

# World Premier International Research Center Initiative (WPI)

## FY 2024 WPI Project Progress Report (The center selected in and before FY2020)

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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 2025) 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 developed techniques and exploring various biological applications, we made intensive efforts on the promising applications that can provide insights otherwise inaccessible with existing methods. For in-cell imaging, **Fukuma** clarified elasticity changes induced by serum depletion, and subsequent TGF- $\beta$  treatment, demonstrating its close correlation with chromatin compaction. For cell-surface imaging, **Watanabe** analyzed the dynamic behavior of subcellular edge structures in migrating breast cancer cells by HS-SICM, identifying three key features of local cell movement (*Nanoscale* 2025b).

**Nanoendoscopic analysis and manipulation:** We are making a continuous effort to develop new technologies focusing on nanoendoscopic analysis and manipulation. **Takahashi** established a nanopipette-based technique for direct sampling of intracellular components, such as multivesicular bodies and exosomes. **Arai** developed fluorescence lifetime imaging (FLIM)-based biosensors for various intracellular signaling molecules. **Hirao, Ogoshi** and **Maeda** have developed new 1-MNA biosensors suitable for urine samples. **Arai, Akine, Ogoshi, Maeda,** and **MacLachlan** developed new molecular machinery systems based on lipid nanoparticles, rotaxane, and helical structures.

**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** modelled AFM studies of water and molecular systems (*Nanoscale* 2024, *ACS Nano* 2024d, *Nano Lett* 2024, *J Chem. Theory Comp* 2024, *JACS* 2024d, *JACS* 2025). **Sumikama** clarified the imaging mechanism of 3D-AFM of soft molecules and elucidated the mechanism of cluster formation of AMPA receptors (*Small Methods* 2024, *ACS Nano* 2024c). **Flechsig** implemented AFM flexible fitting for atomistic-precision understanding of HS-AFM imaging data and contributed analysis methods (*ACS Nano* 2024c). **Okuda** proposed new mathematical models that describe the dynamics of three-dimensional multicellular dynamics (*Nat Commun* 2024b, *Nat Commun* 2024c, *Acta Biomater* 2024). **Beta** revealed the mechanisms of cell motility and the interactions of motile cells (*Phys Rev Lett* 2024, *PNAS* 2024, *Phys Fluids* 2024, *Phys Rev Res* 2024).

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

**Basic cell functions:** **Matsumoto** developed MET-activating protein Fc(mML1), inducing MET dimerization and activation. In a NASH mouse model, Fc(mML1) reduced steatosis, inflammation, and fibrosis, highlighting its therapeutic potential (*iScience* 2024). **Wong** explored intracellular trafficking, showing that NUP153 anchors super-enhancers to nuclear pore complexes, enhancing TP63 expression (*Cell Chem Biol* 2024). They developed a single-molecule imaging method for brain nuclei (*Cells* 2024) and used machine learning to assess viral survival in AFM scans. Their model explains how HIV-1 breaches the nuclear envelope (*Cell Host Microbes* 2024). **Hanayama** advanced exosome research, discovering Rubicon's role in aging-related secretion of microRNA-enriched exosomes (*Nat Cell Biol* 2024). They engineered "designer exosomes" for cancer immunotherapy (*J Extracell Vesicles* 2025) and developed methods to analyze exosome pre-secretion (*Nano Lett* