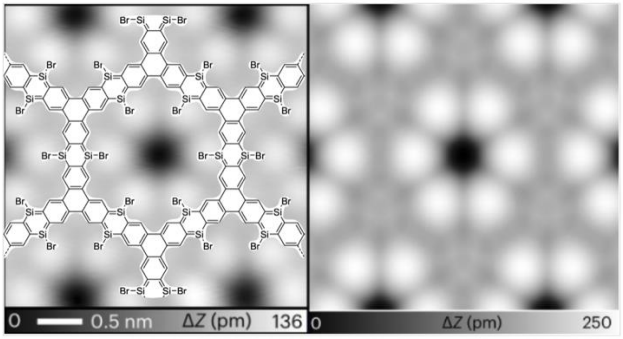

Fig. 19: Comparison of experimental (left) and simulated (right) scanning probe microscopy images of the disilabenzene bridged covalent organic framework.

vi) Mapping nanommechanical properties of basal surfaces in etastatic intestinal 3D living organoids with high-speed scanning ion conductance microscopy (*Small*, 2023a, Wang, Nguyen, Nakayama, Oshima, Sun, Oshima, Watanabe, IF: 13.3**)**

Due to the problems with accessibility of the scanning probe in scanning probe microscopy, mechanical measurements of cells mainly focus on the apical surface, while little is known about the basal surface (BS). To overcome this problem, a method was developed to access the BS in three-dimensional cultured organoids where the BS faces toward the outside surface of organoid cells. The organoids, genotype-defined metastatic cancer cells, were partially embedded into collagen gel to immobilize and stabilize the organoid structures for long-term time-lapse high-speed-SICM measurement (Fig. 20a). The long-term dynamics of subcellular structures, such as ridge-like, stress-fiber, and local elastic modulus distributions on BS, were visualized (Fig. 20b). Furthermore, they demonstrated the possibility that not only the averaged elastic modulus of cells (Fig. 20c) but also local correlations between topography and elastic modulus mapping provide a physical marker to categorize cancer progression (Fig. 20d).

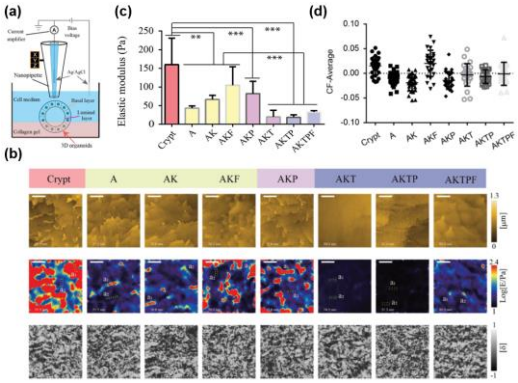

Fig. 20: (a) HS-SICM setup for 3D cell measurement. (b) Snapshots of time-lapse images of height and elastic modulus in genotype-defined (A, AK, AKF, AKP, AKT, AKTP, and AKTPF) 3D organoids of metastasis cancer cells and normal Crypt cells. (c) Elastic modulus of various 3D organoids. (d) Local correlation factor for various 3D organoids.

vii) Multiplexed detection of viral antigen and RNA using nanopore sensing and encoded molecular probes (*Nat Commun* 2023d, Ren, Korchev, IF: 16.6**)**

COVID-19 is an infectious disease caused by SARS-CoV-2 that has swept the globe since it was first identified in December 2019. This has highlighted the need to develop rapid and accurate diagnostic approaches that can be implemented for point-of-care testing of SARS-CoV-2 and relevant variants to minimize virus transmission. In this study, they employ single-molecule nanopore sensing combined with position-encoded DNA molecular probes, with chemistry tuned to simultaneously identify various antigen proteins and multiple RNA gene fragments of SARS-CoV-2 with high sensitivity and selectivity. They show (Fig. 21) that this sensing strategy can directly detect spike (S) and nucleocapsid (N)

proteins in unprocessed human saliva. Moreover, their approach enables the identification of RNA fragments from patient samples using nasal/throat swabs, enabling the identification of critical mutations among viral variants. In particular, it can detect and discriminate between SARS-CoV-2 lineages of wild-type Alpha, Delta, and Omicron within a single measurement without the need for nucleic acid sequencing. The sensing strategy of the molecular probes is easily adaptable to other viral targets and diseases and can be expanded depending on the application required.

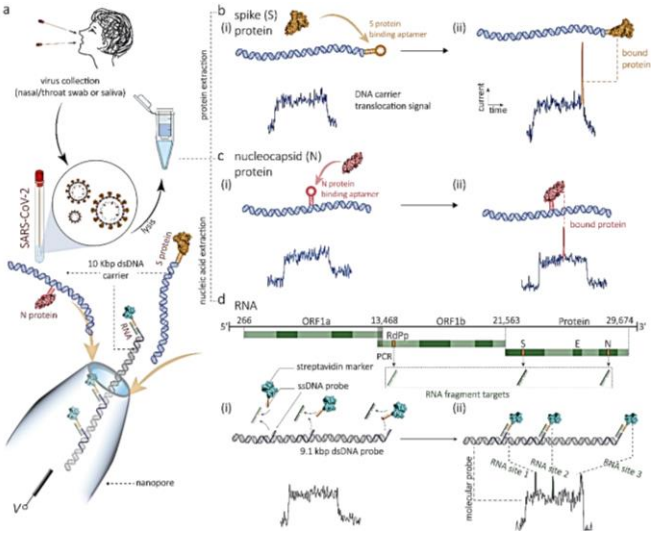

Fig. 21: Multiplexed sensing of SARS-CoV-2 S, N proteins and RNA fragments of critical mutations among viral variants.

viii) Stapling strategy for slowing helicity interconversion of α-helical peptides and isolating chiral auxiliary-free one-handed forms (*Nat Commun* 2023a, Ousaka, MacLachlan, Akine, IF: 16.6**)**

Peptides play important roles in a variety of biological phenomena. The α-helix, one of the important secondary structures, adopts a right-handed structure dictated by chiral L-amino acids. These secondary structures are flexible because they are maintained by only non-covalent interactions, causing thermal denaturation. Therefore, if an α-helical peptide would be composed solely of achiral amino acids, the isolation of a one-handed form has been considered to be impossible due to the rapid racemization equilibrium between the right-handed (P) and left-handed (M) forms. In this study, they employed a stapling strategy to slow down the P/M inversion of the α-helices. They found that the P/M helicity interconversion was slowed down by approximately 10^6 and 10^{12} times by the introduction of one and two stapling groups, respectively, compared to that of the non-stapled analogue. This enabled the successful isolation of an enantiopure α-helical peptide without any chiral L-amino acids, which would retain its optical activity for several years at room temperature. This stapling strategy may be useful for fixing various secondary structures of proteins which could contribute to obtaining clearer images in nanoprobe science. (Fig. 22)

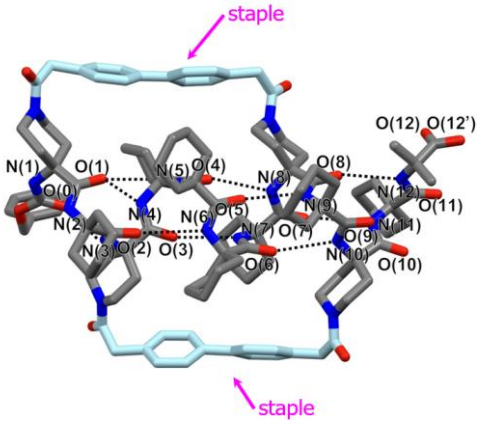

Fig. 22: Molecular structure of doubly-stapled α-helical peptide.

2. Generating Fused Disciplines

* Describe the content of measures taken by the center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields. If any, describe the interdisciplinary research/fused discipline that have resulted from your efforts to generate fused disciplines. You may refer to the research results described concretely in "1. Advancing Research of the Highest Global Level."

Top-down Transdisciplinary Research Promotion (TDRP) Grant

From the second half of FY2020, we have continued to carry out transdisciplinary research that addresses the three priority research themes set out by the NanoLSI Future Planning Board and NanoLSI Faculty Board. The three priority interdisciplinary research themes are as follows:

1. Intracellular imaging and cell monitoring after treatments for observation (coordinators, PIs Fukuma and Wong);
2. Local stimulation/manipulation and chemical mapping (inside cells and on the cell surface) (coordinators, PIs Hirao and Maeda);
3. Cell surface imaging and cell-cell communication (coordinators, PIs Oshima and Hanayama).

For each priority research theme, consumables expenses of up to 4 million yen were provided from the strategic research promotion program from the university headquarters, and personnel expenses of up to 6 million yen were provided from the WPI subsidy.

The above-mentioned efforts for the first phase of priority interdisciplinary research enhancement

were completed in three years as planned, and from FY2024, we set forth efforts on the enhancement of the following three priority research themes.
1. (continued research theme) Local stimulation/manipulation and chemical mapping (inside cells and on the cell surface) (coordinators, PIs Hirao and Maeda);
1-1. Promotion of medical applications of 1-MNA sensors using P6A (PIs Hirao and Ogoshi);
1-2. Visualization of 1-MNA concentration changes around cells associated with metabolism using P6A nanopipette sensor (PI Hirao and Assoc. Prof. Zhang);
1-3. Exploring the development and application of nanopipette sensors for chemicals other than 1-MNA, such as lactate (PIs Akine and Maeda);
1-4. Application of nanopipette usage to life science research through intracellular substance collection and analysis technology (Prof. Takahashi and Assoc. Prof. Arai).
2. Promotion of life science research unique to cell SPM technology;
2-1. Automation of cell nuclear stiffness measurement by nanoendoscopy and contribution to various nuclear envelopathy research (PI Fukuma and Assoc. Prof. Shimi);
2-2. Construction of database of various cell dynamics, cell stiffness, and charge distribution by HS-SICM (PI Oshima and Assoc. Prof. Watanabe).
3. Further advancement of world-class SPM technology of NanoLSI (PIs Kodera and Fukuma, and Assoc. Prof. Watanabe);
3-1. Integration of HS-AFM/SICM and FM/3D-AFM with AI technology (automation, noise removal, and image processing);
3-2. Further improvement in speed and resolution of HS-AFM/SICM and FM/3D-AFM (equipment, method, probe).

Bottom-up Transdisciplinary Research Promotion (TDRP) Grant

In order to support interdisciplinary research by teams consisting of young researchers, the bottom-up TDRP grant was set up, and a total of 20 million yen was provided for 14 research projects via application and selection. Of the 14 research projects supported, 9 are research projects, each led by a graduate student in the Doctoral Course, Division of Nano Life Science. For each research project, the PI corresponding to the research project acts as a supervisor, and at the beginning of the fiscal year following the support, a research report meeting attended by all PIs is held to give advice on future research development.

T-meetings

In order to promote interdisciplinary research, T-meetings were held 24 times in FY2023 by combining 2 research teams out of those individually led by 16 PIs, 6 Jr. PIs, and one Associate PI from different disciplines to allow them to introduce their latest research. Nine of these T-meetings were conducted in combination with 4 overseas PIs and resident PIs or Jr. PIs in NanoLSI.

3. Realizing an International Research Environment

* Describe what's been accomplished in the efforts to raise the center's recognition as a genuine globally visible research institute, along with innovative efforts proactively being taken in accordance with the development stage of the center, including the following points, for example:
- Efforts being developed based on the analysis of number and state of world-leading, frontline researchers (in Appendix 2); exchanges with overseas entities (in Appendix 4); number and state of visiting researchers (in Appendix 5)
- Proactive efforts to raise the level of the center's international recognition
- Efforts to make the center into one that attracts excellent young researchers from around the world (such as efforts fostering young researchers and contributing to advancing their career paths)

Total number of papers by NanoLSI researchers, top 1% papers, top 10% papers, internationally co-authored papers in 2017-2023

The total number of papers in 2023 by NanoLSI researchers was 193, out of which 80 (41.5%) papers were internationally co-authored. Of the total 193 papers, 3 (1.6%) were in the top 1% and 38 (19.7%) in the top 10% in terms of citations. The number of top 1% papers based on field-weighted Citation Impact corrections was 1 (0.5%), and the number of top 10% papers, 18 (9.3%).

During the 7 years from 2017, when NanoLSI was established, to 2023, the total number of papers by the NanoLSI researchers was 1,014, of which 426 (42.0%) were internationally co-authored. Of the total 1,014 papers, 27 (2.7%) were in the top 1% and 263 (25.9%) in the top 10% in terms of citations. The number of top 1% papers based on field-weighted Citation Impact corrections was 7 (0.7%), and the number of top 10% papers was 134 (13.2%).

Number of co-authored papers with overseas PIs in 2017-2023

The total number of papers co-authored by one of the four overseas PIs with resident researchers in NanoLSI was 2 in 2023 alone: one with Prof. Korchev (nanometrology) of Imperial College London, UK, an overseas satellite, and one with Prof. MacLachlan (supramolecular chemistry), the University of British Columbia, Canada, also an overseas satellite.

Twenty-six co-authored papers in the same category were published in the 7 years from 2017 to

2023. Of these 26 papers, 10 were published with Prof. Korchev and 5 with Prof. MacLachlan. In addition, 12 papers were published with Prof. Foster (computational science) of Aalto University, Finland, and one with Prof. Mikhailov (former overseas PI, computational science) of the Fritz Haber Institute of the Max Planck Society, Germany, or with his successor from late 2022, Prof. Beta (computational science and biophysics), University of Potsdam, Germany.

Outreach programs for external researchers in FY2017-FY2023

The Bio-SPM Summer School and Bio-SPM Collaborative Research aim to invite external researchers to disseminate the scanning probe microscope (bio-SPM) technology of NanoLSI, leading to joint research. In FY2023, the Bio-SPM Summer School was held at NanoLSI from Aug. 28 (Mon) through Sept. 2 (Sat) with 15 participants from 9 overseas countries. On the other hand, 17 researchers from Japan participated, and a total number of participants was 32. It should be noted that the number of applicants was 47 from 23 overseas countries and 24 from Japan, i.e., a total of 71. In the Bio-SPM Collaborative Research, 10 joint research projects with overseas researchers from 8 countries were conducted in FY2023.

As a cumulative result from FY2017 to FY2023, a total of 45 overseas researchers from 19 countries participated in the Bio-SPM Summer School. It should be noted that, in FY2020 and FY2021, overseas researchers were not invited due to COVID-19. In the Bio-SPM Collaborative Research, 31 joint research projects with overseas researchers from 15 countries were conducted from FY2017 to FY2023.

The NanoLSI Visiting Fellows Program aims to invite PI-level life science researchers and members of their research groups from overseas to conduct researcher exchanges and joint research, and to establish an organizational cooperative relationship between NanoLSI and the relevant research institutions. In this Program, one research group led by a prominent female researcher (Prof. Zoya Leonenko, University of Waterloo, Canada) consisting of three female researchers, including Prof. Leonenko herself, was invited in FY2023. In addition, a new invitation for a research group (Dr. Sung Pil Hong, CRUK Clinician Scientist Fellow, Imperial College London, UK) was planned, but the group was at Imperial College London, at which a NanoLSI satellite has been established, so arrangements were made for the research group to conduct experiments using SICM at the overseas satellite. As a cumulative result, four research groups were invited from FY2017 to FY2023.

Support for overseas researchers to acquire research funds in FY2017-FY2023

With individual support from the full-time URA of NanoLSI, 23 overseas researchers acquired a total of 29 KAKENHI grants from FY2017 to FY2023. As a result, in FY2023 alone including those whose budgetary support starts in FY2024, overseas researchers belonging to NanoLSI submitted 10 new applications for KAKENHI, of which 5 were approved.

Mobility of and career path for young researchers

One Jr. PI, a tenure-track assistant professor, was promoted to a tenured associate professor in February 2024. In addition, another Jr. PI, a tenure-track assistant professor, moved to Osaka University for the promotion to a tenured associate professor. As of the end of FY2023, the number of postdoctoral researchers (including fixed-term assistant professors) was 31 out of 87 researchers in total in NanoLSI, and 22 out of 31 (74%) were overseas researchers.

Five Assistant Professors (Fixed-term contract) left NanoLSI during FY2023. Of these, 3 have acquired tenured associate professorships, and one has acquired a tenured lecturer-ship. The remaining one has been applying for a researcher position. (For details, refer to Appendix 3.1 FY2023 Records of Center Activities 1.1 Special mention)

Results of overseas researcher visits in FY2023

In FY2023, a total of 68 researchers from 24 countries visited NanoLSI for 1,231 person-days (39 researchers from 17 countries for 1,011 person-days in FY2022).

4. Making Organizational Reforms

* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
* If innovated system reforms generated by the center have had a ripple effect on other departments of the host institutions or on other research institutions, clearly describe in what ways.
* Describe the center's operation and the host institution's commitment to the system reforms.

Continued implementation of successful reforms of NanoLSI

NanoLSI established successful cases of system reform in the first half of the WPI subsidy period. These are; research professorships for concentrating on research, the rigorous evaluation-based salary system, the tenure-track junior PI program, integrated management of NanoLSI and the Graduate School "Division of Nano Life Science," and English-based administration. These successful reforms will be maintained and continued.

Improvement of gender balance among NanoLSI researchers

(Refer to 7. Center's Response to Results of Last Year's Follow-up, Comment 5)

Ripple effect to the host institution: University-wide standardization of administrative correspondence in Japanese and English

Since the establishment of NanoLSI in 2017, the NanoLSI office has been issuing all administrative correspondence in Japanese and English. Kanazawa University, as the host institution, decided to issue administrative correspondence in Japanese and English throughout the University starting in FY2024.

Expected ripple effect to the host institution: Program for Forming Japan's Peak Research Universities (J-PEAKS)

Kanazawa University, the host institution, was selected in FY2023 as part of the Program for Forming Japan's Peak Research Universities (J-PEAKS), a program to promote the strengthening of regional core and distinctive research universities. In this J-PEAKS project, NanoLSI is planned to be used as a leading role model for accepting overseas young researchers and providing know-how for developing support staff members for dealing with and promoting internationalization.

Expected ripple effect to the host institution: Establishment of the Experimental Research Center for Envisioning the Future

Kanazawa University will complete construction of the Experimental Research Center for Envisioning the Future as a new industry-academia collaborative research facility in April 2025. The Center will inherit the basic strategy of NanoLSI to further develop excellence in specific research areas where the University has strengths, promote interdisciplinary research, and bring research and administrative staff together under one roof, aiming at enhancing industry-academia joint research and social implementation of research results. It is planned that this facility will provide research space for NanoLSI researchers to conduct joint industry-academia integrated interdisciplinary research.

5. Efforts to Secure the Center's Future Development over the Mid- to Long-term

* Address the following items, which are essential to mid- to long-term center development:
- Future prospects with regard to the research plan, research organization and PI composition; prospects for fostering and securing of next-generation researchers.
- Prospects for securing resources such as permanent positions and revenues; plan and/or implementation for defining the center's role and/or positioning the center within the host institution's institutional structure
- Measures to sustain the center as a world premier international research center after program funding ends
- Host institution's organizational reforms carried out for the center's autonomous administration simultaneously with the creation of the center.

Research plan, research organization, and PI composition

Regarding the NanoLSI research plan, 6 nanotechnology and 7 life science roadmaps have been updated. Concerning the research organization, the Center Director, the Administrative Director, and four PIs who are the core members of NanoLSI operations hold intensive discussions at the Future Planning Board, the steering committee of NanoLSI, which maintains the balance between top-down and bottom-up operations. As for the PI composition, the structure with 16 PIs has been maintained since the establishment of NanoLSI in 2017.

Fostering and securing of next-generation researchers

In the graduate school, the Division of Nano Life Science, Graduate School of Frontier Science Initiative, which is managed in an integrated manner with NanoLSI, there are 17 students at the Master's Course (including 5 international students; including 3 female students, of which 3 are also internationals) and 36 students at the Doctoral Course (including 27 international students; including 17 female students, of which 15 are internationals), i.e., a total of 53 students (including 32 international students; including 20 female students, of which 18 are internationals) being enrolled as of April 2024.

Concerning the enrollment capacity, it has now been increased from 6 students to 12 at the Master's Course per year and from 6 students to 10 at the Doctoral Course per year in FY2024.

In FY2023, 6 students graduated from the Doctoral Course, Division of Nano Life Science (4 Japanese and 2 international students). Concerning the career path after graduation, one graduate out of 4 Japanese graduates was appointed as a specially appointed assistant professor by Kanazawa University, while the other three were appointed as researchers by companies (Toray, JSR Corporation, Ebara Corporation). In addition, of two international graduates, one was appointed as a specially appointed assistant professor by Kanazawa University, while the other remains in NanoLSI as a postdoctoral researcher.

Securing external funds and revenues

External funding secured by NanoLSI researchers in FY2023 amounts to 1,301 million yen (1,357 million yen previous fiscal year). (For details, refer to Appendix 3-1 5. "Securing external research funding")

Prospect for securing permanent positions

At the President/Center Director meeting in February 2023, the Center Director made a request to the President that 12 positions out of the 22 tenured researcher positions currently placed at NanoLSI

be made permanent in order to stably secure nanometrology researchers who form the core of NanoLSI research. In response to this request, in order to secure long-term, stable positions for NanoLSI researchers, negotiation has started between the President and the Personnel Labor Division of the host institution headquarters.

6. Others

* Describe what was accomplished in the center's outreach activities last year and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 6, describe concretely the contents of these outreach activities. In Appendix 7, describe media reports or coverage, if any, of the activities.
* In addition to the above 1-5 viewpoints, if there is anything else that deserves mention regarding the center project's progress, note it.

Press release of research outcomes

In FY2023, 31 press releases concerning research outcomes were issued, of which 21 were also issued in English. Among the press-released research results published in high impact factor journals, an article by Jr. PI Miyanari, "Genome-wide ATAC-see screening identifies TFDP1 as a modulator of global chromatin accessibility," was published in a very high-ranking journal, Nature Genetics (IF: 30.8)/vol.56/473–482 (2024). In addition, an article by Prof. Takahashi, "1T/1H-SnS_2 Sheets for Electrochemical CO_2 Reduction to Formate," was published in ACS Nano (IF: 17.1)/vol.17(12)/11318-11326.

Outreach activities and their results

(Refer to Appendix 6 FY2023 State of Outreach Activities, Outreach Activities, and Their Results)

7. Center's Response to Results of Last Year's Follow-up

* Transcribe the item from the "Actions required and recommendations" section in the site visit report and the Follow-up report, then note how the center has responded to them.
* If you have already provided this information, indicate where in the report.

Comment 1 ***"NanoLSI is achieving good progress in developing high-end SPM technologies at a top world level. It is now time to apply these technologies to answering still-unanswered questions in life sciences, not just to cancer research. Stiffness and elasticity of membranes are one of the promising targets, and collaborations with experts in cell biology will be key to gaining mechanistic insights."***

We agree with this comment. Indeed, this is perfectly in line with our original plan. Three years ago, we started the top-down Transdisciplinary Research Promotion (TDRP) Grant and set the following three focused subjects aimed at exploring various biological applications of the newly developed live-cell SPM techniques such as (1) in-cell imaging, (2) cell-surface imaging, and (3) chemical mapping. Through these efforts, we have found a few promising applications that may provide new insights inaccessible with existing methods. Based on these findings, we renewed the subjects of the top-down TDRP grant for the next three years, focusing on these promising applications. As suggested in the above comment, nuclear elasticity measurement is one of them. We found it has strong needs in the studies of various diseases known as nuclear envelopathy. We have already started to investigate cardiomyopathy and neuropathy with external researchers. As for the cell-surface imaging, we established a high-throughput analysis method for cell surface structures, dynamics and elasticity by HS-SICM. Although similar studies by AFM were previously reported, attempts to apply such techniques to the cell diagnosis have been impeded by the low throughput. In contrast, HS-SICM is much faster and hence allows to construct a bio-SPM database for cell characterization and diagnosis. As for the chemical mapping, its development schedule is slightly behind that of the other two. However, it has finally entered the stage of exploring biological applications. In this way, we aim to answer unanswered questions in life sciences with the newly developed live-cell imaging techniques.

Comment 2 ***"To realize true nanoendoscopy, continued efforts will be needed in developing sensor systems that can be of practical use in measuring metabolites and other parameters in and around living cells."***

So far, we have established a method for fabricating a 1-MNA nanopipette sensor with P6A molecules integrated into a polymer thin film at its apex. We also confirmed that it has sufficiently high sensitivity and selectivity for diagnosis with a urine test. As suggested in the above comment, we now plan to apply this sensor to map 1-MNA distribution in and around a live cell. We will first try to measure the time response of 1-MNA increase at the cell surface upon addition of a nicotinamide containing solution into the culture medium. In the future, we further aim to map subcellular-level distribution, or cellular-level distribution in a tissue or organoid. We are strongly promoting this work in one of the focused subjects of our top-down TDRP grant over the next three years.

Comment 3 ***"Metric assessment should be made on how effectively the transdisciplinary***

systems, such as TDPR and T-meetings, have worked in leading to fruitful collaborations."

We verified the effectiveness and output of 135 T-meetings conducted between June 2018 and October 2023 using a questionnaire survey. As a result, 21 out of a total of 23 participants, including PIs, Jr. PIs, and others, answered that the implementation of T-meetings led to the start of transdisciplinary research. In addition, 61% of the researchers who participated in the T-meetings answered that they had the impression that it would lead to the start of future transdisciplinary research, and 37% answered that they had in fact started joint research. Furthermore, of the joint research that has begun, 82% of the projects are still ongoing and 44% have resulted in such as research papers. The number of papers resulting from transdisciplinary research triggered by T-meetings was 23, and 6 research grants were acquired from CREST, AMED, etc.

Concerning the bottom-up Transdisciplinary Research Promotion (TDRP) Grant, the Grant has already been integrated into the young researcher training system of NanoLSI. Since the start of this Grant in 2018, a total of 101 teams of young researchers have been supported for transdisciplinary research at a total cost of 140 million yen. Concerning the top-down TDRP grant, although we do not perform metric assessment, the Center Director annually conducts interviews with the PIs to monitor progress and identify problems for improvements. As a result, we have updated top-down TDRP themes focusing on promising applications of three priority issues.

Comment 4 ***"For the future, the Center should begin to consider broader applications of its technologies to non-expert scientists and the non-academic community by seeking further collaborations with industry."***

To broaden the use of our SPM technologies, we have made efforts by setting up many SPM systems dedicated for external use, organizing the annual Bio-SPM Summer School, and running Bio-SPM Collaborative Research program. We also worked with industrial companies in two different ways. One is to collaborate with SPM manufacturers and contract research companies. So far, Ando and Kodera transferred their HS-AFM technology to RIBM and Bruker, while Fukuma transferred his FM-AFM technology to Asylum Research (current Oxford Instrum.) and Hitachi. Takahashi launched his own company to provide SICM systems to private companies and academic institutions. This year, we temporarily installed a Bruker's HS-AFM in our institute, and let NanoLSI members and the Bio-SPM Summer School participants test its performance, giving valuable feedback to the manufacturer. Furthermore, we provided hands-on training on live-cell AFM measurements to researchers of Toray Research, a major contract research company in Japan. In these ways, we are contributing to the use of our techniques by non-expert researchers. The other strategy is to collaborate with companies having demands for SPM analysis. Fukuma has been actively seeking such possibilities and has so far worked with various companies to study metal corrosion, semiconductor device fabrication, detergents, cosmetics, glass, and anti-fouling. This year, they published two papers on Al alloy corrosion studies using SPM with Kobe Steel (***J Phys Chem C* 2023, *Small* 2023b**). Meanwhile, Kodera plans to start collaboration with a pharmaceutical company. In this way, we continue to expand the use of our techniques in the non-academic community.

Comment 5 ***"Improvement of gender balance should also be continued with a strategy. A program to invite senior female and international scientists on a short-term basis to participate in seminars and give presentations may also help in improving this balance."***

Over the past few years, NanoLSI has made improving gender balance one of the key operational goals. NanoLSI has appointed young female researchers as assistant professors or postdoctoral researchers, both Japanese and from overseas, and also appointed a female researcher as an Associate PI in FY2022. Through the accumulation of such efforts, the ratio of female researchers at NanoLSI has increased from 11/83 (13%) in FY2020, 15/81 (19%) in FY2021, 16/82 (20%) in FY2022, to 21/87 (24%) in FY2023, showing improvement in gender balance.

In addition, in FY2024, we have established a working group to study various measures from a medium- to long-perspectives in order to make diversity and inclusion of NanoLSI members, including improving gender balance, to be a permanent system at NanoLSI.

Concerning invitations of senior female and international scientists, Prof. Zoya Leonenko, University of Waterloo, Canada, a prominent female researcher, was invited by the NanoLSI Visiting Fellows Program in FY2023, and a public seminar by Prof. Leonenko was held.

Comment 6 ***"To expand NanoLSI's international networking, it may also be a good idea for the Center to seek more connections to other overseas research institutions."***

So far, we have made tremendous efforts to strengthen connections to overseas researchers and institutions. For example, we have placed overseas satellite research centers in Imperial College London (UK) and the University of British Columbia (Canada) to form connections to the researchers and institutions in Europe and North America. Furthermore, we organized symposia at these institutions in London and Vancouver to promote on-going collaborations. In FY2023, we further organized a

symposium in Berlin, which successfully strengthened our connections to researchers and institutions in Germany and Switzerland. In addition, we have been running the Bio-SPM Collaborative Research and the NanoLSI Visiting Fellows Program, and annually organizing the Bio-SPM Summer School, through which we hosted many overseas visitors from various institutions. For example, in the last year, we hosted approximately 29 visitors from 13 countries and 24 institutions. Through these experiences, we found making many official contracts with other institutions is not necessarily the most efficient or practically effective way. Instead, we believe it is more effective to make the best use of the connections that we have built up through our activities in the past decade. Based on this idea, we are now trying to establish an international forum for a new research field "nanoprobe life science" by making a web site and mailing list for all the previous participants in the previous events and programs. Once it is established, this will be open to the public and should rapidly grow to involve many researchers and eventually institutions. This platform should help expanding connections among various institutions. In this way, we aim to play a pivotal role in this community.

Appendix 1 FY 2023 List of Center's Research Results and Main Awards

1. Refereed Papers

- List only the Center's papers published in 2023. (Note: The list should be for the calendar year, not the fiscal year.)

(1) Divide the papers into two categories, A and B.

A. WPI papers
List papers whose author(s) can be identified as affiliated with the WPI program (e.g., that state "WPI" and the name of the WPI center (WPI-center name)). (Not including papers in which the names of persons affiliated with the WPI program are contained only in acknowledgements.)

B. WPI-related papers
List papers related to the WPI program but whose authors are not noted in the institutional affiliations as WPI affiliated. (Including papers whose acknowledgements contain the names of researchers affiliated with the WPI program.)

Note: On 14 December 2011, the Basic Research Promotion Division (the Basic and Generic Research Division at present) in MEXT's Research Promotion Bureau circulated an instruction requiring paper authors to include the name or abbreviation of their WPI center among their institutional affiliations. From 2012, the authors' affiliations must be clearly noted.

(2) Method of listing paper

- List only refereed papers. Divide them into categories (e.g., original articles, reviews, proceedings).
- For each, write the author name(s); year of publication; journal name, volume, page(s) (or DOI number), and article title. Any listing order may be used as long as format is consistent. (The names of the center researchers do not need to be underlined.)
- If a paper has many authors (say, more than 10), all of their names do not need to be listed.
- Assign a serial number to each paper to be used to identify it throughout the report.
- If the papers are written in languages other than English, underline their serial numbers.
- Order of Listing

A. WPI papers

1. Original articles (1-139)

1. Ackroyd AJ, De Paolis A, Xu YT, Momeni A, Hamad WY, MacLachlan MJ. Self-assembly of cellulose nanocrystals confined to square capillaries. Nanoscale. 2023;15(35):14388-98.
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14. Cai SL, Ren R, He JX, Wang XY, Zhang Z, Luo ZF, et al. Selective Single-Molecule Nanopore Detection of mpox A29 Protein Directly in Biofluids. Nano Letters. 2023;23(24):11438-46.
15. Cho KG, Andrew LJ, MacLachlan MJ. Uniform Growth of Nanocrystalline ZIF-8 on Cellulose Nanocrystals: Useful Template for Microporous Organic Polymers. Angew Chem-Int Edit. 2023;62(24):6.

16. Das Gupta M, Boott CE, Goon JE, Patrick BO, MacLachlan MJ, Reid JP. Controlled Supramolecular Self-Assembly of Uniform Nanostructures from Trimetallic Complexes. Acs Applied Nano Materials. 2023;6(6):4672-80.
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149. Vu CQ, Arai S. Quantitative Imaging of Genetically Encoded Fluorescence Lifetime Biosensors. Biosensors-Basel. 2023;13(10):15.
150. Wada K, Ogoshi T. Functionalization of pillar n arenes towards optically responsive systems via host-guest interactions. Materials Chemistry Frontiers. 2024;8(5):1212-29.

3. Proceedings

None

4. Other English articles(151)

151. Nakajima M, Tamai I. Roles and Application of Extracellular Vesicles Occurring Endogenously and Naturally. Pharmaceutical Research. 2023;40(4):793-4.

B. WPI-related papers

1. Original articles(152-189)

152. Asano Y, Yamamoto N, Demura S, Hayashi K, Takeuchi A, Kato S, et al. Novel predictors of immune checkpoint inhibitor response and prognosis in advanced non-small-cell lung cancer with bone metastasis. Cancer Medicine. 2023;12(11):12425-37.
153. Cheng XX, Gan YJ, Zhang G, Song QP, Zhang ZB, Zhang W. Conformationally supramolecular chirality prevails over configurational point chirality in side-chain liquid crystalline polymers. Chemical Science. 2023;14(19):5116-24.
154. Cheng XX, Miao TF, Zhang G, Guo JY, Zhou ZY, Zhang W. Switchable Phase Helicity Independent of the Absolute Configuration of the Stereocenter: Anomalous Induction between Sergeants and Soldiers in Chiral Liquid-Crystalline Polymers. Journal of the American Chemical Society. 2023;145(30):16474-87.
155. Dai HB, Hong R, Ma YF, Cheng XX, Zhang W. A Subtle Change in the Flexible Achiral Spacer Does Matter in Supramolecular Chirality: Two-Fold Odd-Even Effect in Polymer Assemblies. Angew Chem-Int Edit. 2023;62(50):9.
156. Das S, Paramane A, Chatterjee S, Rao UM. Accurate Identification of Transformer Faults From Dissolved Gas Data Using Recursive Feature Elimination Method. Ieee Transactions on Dielectrics and Electrical Insulation. 2023;30(1):466-73.
157. Das S, Paramane A, Rao UM, Chatterjee S, Kumar KS. Corrosive Dibenzyl Disulfide Concentration Prediction in Transformer Oil Using Deep Neural Network. Ieee Transactions on Dielectrics and Electrical Insulation. 2023;30(4):1608-15.
158. Fan J, Xu MC, Xu YT, Hamad WY, Meng ZH, MacLachlan MJ. A visible multi-response electrochemical sensor based on cellulose nanocrystals. Chemical Engineering Journal. 2023;457:10.
159. Fujiwara Y, Kuboki Y, Furukawa M, Mizuno N, Hara H, Ioka T, et al. FIGHT-102: A phase 1 study of pemigatinib in Japanese patients with advanced malignancies. Cancer Medicine. 2023;12(9):10597-611.
160. Fukuda K, Shimi T, Shimura C, Ono T, Suzuki T, Onoue K, et al. Epigenetic plasticity safeguards heterochromatin configuration in mammals. Nucleic Acids Research. 2023;51(12):6190-207.
161. Guo YQ, Cheng XX, He ZX, Zhou ZY, Miao TF, Zhang W. Simultaneous Chiral Fixation and Chiral Regulation Endowed by Dynamic Covalent Bonds. Angew Chem-Int Edit. 2023;62(52):7.
162. Hirose D, Kusuma SBW, Yoshizawa A, Wada N, Takahashi K. Dehydrogenative silylation of cellulose in ionic liquid. Green Chemistry. 2023;25(18):7.
163. Ide T, Nishino Y, Takiguchi T, Kanda S, Otsuki K, Hayashi R, et al. Multi-institutional survey of antiemetic therapy in lung cancer patients treated with carboplatin in Hokushin region. Bmc Pulmonary Medicine. 2023;23(1):9.
164. Kakuta T, Miyazaki R, Shinjo Y, Ueno Y, Yamagishi TA. Acceptor-Induced Fluorescence of Phenolic Polymers Based on Triphenylamine Derivatives. Chempluschem. 2023;88(9):5.
165. Kemeth FP, Alonso S, Echebarria B, Moldenhawer T, Beta C, Kevrekidis IG. Black and gray box learning of amplitude equations: Application to phase field systems. Physical Review E. 2023;107(2):8.
166. Kerzel T, Giacca G, Beretta S, Bresesti C, Notaro M, Scotti GM, et al. In vivo macrophage engineering reshapes the tumor microenvironment leading to eradication of liver metastases. Cancer Cell. 2023;41(11):1892-+.
167. Kitagawa K, Shibata E, Yamamoto M, Harada H, Yoshino K, Iwashita T, et al. Subacute exposure to bisphenol F diglycidyl-ether induces chronic dermatitis characterized by psoriasis-like skin inflammation in mice. Genes to Cells. 2023;28(1):42-52.
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172. Miao TF, Cheng XX, Zhang G, Wang YQ, He ZX, Wang Z, Zhang W. Self-recovery of chiral microphase separation in an achiral diblock copolymer system. Chemical Science. 2023;14(7):1673-8.
173. Milotskyi R, Sharma G, Fujie T, Hirose D, Wada N, Takahashi K. Continuous process of cellulose dissolution and transesterification reaction catalysed by ionic liquid in twin screw extruder. React Chem

Eng. 2023;8(6):1395-402.
174. Nagayama S, Kobayashi Y, Fukunaga M, Sakimura S, Sugimachi K, Sasaki S, et al. Mutated genes on ctDNA detecting postoperative recurrence presented reduced neoantigens in primary tumors in colorectal cancer cases. Scientific Reports. 2023;13(1):11.
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179. Suzuki T, Akiba C, Izawa M, Iwami M. Steroid hormone-dependent changes in trehalose physiology in the silkworm, Bombyx mori. J Comp Physiol B-Biochem Syst Environ Physiol. 2023;193(4):383-90.
180. Taira J, Yamaguchi M, Tashiro A, Kida A, Suzuki K, Sakai K, et al. Computer-Assisted Identification of Inhibitor with Novel Pharmacophore Targeting First Kringle Domain of Hepatocyte Growth Factor. Chemistryselect. 2023;8(36):6.
181. Takayanagi-Kiya S, Shioya N, Nishiuchi T, Iwami M, Kiya T. Cell assembly analysis of neural circuits for innate behavior in Drosophila melanogaster using an immediate early gene stripe/egr-1. Proceedings of the National Academy of Sciences of the United States of America. 2023;120(33):11.
182. Tamai S, Ichinose T, Jiapaer S, Hirai N, Sabit H, Tanaka S, et al. Therapeutic potential of pentamidine for glioma-initiating cells and glioma cells through multimodal antitumor effects. Cancer Science. 2023;114(7):2920-30.
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1. Review articles(190)

190. Beta C, Edelstein-Keshet L, Gov N, Yochelis A. From actin waves to mechanism and back: How theory aids biological understanding. Elife. 2023;12:37.

2. Proceedings

None

4. Other English articles(191-193)

191. Ogoshi T. Hierarchical Materials from High Information Content Macromolecular Building Blocks: Construction, Dynamic Interventions, and Prediction. Chemical Reviews. 2023;123(13):8041-3.
192. Tsukida S, Watanabe S, Hongo M, Murase Y, Yamamoto Y, Kase K, et al. Unexpected Diffuse Alveolar Hemorrhage After Bronchoscopy. Chest. 2023;164(3):E71-E4.
193. Fukuoka M, Yano S, Giaccone G, Tamura T, Nakagawa K, Douillard JY, et al. Multi-Institutional Randomized Phase II Trial of Gefitinib for Previously Treated Patients With Advanced Non-Small-Cell Lung Cancer (Reprinted from vol 21, pg 2237-2246, 2003). Journal of Clinical Oncology. 2023;41(6):1162-71.

(3) Submission of electronic data
- In addition to the above, provide a .csv file output from the Web of Science (e.g.) or other database giving the paper's raw data including Document ID. (Note: the Document ID is assigned by paper database.)
- The papers should be divided into A or B categories on separate sheets, not divided by paper categories.

(4) Use in assessments
- The lists of papers will be used in assessing the state of WPI project's progress.
- They will be used as reference in analyzing the trends and whole states of research in the said WPI center, not to evaluate individual researcher performance.
- The special characteristics of each research domain will be considered when conducting assessments.

(5) Additional documents
- After all documents, including these paper listings, showing the state of research progress have been submitted, additional documents may be requested.

2. Invited Lectures, Plenary Addresses (etc.) at International Conferences and International Research Meetings

- List up to 10 main presentations during FY 2023 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
2024/3/28	Adam S. Foster	Machine Learning Analysis and Automation in High-resolution Scanning Probe Microscopy	AFM & SPM Meeting 2024, Durham, UK
2024/2/20	Shigehisa Akine	Control of chirality inversion kinetics of helical cage complexes by guest binding	The 9th Asian Conference on Coordination Chemistry (ACCC9), Bangkok, Thailand
2024/1/18	Mark J. MacLachlan	Responsive photonic materials from cellulose nanocrystals	CEMSupra Symposium, Tokyo, Japan
2023/12/6	Mikihiro Shibata	Activity-dependent structural dynamics of CaMKIIα visualized by High-speed atomic force microscopy	2023 Annual Meeting of the Australian Society of Biophysics, Wollongong, Australia
2023/9/21	Richard Wong	Nano imaging of Genomic modality in nuclear pore territories	The 4th "Genome Modality" Annual meeting, Karolinska Institute, Stockholm, Sweden
2023/8/7	Takeshi Fukuma	AFM study on the hydration of PVA brush surface and its impact on the interaction with abrasive nanoparticles	25th International Symposium on Chemical-Mechanical Planarization (CMP), Lake Placid, USA
2023/7/7	Toshio Ando	Directly watching protein molecules in dynamic action by high-speed AFM	The partnership for structural biology symposium "Dynamics in Structural Biology", Grenoble, France

2023/6/21	Hanae Sato	The potential role of mRNA decay in transcription	Cold Spring Harbor Asia conference “The Now and Future of RNA Therapeutics ”, Awaji, Japan
2023/6/14	Noriyuki Kodera, Kenichi Umeda, Kazuma Tatsumi, Karen Kamoshita	Recent progress in high-speed atomic force microscopy	9th Multifrequency AFM Conference, Madrid, Spain
2023/5/10	Carsten Beta	Composite active matter — How motile cells move passive micro-cargo	Mathematical Cell Biology Symposium, UBC, Vancouver, Canada

3. Major Awards

- List up to 10 main awards received during FY 2023 in order from the most recent.
- For each, write the date issued, the recipient’s name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
2023/11/15	Shingo Fukuda	Early Research in Biophysics Award, The Biophysical Society of Japan
2023/9/15	Richard Wong	Best Oral Presentation Award, The 20th International Microscopy Congress (in Busan, KOREA)
2023/5/20	Miki Nakajima	Most Prolific Author in Drug Metabolism and Disposition, The American Society for Pharmacology and Experimental Therapeutics
2023/5/20	Keisuke Miyazawa	JVSS Excellent Presentation Awards, The Japan Society of Vacuum and Surface Science
2023/4/29	Toshio Ando	Medal with Purple Ribbon, The Cabinet Office, Government of Japan
2023/4/19	Takeshi Fukuma	The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology, Research Category

Appendix 2　FY 2023 List of Principal Investigators

NOTE:

*Underline names of principal investigators who belong to an overseas research institution.

*In the case of researcher(s) not listed in the latest report, attach a "Biographical Sketch of a New Principal Investigator"(Appendix 2a).

*Enter the host institution name and the center name in the footer.

<Results at the end of FY2023> **Principal Investigators Total: 16**

Name	Age	Affiliation (Position title, department, organization)	Academic degree, specialty	Effort (%)*	Starting date of project participation	Status of project participation (Describe in concrete terms)	Contributions by PIs from overseas research institutions
Center Director Takeshi Fukuma	47	Nano Life Science Institute, Kanazawa University	Doctor of Engineering, Electrical engineering, Nanometrology	90	October, 2017	usually stays at the institute	
Noriyuki Kodera	45	Nano Life Science Institute, Kanazawa University	Doctor of Science, Biophysics and Nano-Bioscience	90	April, 2022	usually stays at the institute	
Yuri Korchev	63	Department of Medicine, Imperial College London	Ph.D. in Biophysics and Cytology, Biophysics	30	October, 2017	Under contract, stays at the institute 30 days or more/per fiscal year	-Engaged in measuring the distribution of substances inside and outside the cell while working toward the development of new nanoprobe technology -In charge of the 2nd NanoLSI International Symposium in London held on November 19, 2018.
Atsushi Hirao	60	Nano Life Science Institute, Kanazawa University	Doctor of Medicine, Stem Cell Biology	90	October, 2017	usually stays at the institute	
Masanobu Oshima	62	Nano Life Science Institute, Kanazawa University	D.V.M., Ph.D., Cancer research, Genetics for Cancer modeling	90	October, 2017	usually stays at the institute	
Seiji Yano	58	University Hospital, Kanazawa University	MD, PhD, Medical Oncology, Circumvention of targeted drug resistance	50	October, 2017	usually stays at the institute	
Kunio Matsumoto	65	Nano Life Science Institute, Kanazawa University	Doctor of Philosophy, Biological Chemistry, Tumor Biology	90	October, 2017	usually stays at the institute	
Rikinari Hanayama	49	Nano Life Science Institute, Kanazawa University	MD, PhD, Immunology, Cell Biology	90	October, 2017	usually stays at the institute	

Richard W. Wong	49	Nano Life Science Institute, Kanazawa University	Doctor of Medicine, Molecular cell biology	90	October, 2017	usually stays at the institute	
Miki Nakajima	54	Nano Life Science Institute, Kanazawa University	Doctor of Pharmaceutical Sciences, Drug Metabolism and	90	October, 2017	usually stays at the institute	
Shigehisa Akine	51	Nano Life Science Institute, Kanazawa University	Doctor of Science, Supramolecular chemistry, Coordination chemistry	90	October, 2017	usually stays at the institute	
Katsuhiro Maeda	53	Nano Life Science Institute, Kanazawa University	Doctor of Engineering, Polymer chemistry	90	October, 2017	usually stays at the institute	
Tomoki Ogoshi	47	Graduate School of Engineering, Kyoto University / Nano Life Science Institute, Kanazawa Univeristy	Doctor of Engineering, Supramolecular Chemistry, Structural Organic Chemistry	20	October, 2017	Works at the institute 20% of the total working days / per year based on the cross-appointment agreement between Kyoto univ. and Kanazawa univ.	
Mark MacLachlan	50	Department of Chemistry, University of British Columbia	PhD in Chemistry	30	October, 2017	Under contract, stays at the institute 30 days or more/per fiscal year	-Engaged in development of supramolecular nanoprobes while working toward the development of new nanoprobe technology - In charge of Selection Committee of Jr.PI -In charge of the 3rd NanoLSI International Symposium held on August 8, 2019 at UBC
Adam Stuart Foster	48	Department of Applied Physics, Aalto University	PhD in Theoretical Solid State Physics	30	October, 2017	Under contract, stays at the institute 30 days or more/per fiscal year	-Promotes understanding of the real image from the observation image while working toward the development of new nanoprobe technology -In charge of NanoLSI Educational Program at the Graduate School - In charge of Selection Committee of Jr.PI
Carsten Beta	49	Biological Physics Group, University of Potsdam	Doctor of Natural Sciences, Biophysics, Pattern formation	20	April, 2022	Under contract, stays at the institute 30 days or more/per fiscal year	-Promotes understanding of the real image from the observation image while working toward the development of new nanoprobe technology -In charge of Selection Committee of Jr.PI -In charge of the 7th NanoLSI International Symposium in Berlin held on November 2-3, 2023.

Appendix 3-1 FY 2023 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

1-1. Number of researchers in the "core" established within the host institution

- Regarding the number of researchers at the Center, fill in the table in Appendix 3-1a.

Special mention

- Enter matters warranting special mention, such as concrete plans for achieving the Center's goals, established schedules for employing main researchers, particularly principal investigators.
- As background to how the Center is working on the global circulation of world's best brains, give good examples, if any, of how career paths are being established for the Center's researchers; that is, from which top-world research institutions do researchers come to the Center and to which research institutions do the Center's researchers go, and how long are their stays at those institutions.

The career path development of the NanoLSI researchers in FY2023 is as shown in the table cited below.

	Name (M/F)	From which institution	Position at NanoLSI	How long	To which institution	Position
1	TANIGUCHI TSUYOSHI (M)	Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University (Japan)	Assistant professor (Fixed-term contract)	10 months	National Institute of Advanced Industrial Science and Technology (AIST), Research Center for Integrated Catalytic Chemistry (Japan)	Senior research scientist (Tenured position) *Equivalent to associate professor
2	HALL DAMIEN RICHARD (M)	Nagoya Institute of Technology (Japan)	Assistant professor (Fixed-term contract)	3.0 years	Applying for a researcher position	
3	TODA SATOSHI (M)	University of California San Francisco (USA)	Assistant professor (Jr. PI) (Fixed-term contract)	4.5 years	Institute for Protein Research, Osaka University (Japan)	Associate professor (Tenured position)
4	OUSAKA NAOKI (M)	Kyushu Institute of Technology (Japan)	Assistant professor (Fixed-term contract)	3.0 years	Research Center for Negative Emission Technology, Kyushu University (Japan)	Associate professor (Tenured position)
5	SAJIDAH ELMA SAKINATUS (F)	Doctoral student at Kanazawa University (Japan)	Assistant professor (Fixed-term contract) *Promising researcher	6 months	State University of Surabaya (Indonesia)	Lecturer (Tenured position)

1-2. Satellites and partner institutions

- List the satellite and partner institutions in the table below.
- Indicate newly added and deleted institutions in the "Notes" column.
- If satellite institutions have been established overseas, describe by satellite the Center's achievements in coauthored papers and researcher exchanges in Appendix 4.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes
Imperial College London	Yuri Korchev	Established the Agreement in January 2019 (The effective date is January 15 2019)
University of British Columbia	Mark MacLachlan	Established the Agreement in October 2018 (The effective date is April 2019)

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
RIKEN Center for Biosystems Dynamics Research		Established the collaborative research agreement in May 2018
Nikon Instech Co., Ltd.		Established the collaborative research agreement in May 2019
MicroBiology Research Center for Sustainability, Tsukuba University		Established the collaborative research agreement in June 2019
National Institutes for Quantum Science and Technology (QST), Institute of Quantum Life Science		Established the collaborative research agreement in June 2021

2. Holding international research meetings

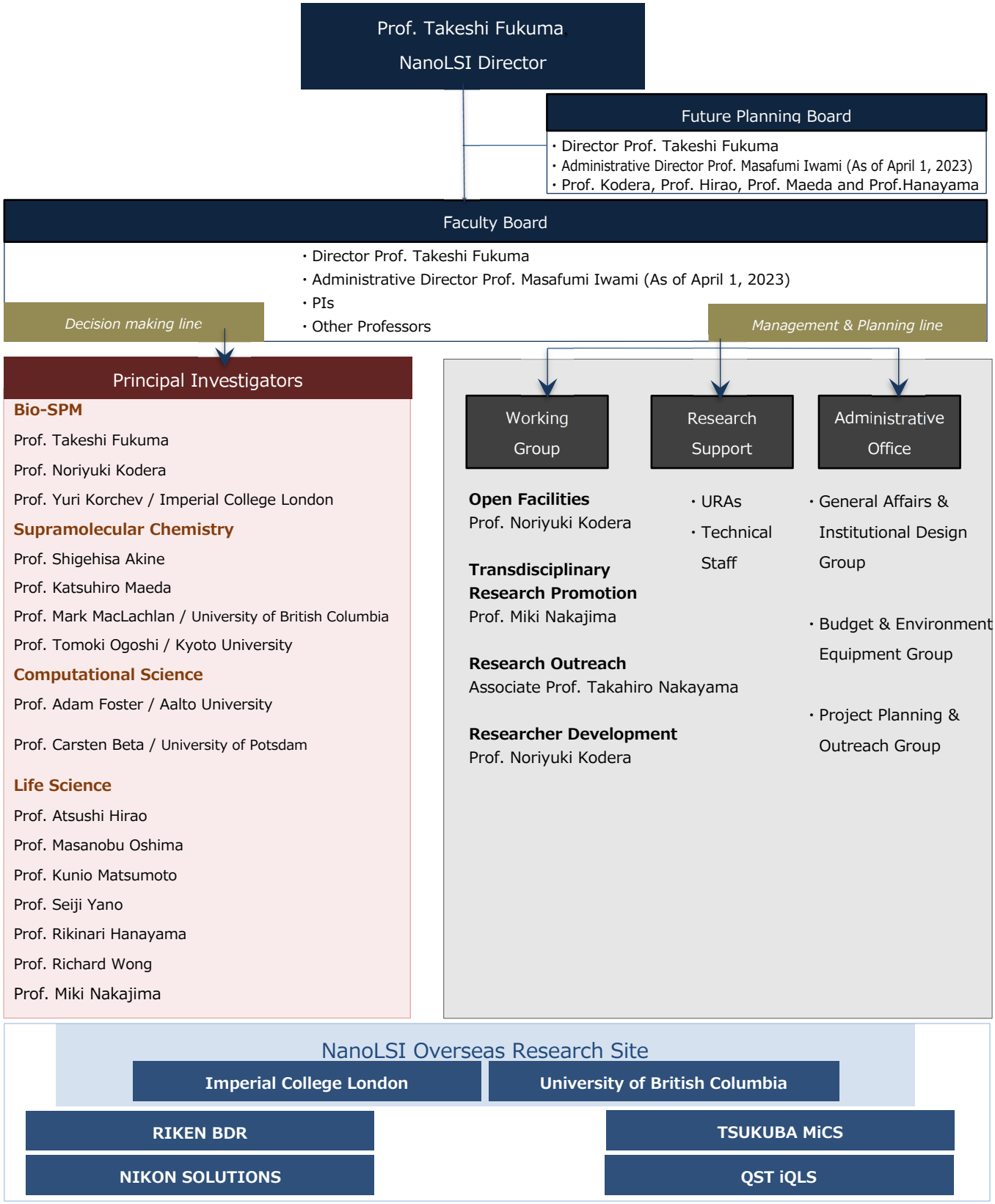
- Indicate the number of international research conferences or symposiums held in FY2023 and give up to three examples of the most representative ones using the table below.

FY 2023: 4 meetings

Major examples (meeting titles and places held)	Number of participants
7th NanoLSI Symposium - From Molecules to Cells and Tissue - Bridging Scales with Nanoprobe Technology – Harnack House, The Conference Venue of The Max Planck Society, Berlin, Germany	From domestic institutions: 20 From overseas institutions: 19
The first International Symposium of Nano Life Science: Nano Biotechnology, Biosensor, Computation (NanoBioCoM2023) International Centre for Interdisciplinary Science and Education (ICISE), Quy Nhon, Vietnam	From domestic institutions: 27 From overseas institutions: 77
SANTO Project, Next Generation Hokushin Cancer Pro, WPI International Seminar, Cancer Research Institute Seminar - Overcoming drug resistance in lung cancer – CPD Center (Day-1) & Nano Life Science Institute (Day-2), Kanazawa University, Kanazawa and Online	From domestic institutions: 51 From overseas institutions: 3

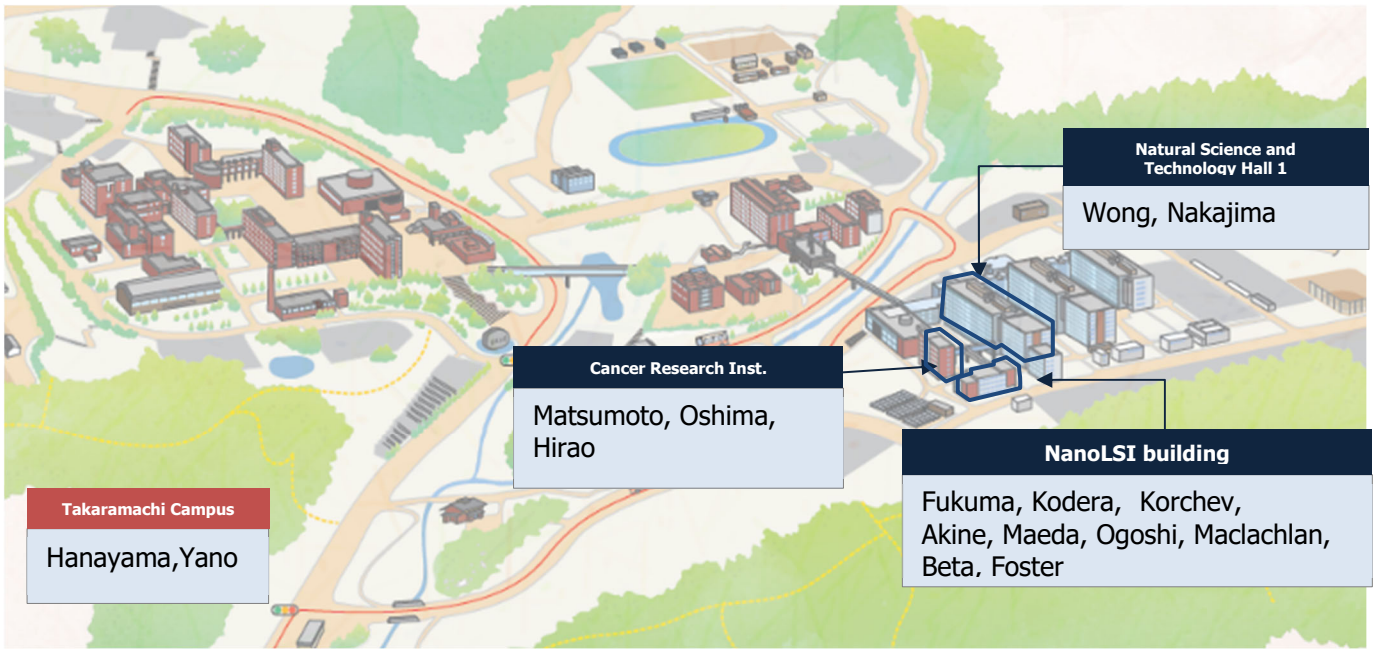
3. Diagram of management system

- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any new changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such as the center director, administrative director, head of host institution, and officer(s) in charge at the host institution (e.g., executive vice president for research).



4. Campus Map

- Draw a simple map of the campus showing where the main office and principal investigator(s) are located.



Wong, Nakajima and Hanayama have their offices and laboratories in both NanoLSI building and in other buildings.

5. Securing external research funding*

External research funding secured in FY2023

NanoLSI External Research Funding Secured in FY2023 by type of funding source CONFIDENTIAL

※Including Indirect funding

■Grants-in-Aid for Scientific Research	PI（Including Associate PI）		Jr.PI		Full time researcher		Associated researcher		Total	
	number	amount(JPY)	number	amount(JPY)	number	amount(JPY)	number	amount(JPY)	number	amount(JPY)
Grant-in-Aid for Transformative Research Area(A)	5	33,670,000	3	21,489,000	1	3,380,000	1	5,590,000	10	64,129,000
Grant-in-Aid for Transformative Research Area(B)					2	10,192,000			2	10,192,000
Grant-in-Aid for Scientific Research (S)					1	6,760,000			1	6,760,000
Grant-in-Aid for Scientific Research (A)	9	52,830,000	2	9,490,000	2	10,140,000	3	2,470,000	16	74,930,000
Grant-in-Aid for Scientific Research (B)	9	35,310,900	4	5,746,000	12	25,530,000	8	23,120,000	33	89,706,900
Grant-in-Aid for Scientific Research (C)	1	260,000			12	21,913,729	14	17,217,423	27	39,391,152
Challenging Research (Pioneering)	1	9,907,941							1	9,907,941
Challenging Research (Exploratory)	8	15,066,432	3	7,020,000	4	12,088,545	6	10,782,172	21	44,957,149
Early-Career Scientists					3	4,030,000	2	3,640,000	5	7,670,000
Grant-in-Aid for Research Activity Start-up					4	5,802,634			4	5,802,634
Grant-in-Aid for Scientific Research on Innovative Areas			1	4,550,000					1	4,550,000
Fund for the Promotion of Joint International Research (Fostering Joint International Research （B）)	1	330,000	1	2,600,000	2	2,193,606	3	10,922,513	7	16,046,119
Grant-in-Aid for JSPS Fellows	4	3,100,000							4	3,100,000
Total	38	150,475,273	14	50,895,000	43	102,030,514	37	73,742,108	132	377,142,895
■Commissioned research projects										
AMED Practical Research for Innovative Cancer Control	2	3,640,000					1	16,900,000	3	20,540,000
AMED Advanced Research & Development Programs for Medical Innovation	1	8,450,000			1	6,240,000	1	9,100,000	3	23,790,000
AMED Project for Promotion of Cancer Research and Therapeutic Evolution	2	54,365,000	1	3,900,000			1	41,000,000	4	99,265,000
AMED Science and Technology Platform Program for Advanced Biological Medicine	1	29,900,000							1	29,900,000
AMED Research on Development of New Drugs	1	26,000,000							1	26,000,000
AMED Research Center Network for Realization of Regenerative Medicine			1	14,300,000					1	14,300,000
AMED Research Program on Hepatitis							1	15,600,000	1	15,600,000
AMED Project of Translational and Clinical Research Core Centers	1	1,780,000							1	1,780,000
AMED The iD3 Booster	1	2,500,000							1	2,500,000
AMED Research on Regulatory Science of Pharmaceuticals and Medical Devices	1	1,300,000							1	1,300,000
AMED Cyclic Innovation for Clinical Empowerment	1	4,290,000							1	4,290,000
AMED Strategic Research Program for Brain Sciences					1	2,600,000			1	2,600,000
AMED Program for Promoting Platform of Genomics based Drug Discovery							1	2,600,000	1	2,600,000
JST Strategic Basic Research Programs (CREST)	3	101,001,988	1	32,000,847	1	791,477	1	3,900,000	6	137,694,312
JST Strategic Basic Research Programs (SAKIGAKE)			2	19,520,985	3	22,457,022			5	41,978,007
JST Strategic Basic Research Programs (ACT-X)							1	6,500,000	1	6,500,000
JST Fusion Oriented Research for disruptive Science and Technology			1	7,156,723	1	11,024,000	1	6,360,000	3	24,540,723
JST Outline of the Program on Open Innovation Platforms for Industry-academia Co-creation (COI-NEXT)							1	1,000,000	1	1,000,000
NEDO Research and Development Initiative for Scientific Innovation of New Generation Batteries3					1	16,957,200			1	16,957,200
Others	6	14,685,317					11	9,209,549	17	23,894,866
Total	20	247,912,305	6	76,878,555	8	60,069,699	20	112,169,549	54	497,030,108
■Joint research projects										
Joint research projects(New)	18	61,772,823	3	12,800,000	4	20,749,400	4	24,688,000	29	120,010,223
Joint research projects(Carry-forward)	6	6,102,093					1	12,253,196	7	18,355,289
Total	24	67,874,916	3	12,800,000	4	20,749,400	5	36,941,196	36	138,365,512
■Donations										
Donations(New)	28	13,150,000	8	7,000,000	14	6,400,000	38	14,938,000	88	41,488,000
Donations(Carry-forward)	28	148,345,720	8	9,235,445	14	52,511,635	38	36,830,597	88	246,923,397
Total	56	161,495,720	16	16,235,445	28	58,911,635	76	51,768,597	176	288,411,397

Securing external research funding

	PI		Jr.PI		Full time researcher		Associated researcher		Total	
Total	132	627,758,214	39	156,809,000	83	241,761,248	137	274,621,450	391	1,300,949,912

Total: 1,300,949,912 yen

- Describe external funding warranting special mention. Include the name and total amount of each grant.

* External research funding includes "KAKENHI," funding for "commissioned research projects," "joint research projects," and for others (donations, etc.) as listed under "Research projects" in Appendix 3-2, Project Expenditures.

Appendix 3-1a FY 2023 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

* Fill in the number of researchers and other center staff in the table blow.
* Describe the final goals for achieving these numbers and dates when they will be achieved described in the last "center project."

a) Principal Investigators

(full professors, associate professors or other researchers of comparable standing)

(number of persons)

	At the beginning of project	At the end of FY 2023	Final goal (Date: March, 2027)
Researchers from within the host institution	12	11	11
Researchers invited from overseas	4	4	4
Researchers invited from other Japanese institutions	0	1	1
Total principal investigators	16	16	16

b) Total members

	At the beginning of project		At the end of FY 2023		Final goal (Date: March, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	49		87		85	
Overseas researchers	8	16	30	34	34	40
Female researchers	6	12	21	24	19	22
Principal investigators	16		16		16	
Overseas PIs	5	31	5	31	5	31
Female PIs	1	6	1	6	2	13
Other researchers	27		40		38	
Overseas researchers	1	4	2	5	3	8
Female researchers	5	19	10	25	10	26
Postdocs	6		31		31	
Overseas postdocs	2	33	23	74	26	84
Female postdocs	0	0	10	32	7	23
Research support staffs	8		26		32	
Administrative staffs	13		18		18	
Total number of people who form the "core" of the research center	70		131		135	

	At the beginning of project		At the end of FY 2023		Final goal (Date: March, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	0		34		30	
Employed	0	-	14	41.2	15	50.0

※b) The number of doctoral students in the lower table can be duplicated in the upper table of overall composition.

Appendix 3-2 Project Expenditures

1) Overall project funding

* In the "Total costs" column, enter the total amount of funding required to implement the project, without dividing it into funding sources.
* In the "Amount covered by WPI funding" column, enter the amount covered by WPI within the total amount.
* In the "Personnel," "Project activities," "Travel," and "Equipment" blocks, the items of the "Details" culumn may be changed to coincide with the project's actual content.

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center director and administrative director	39.1	10.9
	Principal investigators (no. of persons):10	182.6	40.6
	Associate Principal investigators (no. of persons):1	11.1	11.1
	Junior Principal investigators (no. of persons):5	60.1	60.1
	Other researchers (no. of persons):63	294.0	205.0
	Research support staff (no. of persons):11	56.0	56.0
	Administrative staff (no. of persons):16	113.7	55.6
	Remuneration for RA(Research Assistant)	10.9	10.9
	Labor insurance premium adjustment amount	0.0	0.0
	Subtotal	767.5	450.2
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):3	5.5	5.5
	Research startup cost (no. of persons):9	33.8	33.8
	Cost of satellite organizations (no. of satellite organizations):2	26.7	27.3
	Cost of international symposiums (no. of symposiums):1	4.3	4.2
	Facility expenses	25.5	3.3
	Cost of consumables	16.4	16.4
	Cost of utilities	40.6	38.7
	Other costs	41.1	34.5
	Subtotal	193.9	163.7
Travel	Domestic travel costs	2.9	2.9
	Overseas travel costs	10.8	10.8
	Travel and accommodations cost for invited scientists		
	(no. of domestic scientists):40	2.8	2.8
	(no. of overseas scientists):44	17.3	17.2
	Travel cost for scientists on transfer		
	(no. of domestic scientists):1	0.1	0.1
	(no. of overseas scientists):1	0.2	0.2
	Subtotal	34.1	34.0
Equipment	Depreciation of buildings	0.4	0.4
	Depreciation of equipment	164.7	164.7
	Subtotal	165.1	165.1
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	108.4	0
	KAKENHI	228.1	0
	Commissioned research projects, etc.	250.7	0
	Joint research projects	54.7	0
	Ohers (donations, etc.)	42.2	0
	Subtotal	684.1	0
Total		1,844.7	813.0

Costs (Million yens)

WPI grant in FY 2023	700
Costs of establishing and maintaining facilities	5.1
Establishing new facilities	0.4
Repairing facilities	1.4
Others	3.3
Costs of equipment procured	164.7
High-speed Single-Molecule Fluorescence Microscopy Two-Color Simultaneous Imaging System 1Set	30.0
Biacore X100 Plus Package 1set	11.9
Others	122.8

*1. Management Expenses Grants (including Management Enhancements Promotion Expenses (機能強化経費)), subsidies including National university reform reinforcement promotion subsidy (国立大学改革強化推進補助金) etc., indirect funding, and allocations from the university's own resources.
*2 When personnel, travel, equipment (etc.) expenses are covered by KAKENHI or under commissioned research projects or joint research projects, the amounts should be entered in the "Research projects" block.

*1 運営費交付金（機能強化経費を含む）、国立大学改革強化推進補助金等の補助金、間接経費、その他大学独自の取組による学内リソースの配分等による財源
*2 科研費、受託研究費、共同研究費等によって人件費、旅費、設備備品等費を支出している場合も、その額は「研究プロジェクト費」として計上すること

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):1		
	Other researchers (no. of persons):2		
	Subtotal	21.4	21.4
Project activities	Subtotal	2.6	2.6
Travel	Subtotal	0	0
Equipment	Subtotal	0	0
Research projects	Subtotal	0	0
Total		24.0	24.0

Appendix 4 FY 2023 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2023 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2024 and not described in Appendix 1.

Overseas Satellite 1 **Imperial College London, UK** (Total: one paper)

1) Takahashi, Y., Sasaki, Y., Yoshida, T., Honda, K., Zhou, Y.S., Miyamoto, T., Motoo, T., Higashi, H., Shevchuk, A., Korchev, Y., et al. (2023). Nanopipette Fabrication Guidelines for SICM Nanoscale Imaging. Analytical Chemistry, 9. 10.1021/acs.analchem.3c01010.

Overseas Satellite 2 **University of British Columbia, Canada** (Total: one paper)

1) Ousaka, N., Maclachlan, M.J., and Akine, S. (2023). Stapling strategy for slowing helicity interconversion of α-helical peptides and isolating chiral auxiliary-free one-handed forms. Nature Communications 14, 12, 6834. 10.1038/s41467-023-42493-y.

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2023. Enter by institution and length of exchange.
- Write the number of principal investigator visits in the top of each space and the number of other researchers in the bottom.

Overseas Satellite 1: Imperial College London

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	0	0	0	0	0
	0	1	0	0	1

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	0	1	0	0	1
	0	0	0	0	0

Overseas Satellite 2: University of British Columbia

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	0	0	0	0	0
	0	0	0	0	0

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2023	0	2	0	0	2
	0	0	0	0	0

Appendix 5　FY 2023 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.
* Enter the host institution name and the center name in the footer.

Total: 68

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
1	Amyot Romain Felix Emile	30	Researcher, Adhesion and Inflammation Lab (LAI)	France	PhD / Biophysics	BioAFMviewer: An interactive interface for simulated AFM scanning of biomolecular structures and dynamics; PLoS Comput Biol, 16(11), e1008444 (Nov 2020)	2022/10/1~2024/9/30	JSPS Postdoctoral Fellowship for Research in Japan (Standard)
2	Alessio Carmignani	34	PhD student, The BioRobotics Institute of Sant'Anna School of Advanced Studies	Italy	PhD student, Molecular Biotechnology	In Vitro and Ex Vivo Investigation of the Effects of Polydopamine Nanoparticle Size on Their Antioxidant and Photothermal Properties: Implications for Biomedical Applications, ACS Appl. Nano Mater, 5, 1702-1713 (Jan 2022)	2023/3/8~6/5	Collaborative Research
3	Nanqin Mei	28	PhD student, Waterloo Institute of Nanotechnology, University of Waterloo	Canada	PhD student, Physics - Nanotechnology	・2021 the WIN Nanofellowship	2023/4/3~4/28	Visiting Fellows Program
4	Filice Carina Teresa	28	PhD student, Waterloo Institute of Nanotechnology, University of Waterloo	Canada	PhD student, Biology	・2021 the UW Graduate Scholarship ・2019 Waterloo Pioneers of Microbiology Award	2023/4/3~4/28	Visiting Fellows Program
5	Zoya Leonenko	61	Professor, University Research Chair, Waterloo Institute for Nanotechnology, University of Waterloo	Canada	PhD / Chemical Physics	・2020-2027 University Research Chair, ・2012 Invited Professorship Award, University of Burgundy, ・2007-2012 NSERC University Faculty Award	2023/4/17~4/21	Visiting Fellows Program and NanoLSI Open Seminar
6	Fredrik Elinder	57	Professor, Linköping University	Sweden	PhD, Department of Clinical and Experimental Medicine (IKE)	Onkel Adam Award for 2021	2023/4/24	NanoLSI Open Seminar
7	Oscar Domenech Cabrera	46	Associate Professor, Faculty of Pharmacy and Food Sciences, University of Barcelona	Spain	PhD, Physical Chemistry	Endogenous Antioxidant Cocktail Loaded Hydrogel fro Topical Wound Healing of Burns; Pharmaceutics, 2021, 13, 8	2023/5/4~5/25	Bio-SPM Collaborative Research Program
8	Isabella Guido	46	Associate Professor, Department of Physics, Faculty of Engineering and Physical Sciences, University of Surrey	United Kingdom	PhD, Synthetic Biology	Metal-Induced Energy Transfer (MIET) for Live-Cell Imaging with Fluorescent Proteins, In: ACS Nano17(9)pp. 8242-8251 American Chemical Society (2023)	2023/6/3~6/21	Bio-SPM Collaborative Research Program
9	Antonina Roll-Mecak	-	Senior Investigator and Chief, NIH(USA)	USA	Ph. D. Cell Biology and Biophysics Section	・NINDS Director Award (2019) ・NIH Director Award for service on the NIH Equity Committee (2019) ・NINDS Director Award (2020) ・International Award from the Biochemical Society (2023) ・NIH Director's Innovation Challenge Award (2022-2024)	2023/6/26	NanoLSI Open Seminar
10	Yusuke Toyama	-	Associate Professor, National University of Singapore	Singapore	Ph. D. in Engineering	Epithelial homeostasis: Cell size shapes cell fate. Curr Biol;33(22):R1205-R1207, 2023	2023/6/19	NanoLSI Open Seminar
11	Beta Carsten	49	Professor, University of Potsdam	Germany	Ph. D. Natural Sciences	From actin waves to mechanism and back: How theory aids biological understanding, Elife 12, e87181, 2023	①2023/7/13~7/28 ②2024/2/1~2/25	Participation as principal investigator
12	Mark Maclachlan	50	Professor, The University of British Columbia	Canada	Ph. D. Supramolecular Chemistry, Nanomaterials chemistry	・2016　Award for Research Excellence in Materials Chemistry (Canadian Society for Chemistry) ・2015-2022　Tier 1 Canada Research Chair in Supramolecular Materials ・2014　Steacie Prize for Natural Sciences (E.W.R. Steacie Memorial Fund) ・2014　Elected Fellow of the Royal Society of Canada (FRSC)	①2023/7/11~8/5 ②2023/9/16~10/6	Participation as principal investigator
13	Adam Foster	48	Professor, Aalto University	Finland	Ph. D. Department of Applied Physics	Väisälä Prize: Award or honor granted for academic or artistic career　Surfaces and Interfaces at the Nanoscale　Jan 2009	①2023/7/16~7/30 ②2024/1/5~1/21	Participation as principal investigator
14	Yuri Korchev	63	Professor, Imperial College London	United Kingdom	Ph. D. Biophysics	Release of insulin granules by simultaneous, high-speed correlative SICM-FCM, Journal of Microscopy, Vol: 282, 21-29, 2020	①2023/7/13~7/22	Participation as principal investigator
15	Farzin Irandoost Mohammad	28	Doctoral Researcher, Aalto University	Finland	Doctoral Researcher /Applied Physics	Project: Academy of Finland: Other research funding "Autoatomic: Atomic force microscopy, surface chemistry, organic molecules, biomolecules, machine learning, computer vision", 01/09/2022 → 31/08/2026	①2023/7/18~7/28 ②2024/1/9~1/19	Collaborative Research
16	Fabio Priante	29	PhD Graduate Student, Aalto University, School of Science and Technology	Finland	PhD Graduate Student	Molecular insights on the crystalline cellulose-water interfaces via three-dimensional atomic force microscopy; SCIENCE ADVANCES, 8(41) (Oct 202)	①2023/7/18~7/28 ②2024/1/9~1/19	Collaborative Research
17	Das Tamoghna	42	Research Fellows, KIAS(Korea Institute for Advanced Study)	Korea	Computational Soft Condensed Matter Physics	Acceleration of enzymatic catalysis by active hydrodynamic fluctuations, Communications Physics 5(1), April 2022	2023/7/24	NanoLSI Open Seminar
18	Mingbo Qu	40	Associate Professor, School of Bioengineering, Dalian University of Technology	China	PhD / Biochemical Engineering	The National Natural Science Foundation of China (2022-2025), No. 32170501	2023/7/1~7/29	Bio-SPM Collaborative Research Program
19	Valeriia Muraveva	28	Institute of Physics and Astronomy University of Potsdam	Germany	PhD Student	The International Conference on Biological Physics, ICBP 2023, Seoul, Korea	2023/7/27~8/10	Collaborative Research
20	Motoyuki Hattori	-	Professor, Fudan University (復旦大学)	China	Ph. D. School of Life Sciences	Early Carrer Award in Protein Science Society in Japan, 2008	2023/7/3	NanoLSI Open Seminar
21	Prasanna Venkatraman	-	Deputy Director, Advanced Centre for Treatment, Research and Education in Cancer (CRI ACTREC), Tata Memorial Centre	India	PhD, Molecular Biophysics Unit	Novel Nexus with NFκB, β-catenin, and RB1 empowers PSMD10/Gankyrin to counteract TNF-α induced apoptosis establishing its oncogenic role. The International Journal of Biochemistry & Cell Biology, 146, 106209 (2022)	2023/7/24~7/27	short-term stay for joint research; participation in India–Japan Cancer Symposium

22	Kulbhushan Tikoo	-	Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research (NIPER)	India	PhD, Biochemistry	OPPI Scientist Award in the year 2011	2023/7/24~7/27	short-term stay for joint research; participation in India–Japan Cancer Symposium
23	Surajit Karmakar	-	Professor and Scientist-F Dean R&D Institute of Nano Science and Technology (INST)	India	PhD, Physiology	・New staff development grant from University of Queensland, Australia, 2013. ・Young Investigator Award, American Society for Neurochemistry, 2005. ・Senior Research Fellowship, Indian Council of Medical Research, New Delhi, India, 2002-2004.	2023/7/24~7/27	short-term stay for joint research; participation in India–Japan Cancer Symposium
24	Swapnil Ulhas Rane	-	Professor & Pathologist, Tata Memorial Centre, HBNI	India	Doctor of Medicine	・Silver Medal during MD Pathology, PGIMER, Chandigarh ・Distinction at MRes (TCM), King's College London ・GAPIO Excellence in Diagnostics Award-Young Category, 2022	2023/7/24~7/27	short-term stay for joint research; participation in India–Japan Cancer Symposium
25	Srinivas Gopala	-	Sree Chitra Tirunal Institute for Medical Sciences and Technology	India	PhD, Biochemistry	IndoUS Science and Technology Forum Research Fellowship (2009-10), Indian Council for Medical Research (ICMR) International Fellowship (2013-14)	2023/7/24~7/27	short-term stay for joint research; participation in India–Japan Cancer Symposium
26	Yuta Koui	-	Laboratory of Stem Cell and Neuro-Vascular Biology, Cell and Development Biology Center (CDBC), National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH)	USA	Master of Science and Doctor of Philosophy, Department of Biological Sciences, Graduate School of Science	・2016-2019: Research fellow of Japanese Society for the Promotion of Science (JSPS) ・2019: Research encouragement award (Graduate school of science, The University of Tokyo) ・2020-2022: Kaitoku Research Fellowship for Japanese Biomedical and Behavioral Researchers at NIH (JSPS) ・2022-2023: Uehara Postdoctoral Fellowship Award (The Uehara Memorial Foundation) ・2022-present: Lenfant Fellowship Award (NHLBI)	2023/7/25(online)	participation in India–Japan Cancer Symposium
27	Akiko Omori	-	University of Padua	Italy	Ph.D. in Life Science	・2015 DTI International Postdoctoral fellowship, Telethon D. The European Union Seventh Framework ・Programme, Marie Curie Co-funding of Regional, National and International Programmes ・2020 IBSA foundation postdoctoral fellow, Swiss ・2021 Foundazione Umverto Veronesi foundation postdoctoral fellow, Italy ・2022 JSPS RPD fellow, Japan	2023/7/24~7/25	participation in India–Japan Cancer Symposium
28	Daniel Mindiola	49	Brush Family Professor of Chemistry, Graduate Chair, University of Pennsyrvania	USA	Ph. D. Inorganic and Organometallic Synthesis, Catalysis, and Mechanistic Chemistry	・F. Albert Cotton Award in Synthetic Inorganic Chemistry (2020) ・Friedrich Wilhelm Bessel Research Award, Alexander von Humboldt Foundation (2009-2010) ・National Fresenius Award, Phi Lambda Upsilon (2009) ・Camille Dreyfus Teacher-Scholar Award, Camille and Henry Dreyfus Foundation (2005-2012) ・Presidential Early Career Award for Scientists and Engineers (PECASE) (2004) ・National Science Foundation CAREER Award (2003-2008)	2023/8/23	NanoLSI Open Seminar
29	AHMED IkhlasMohamed Mohamud	33	University of Strathclyde	United Kingdom	Postdoctoral Research Associate	Native mass spectrometry interrogation of complexes formed during targeted protein degradation: 30 Nov 2023, In: Rapid Communications in Mass Spectrometry . 37, 22, 9 p., e9604.	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
30	AL-SHAER Alaa	28	Simon Fraser University	Canada	D4 Student	Sequence-dependent mechanics of collagen reflect its structural and functional organization Open ArchivePublished:August 11, 2021	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
31	BRULE Mael	25	Helmholtz Zentrum Berlin / Fritz Haber Institute	Germany	PhD Students/ Engineering Physics	-	①2023/8/28~9/2 ②2024/2/3~2/20	①11th NanoLSI Bio-SPM Summer School ②Bio-SPM Collaborative Research Program
32	COLCLOUGH Cameron	25	University of Sheffield	United Kingdom	M1 Student/ Physics and Astronomy	-	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
33	DIEZ Alejandro	30	Autonomous University of Madrid	Spain	D1 Student	-	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
34	JIRIKOVA Katerina	25	Institute of Photonics and Electronics,Czech Academy of Sciences	Czech Republic	M2 Student	-	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
35	KIM Chae-eun	28	University of Ulsan	SouthKorea	M2 Student	-	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
36	LAFARGUE Elodie	28	Aix-Marseille University, INSERM	France	PhD student/ Biophysic	-	2023/8/26~9/9	11th NanoLSI Bio-SPM Summer School
37	MARTIN CUEVAS Eva Maria	27	Spanish National Centre forBiotechnology (CSIC)	Spain	D2 Student	CTP promotes efficient ParB-dependent DNA condensation by facilitating one-dimensional diffusion from parS. eLife (July 2021)	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
38	ONDOY Rica Jan C.	33	University of the Philippines Diliman	Philippines	M2 Student	Electrocoagulation for the treatment of textile industry effluent e A review	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
39	PAVELKA Vit	30	Masaryk University	Czech Republic	D6 Student	Complex evaluation of Raman spectra using morphological filtering: Algorithms, software implementation, and experimental verification of baseline correction, peak recognition, and cosmic ray removal in SERS spectra of designer drugs. Journal of Raman Spectroscopy 53(12) (Sep 2022)	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
40	ROTH Jonathan	29	Rutgers University	USA	Postdoctoral Researcher	Design of synthetic collagens that assemble into supramolecular banded fibers as a functional biomaterial testbed. Nature Communications volume 13, Article number: 6761 (2022)	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
41	SAHA Prithwidip	33	Aix-Marseille University, INSERM	France	Postdoctoral Researcher	・Selected for Participation in 70th Lindau Nobel Laureate Meetings 2021 ・Solvent- and Temperature-Dependent Assembly in Monolayer Films of a Ferrocene-Naphthyridine Hybrid on HOPG. Chemistry – An Asian Journal, Vol 16, Issue 11. 1430-1437 (April 2021)	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
42	SEIER Florian	30	Leibniz Institute of PhotonicTechnology	Germany	Doctoral Researcher	–	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School
43	TABARES Jonathan	28	Florida International University	USA	B4 Student	2022 GEM Fellowship (https://www.gemfellowship.org/students/gem-fellowship-program/)	2023/8/28~9/2	11th NanoLSI Bio-SPM Summer School

44	Li Minjie	43	Professor, State Key Lab of Supramolecular Structure and Materials, College of Chemistry, Jilin University	China	PhD, Supramolecular self-assembly and chiroptics	Highly Stable Triangular Single-Layer 2D Assemblies: Synthesis and Their Stimuli-Responsive Elastic and Anisotropic Curling; Angew. Chem. Int. Ed., 2023, e202302365 (2023)	2023/9/25~9/30	Bio-SPM Collaborative Research Program
45	Zhang Shengrui	29	PhD student, State Key Lab of Supramolecular Structure and Materials, College of Chemistry, Jilin University	China	PhD student	Wide-Range and Highly Sensitive Chiral Sensing by Discrete 2D Chirality Transfer on Confined Surfaces of Au(I)-Thiolate Nanosheets. ACS Nano 16(1) (Dec 2021)	2023/9/25~9/30	Bio-SPM Collaborative Research Program
46	Huijuan Yang	52	Professor,Fudan University Shanghai Cancer Center	China	M.D., Ph.D	•2021 Shanghai Medical Science and Technology Prize 2021 (3rd prize) •2022 Shanghai Medical Science and Technology Prize 2022 (1st prize) •2022 Shanghai Anticancer Science and Technology Prize 2022	2023/9/12~9/15	short-term stay for joint research; participation in The 11th KUCRI-FUSCC Joint Symposium on Tumor Biology 2023
47	Tong Tong	42	Professor,Fudan University Shanghai Cancer Center	China	Ph.D	•2017 Third Prize, Shanghai Anti-Cancer Science and Technology Award, Shanghai Anti-Cancer Association. •2016 Third Prize, Fudan University Shanghai Cancer Center "Tianheng Cup", FUSCC	2023/9/12~9/15	short-term stay for joint research; participation in The 11th KUCRI-FUSCC Joint Symposium on Tumor Biology 2023
48	Yong Chen	45	Professor,Fudan University Shanghai Cancer Center	China	M.D., Ph.D	•2008 The 3rd class excellent paper in 5th Chinese conference on oncology •2021 The 2nd Prize of Science and Technology Award of China Anti-Cancer Association	2023/9/12~9/15	short-term stay for joint research; participation in The 11th KUCRI-FUSCC Joint Symposium on Tumor Biology 2023
49	Zikiou Abdellah	36	Leader, Food Biotechnology Division, Biotechnology Research Center – C.R.Bt, Constantine	Algeria	PhD, Food Science	Algerian cardoon flowers express a large spectrum of coagulant enzymes with potential applications in cheesemaking; International Dairy Journal, 105, 104689	2023/10/18~11/23	Bio-SPM Collaborative Research Program
50	Berker Daniel	25	University of Siegen	Germany	M2	–	2023/10/2~2024/2/16	KU Exchange Program-Science and Engineering Sciences/Medical, Pharmaceutical and Health Sciences
51	Bartolome Soberats	53	University of the Balearic Islands	Spain	PhD, Chemistry/ Associate Professor	Two-Dimensional Supramolecular Polymerization of a Bis-Urea Macrocycle into a Brick-Like Hydrogen-Bonded Network. Angewandte Chemie International Edition in English 135(46) (Sep 2023)	2023/10/30~11/1	Short-term stay for joint research
52	Antonio Pedro da Rocha Cardoso Goncalves	37	Visiting assistant professor and Assistant research fellow, College of Medicine, National Cheng Kung University	Taiwan	PhD, Molecular Pathology and Genetics	Conflict, Competition, and Cooperation Regulate Social Interactions in Filamentous Fungi; Annual Review of Microbiology, 2020	2023/10/29~12/15	Bio-SPM Collaborative Research Program
53	Antonio Jose Capezza	31	KTH Royal Institute of Technology, Department of Fiber and Polymer Technology, Division of Polymeric Materials	Sweden	PhD (double degree), Agricultural Science and Fiber and Polymer Technology / Postdoctoral Fellow	Biodegradable Fiber-Reinforced Gluten Biocomposites for Replacement of Fossil-Based Plastics. ACS Omega, E-ISSN 2470-1343, Vol. 9, no 1, 1341-1351. (2023)	2023/11/13	Meeting for a future joint research project (BioSPM Collaborative Research)
54	Luo Changfeng	25	PhD student, School of Life Science and Technology, ShanghaiTech University	China	PhD student	–	2023/11/5~11/12	Bio-SPM Collaborative Research Program
55	Antonio Benedetto	39	Professor, School of Physics University College Dublin, University Roma Tre	Ireland	Ph.D. in Physics (University of Messina, Italy)	・The Michèle Auger Award for Young Scientists' Independent Research 2023 of Biophysical Reviews (Spinger-Nature) ・Lindau Nobel Laureate Meeting Award awarded in 2016, EBSA Bursary awarded in 2015 ・Borsellino-Menestrina Prize awarded in 2012	2023/12/13	NanoLSI Open Seminar
56	Khin Mar MYINT	-	University of Medicine-1, Yangon	Myanmar	PhD/ Vice President, Professor	High sensitivity-CRP lowering effects of ramipril, valsartan and amlodipine in hypertensive patients. Burma Medical Journal 58(1):41-49 (March 2016)	2023/12/8	Discussion and observation of the research activities at NanoLSI
57	Pastsakorn KITIYODOM	-	ATT Consultants Co., Ltd	Thailand	PhD Engineering/ Geotechnical & Foundation Engineering Co., Ltd	Challenges in design and construction of Bangkok MRT Orange Line project. Geomechanik und Tunnelbau 16(3):265-271 (June 2023)	2023/12/8	Discussion and observation of the research activities at NanoLSI
58	Wenxiang WEI	-	Soochow University, School of Biology and Basic Medical Science	China	PhD/ Professor	URI1 suppresses irradiation-induced reactive oxygen species (ROS) by activating autophagy in hepatocellular carcinoma cells. Int J Biol Sci 2021; 17(12):3091-3103.	2023/12/8	Discussion and observation of the research activities at NanoLSI
59	Acep PURQON	-	Bandung Institute of Technology	Indonesia	PhD Physics/ Associate Professor	Effect of Scaling the Electrostatic Interactions on the Free Energy of Transfer of Azurin from Water to Lipid Membrane Determined by Coarse-Grained Simulations. Pertanika Journal of Science and Technology 31(6):2735-2750 (Sep 2023)	2023/12/8	Discussion and observation of the research activities at NanoLSI
60	Jambaldorj Boldbaatar	-	National University of Mongolia, School of Engineering and Technology	Mongolia	PhD/ Senior Lecturer	Fabrication of wet-spun wool keratin/poly (vinyl alcohol) hybrid fibers: Effects of keratin concentration and flow rate. Journal ACS omega.8(13) 12327-12333 (March 2023)	2024/1/23	Meeting for a future joint research project
61	Le Thi Phuong Ngan	32	Researcher, Center for Bioscience and Biotechnology, University of Science, Vietnam National University, Ho Chi Minh City	Vietnam	PhD, Microbiology, Biotechnology	Influence of N-terminal His-tags on the production of recombinant proteins in the cytoplasm of Bacillus subtilis, Biotechnology Reports 35: e00754. (2022)	2024/2/14~4/13	Bio-SPM Collaborative Research Program
62	金京春 Kim Kyung-chun	-	Yanbian University, Yanbian Hospital（延辺大学, 付属医院）	China	MD, PhD/ Professor	・Jilin Provincial Natural Science Academic Achievement Award, Excellence Award 2013 ・Yanbian Korean Autonomous Prefecture Science and Technology Progress Award, Second Prize 2014	2024/2/6	Short-term stay for joint research
63	朴英実 Park Young-sil	50	Yanbian University, Yanbian Hospital（延辺大学, 付属医院）	China	PhD/ Associate Professor	・Yanbian Korean Autonomous Prefecture Science and Technology Progress Second Prize (first), 2014 ・Yanbian Korean Autonomous Prefecture Science and Technology Progress Second Prize (Second), 2014	2024/2/6	Short-term stay for joint research
64	Zong-Quan Wu (吴宗铨)	45	Professor, Jilin University (吉林大学)	China	Ph.D. Organic Chemistry	・Excellent young talents overseas ・Excellent Young Scientist funding of NSFC ・Chiral Chemistry Award for Young Scientist by Chinese Chemical Society ・Young Science & Technology Award by Anhui province	2024/3/17~3/18	NanoLSI Open Seminar
65	Ron Naaman	74	Weizmann Institute of Science, Israel	Israel	Professor	Foreword to the Special Issue Chiral Induced Spin Selectivity Journal of Chemical Physics. 160, 9, 096101. (2024)	2024/3/24~3/26	NanoLSI Open Seminar
66	Trever Bivona	-	University of California San Francisco	USA	Professor	・2022 Chan-Zuckerberg Biohub Senior Investigator ・Long Non-Coding RNAs as Emerging Targets in Lung Cancer. Cancers (Basel). 15(12), Jun 2023	2024/3/18,19	SANTO Project, Next Generation Hokushin Cancer Project, WPI International Seminar
67	Daniel Lucas Kerr	-	University of California San Francisco	USA	Junior Specialist, Medicine	AXL and Error-Prone DNA Replication Confer Drug Resistance and Offer Strategies to Treat EGFR-Mutant Lung Cancer. Cancer Discov. 12(11):2666-2683 (Nov 2022)	2024/3/18,19	SANTO Project, Next Generation Hokushin Cancer Project, WPI International Seminar
68	Tadashi Manabe	-	University of California San Francisco	USA	Postdoctoral Research Fellow	・Fellowship Award, Damon Runyon Cancer Research Foundation (Jul 2022) ・Remodeling of the tumor/tumor microenvironment ecosystem during KRAS G12C inhibitor clinical resistance in lung cancer. The Journal of clinical investigation, 132(4), Feb 2022	2024/3/18,19	SANTO Project, Next Generation Hokushin Cancer Project, WPI International Seminar

Appendix 6 FY2023 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2023 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2023 (number of activities, times held)
PR brochure, pamphlet	*NanoLSI Leaflet (1) (EN) *NanoLSI Visiting Fellows Program Leaflet (1) (EN) (Total: 2)
Lectures, seminars for general public	*NanoLSI Open Seminar (16) *Kanazawa University Open Lecture（1 by Oshima） (Total:17)
Teaching, experiments, training for elementary, secondary and high school students	*NanoLSI Research Exchange (presentation workshop) for Kanazawa Izumigaoka High School (6/23, 11/3) and for Komatsu High School (11/3) *Cancer research Early Exposure Program (8/1-8/4) *Rigakuno-Hiroba（Hands-on Science Seminar for High School Students) (8/8) (Akine, Furutachi, Sakata, Iwami) *Annual Presentation Workshop of Ishikawa Super Science High Schools and Ishikawa New Super High School (1/23) *Komatsu High School (instruction for experiment) (Total: 8)
Open houses	*NanoLSI Open House for Komatsu High School SSH (12/12) and visit to Toda Lab (3/15) *NanoLSI Facility Tour for G7 Education Ministers' Meeting in Toyama and Kanazawa (5/15) *NanoLSI Facility Tour for Ishikawa Chemical Education (8/17) *NanoLSI Facility Tour for Alumni of 1973 graduates of the Dept. of Mechanical Engineering, Kanazawa University (9/11) *NanoLSI Facility Tour for Kanazawa University STELLA Program participants (9/18) *NanoLSI Facility Tour for Summer School by Molecular Electronics and Bioelectronics, The Japan Society of Applied Physics (9/19) *NanoLSI Facility Tour for Overseas Alumni Associations, Kanazawa University (12/8) *NanoLSI Facility Tour for Kinka Chemical Society (12/15) *Visit by Consul General of the Republic of Turkey in Nagoya (6/1) *Visit by the Ambassador Extraordinary and Plenipotentiary of the European Union (EU) to Japan (10/20) *Visit by the Yoshida Scholarship Foundation (11/22) *Visit by Delegation from the Taipei Economic and Cultural Representative Office in Japan (3/13) *Visits by MEXT, other ministries (or national organizations), and university officials (4/18,25, 6/27, 7/11, 8/8,25 9/19, 10/13,17) - Visit by State Minister of Education, Culture, Sports, Science and Technology (MEXT) (7/11) (Total: 22)
Participating, exhibiting in events	*12th WPI Science Symposium (11/23) (Total: 1)
Press releases	Flechsig/Ando, Arai, Nakayama, Sumino, Okuda, Takahashi (2), Kodera (2), Shibata/Sumino, Sumikama, Miyazawa, Ichikawa/Fukuma, Hazawa/Wong (2), Takahashi/Korchev/Fukuma, Wong, Konno/Nakayama, Sakai, Oshima, Ousaka/MacLachlan/Akine, Ikbal/Akine, Foster, Flechsig/Kodera, Sumino/Sumikama, Flechsig/Franz, Franz, Ayhan/Sun/Fukuma. (Total: 31)
Others（Radio & TV program, podcast）	*Radio program (1) MRO "Tad Mitani's Innovation Now" *TV program (1) NHK World "Science View" *Podcast (21); Holger, Takahashi (3), Sumino (2), Nakayama, Shibata, Fukuma, Lyu, Arai, Ando, Ichikawa, Wong (2), Sumikama, Miyazawa, Akine, Oshima, Ousaka, Kodera. (Total: 23)

*If there are any rows on activities the center didn't implement, delete that (those) row(s). If you have any activities other than the items stated above, fill in the space between parentheses after "Others" on the bottom with the name of those activities and state the numbers of activities and times held in the space on the right. A row of "Others" can be added, if needed.

Outreach Activities and Their Results

List up to three of the Center's outreach activities carried out in FY 2023 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, and describe its concrete contents and effect in narrative style. (Where possible, indicate the results in concrete numbers.)

Examples:
- As a result of using a new OO press-release method, a OO% increase in media coverage was obtained over the previous year.
- By holding seminars for the public that include people from industry, requests for joint research were received from companies.
- We changed our public relations media. As a resulting of using OO to disseminate information, a OO% increase in inquiries from researchers was obtained over the previous year.
- As a result of vigorously carrying out OO outreach activity, ¥OO in external funding was acquired.

I. Holding research meetings abroad

1. NanoBioCoM2023 in Viet Nam

We held the first symposium in Southeast Asia in cooperation with the Rencontres du Vietnam. The symposium, entitled 'The first International Symposium of Nano Life Science: Nano Biotechnology, Biosensor, Computation (NanoBioCoM2023), was organized to discuss cutting-edge nanobiotechnology and fundamental knowledge in order to solve life science challenges. The three-day program welcomed more than 100 researchers from 15 countries, including ten researchers and ten students from the NanoLSI presented their research. The symposium is scheduled to be held continuously from 2024 onwards, contributing to forming an academic community in the field of nano life sciences, particularly nanoprobes and nanobiotechnology, in Viet Nam.
The symposium had also received support from the JSPS Bangkok Office. In addition, we were able to help raise awareness of the JSPS and the WPI projects at the symposium by welcoming the Deputy Director to make a speech and to have a booth.

2. The 7th NanoLSI Symposium

The 7th NanoLSI Symposium was held in Berlin in cooperation with Prof. Carsten Beta, University of Potsdam, Germany, who joined NanoLSI as an overseas PI in FY2022, and NanoLSI Assoc. Prof. Clemens M. Franz as the organizers.
Previously, the NanoLSI Symposia have been held in London and Vancouver to strengthen overseas collaboration, mainly with overseas PIs. 'From Molecules to Cells and Tissue – Bridging Scales with Nanoprobe Technology' was the theme of this symposium. Eight German researchers in biomechanics, cell biology and biophysics were invited as speakers while also seeking the development of future collaborative research.
The total number of participants was 39 (eight invited speakers, ten local participants, and from the NanoLSI, seven speakers, seven poster presenters, and six administrative staff attended).

II. Contribution to the region (support for high school students of SSH-designated schools in their research projects

As a local research institute with world-leading outstanding technology, the NanoLSI has supported research activities mainly for high school students in science and mathematics at schools designated as Super Science High Schools (SSH) in Ishikawa Prefecture, and high school teachers and students have high expectations of NanoLSI.

1. Ishikawa Prefectural Kanazawa Izumigaoka High School

In response to requests for support from NanoLSI researchers, the following support was provided in 2023 to the three-year research projects of the students of the Dept. of Science and Mathematics.

- ✧ 6/23 Support for organizing Oral presentations of the results of third-year students of the Dept. of Science and Mathematics research project and advice from researchers (in English).
  No. of students: Third-year students (presentation) 40, Second-year students (audience) 38, total 78.
  Supported by: Nakayama, Sandhu (NanoLSI PR advisor), and several others.
- ✧ 11/3 In-school Interim Oral Presentations for Second-year students of the Dept. of Science and Mathematics.
  No. of students: Second-year students (presentation) 39, First-year students (audience) 41, total 80.
  Supported by: Nakayama

- ✧ 1/23 Ishikawa Super Science High School Research Presentation and Ishikawa New Super High School Research Presentation
  No. of students: Second year students (presentation) 87, First year students (audience) 41.
  Supported by: Nakayama, Sandhu
  *A total of 640 high school students presented at this presentation, and NanoLSI researchers mainly provided advice to the Izumigaoka students. The advice from a researcher's perspective contributed to raising the students' motivation for research and acquiring of a way of thinking unique to researchers. This event was also open to the public as well as junior high and high school teachers throughout Japan. These support activities have helped to raise awareness of the NanoLSI in the general public.

2. Ishikawa Prefectural Komatsu High School

Komatsu High School is an exceptionally highly reputed school among the current SSH schools. This Komatsu High School also has high expectations of NanoLSI in executing its students' research projects. We responded to its strong requests for examination and advising at research presentations and facility/laboratory visit, as follows.

- ✧ 11/3 In-school Interim Oral Presentations for Second-year students of the Dept. of Science and Mathematics.
  No. of students: Second-year students (presentation) 40 (Total No. of participants 140 including students from other schools.)
  Supported by: Miyata
- ✧ 12/12 Facility visit
  No. of students: 15
- ✧ 3/15 Lab. Visit
  No. of students: 4
  *Assisted with advice on experimental techniques connecting the December facility visit.

III. Continuing program for fostering future young researchers

The Cancer Research Early Exposure Program for high school students, was organized by researchers of the NanoLSI and the Cancer Research Institute, Kanazawa University, following on from the previous year's program. The NanoLSI conducted seven programs out of total 11, which started with a classroom lecture and included actual observation of samples using HS-AFM and SICM. In the seminar on the final day, three researchers of the NanoLSI talked to high school students about their careers as researchers and other topics, including what motivated them to become researchers from the perspective of high school students. Some students who had been unsure about their future career paths were inspired to become researchers after taking part in this research experience program, and their interest in research was greatly stimulated, creating a positive attitude toward future scientific research activities. During the course, a promotional video was simultaneously filmed, and a video with student interviews was made for public release. It is widely expected that the students' enthusiasm after their experience of the program will be expressed through the video.

- ✧ Cancer Research Early Exposure Program promotional video

  https://ganken.cri.kanazawa-u.ac.jp/graduate/gankeneep/

  No. of students: 38 in the research experience program and 18 in the seminar
  Supported by: Hirao, Oshima, Matsumoto, Shibata, Hirata, Nakayama, Arai, Watanabe, Miyanari, Sato, and Vu (11)

Appendix 7 FY 2023 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2023.

* Enter the host institution name and the center name in the footer.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2023.4.8	Newspaper (1)	Award: Prof. Takeshi Fukuma, Awards for Science and Technology Research Category, The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science, and Technology 2023 (Hokkoku)
2	2023.4.28	Newspaper (5)	Award: Prof. Toshio Ando, the Medal of Honor with the Purple Ribbon (Hokkoku (2), Yomiuri, Mainichi, Nikkei)
3	2023.4.28	Newspaper (1)	Research result: Asst. Prof. Atsuko Kasahara, Identification of proteins involved in anticancer drug resistance (Hokkoku)
4	2023.5.9-8.22	Newspaper (3), television (2)	Research result: Assoc. Prof. Takahiro Nakayama, Zooming in on neurotoxic aggregates (Hokkoku (2), Asahi, ITC, TBS)
5	2023.6.11	Newspaper (1)	Research result: Prof. Yasufumi Takahashi, Enhancing carbon dioxide reduction (Hokkoku)
6	2023.6.11	Newspaper (1)	Research result: Assoc. Prof. Satoru Okuda, Results revealing the deformation factors of cultured organs (Hokkoku)
7	2023.6.3-8.29	Newspaper (9)	Others: Vice President Prof. Kunio Matsumoto, Establishment of a venture capital company wholly investied by Kanazawa University (Hokkoku (2), Hokuriku Chunichi (3), Nikkei, Mainichi, Yomiuri, Kensetsu Kogyo)
8	2023.7.1	Newspaper (1)	Research result: Prof. Mikihiro Shibata, Experiments provide insights into the molecular mechanism for memory and learning (Hokkoku)
9	2023.8.1	Newspaper (1)	Research result: Asst. Prof. Takashi Sumikama, Ion channel block unraveled (Hokkoku)
10	2023.8.2	Newspaper (2)	Event: Prof. Masanobu Oshima, Cancer Research Early Exposure Program for High School Students (Hokkoku, Hokuriku Chunichi)
11	2023.8.8	Newspaper (1)	Research result: Prof. Richard Wong, Brain cancer linked to nuclear pore alterations (hokkoku)
12	2023.8.23	Newspaper (1)	Research result: Prof. Yasufumi Takahashi, Researchers define a nanopipette fabrication protocol for high resolution cell imaging (Hokkoku)
13	2023.9.27	Newspaper (1)	Research result: Prof. Richard Wong, Researchers identify the dynamic behavior of a key SARS-CoV-2 accessory protein (Hokkoku)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
14	2023.10.7	Newspaper (1)	Research result: Assoc. Prof. Hiroki Konno, Assoc. Prof. Takahiro Nakayama Molecular mechanisms of plant root hair lateral surfaces observed by AFM (Hokkoku)
15	2023.10.15	Newspaper (1)	Research result: Prof. Richard Wong, Researchers identify the dynamic behavior of a key SARS-CoV-2 accessory protein (Hokuriku Chunichi)
16	2023.10.27	Newspaper (1)	Research result: Assoc. Prof. Katsuya Sakai, Results elucidating the role of the Met receptor double (Science News)
17	2023.10.31	Newspaper (1)	Others: Prof. Takeshi Fukuma, Prof. Toshio Ando, Featured article: The future of regional universities (2) (Asahi)
18	2023.12.15	Newspaper (1)	Research result: Asst. Prof. Naoki Ousaka, Prof. Shigehisa Akine, Prof. Mark J. MacLachlan, Researchers fix the chirality of helical proteins (Science News)
19	2023.12.20	Newspaper (1)	Research result: Prof. Adam S. Foster, Structural isomerization of individual molecules using a scanning tunneling microscope probe (Hokkoku)
20	2023.12.24	Newspaper (1)	Research result: Asst. Prof. Ayumi Sumino, Asst. Prof. Takashi Sumikama, Sodium channel investigation (Hokkoku)
21	2024.1.1	Newspaper (1)	Research result: Prof. Rikinari Hanayama AMED: successful corporate licensing (Science News)
22	2024.3.14	Newspaper (1)	Research result: Prof. Rikinari Hanayama AMED: successful corporate licensing (Science News)
23	2024.3.19	Newspaper (1)	Award: Asst. Prof. Kee Siang Lim, The Grant-in-Aid for Young Scientists provided by Hokuriku Band (Hokkoku)

Erratta（正誤表）

Corrections and Clarifications for the FY2023 WPI Project Progress Report of NanoLSI

Date: 2024/12/10

Page	Line	Original	Corrected	Reason
2	7th line	They also discovered that the basal surfaces of metastatic colon tumor organoids had comparable ridge-like features and softer cell membranes. (Small 2023a).	*dele*	This sentence corresponds to the summary section of Page 9, “Oncogenes and Cancer Cell Dynamics (Oshima),” but since the "Small 2023a" paper is not mentioned in the “Oncogenes ~” section (it was deleted during editing), we decided that it would be better to delete this sentence from the summary section as well.
19	the 15th line from the bottom	Furthermore, of the joint research that has begun, 82% of the projects are still ongoing and 34% have resulted in such as research papers.	Furthermore, of the joint research that has begun, 82% of the projects are still ongoing and 44% have resulted in such as research papers.	writing error (underlined part)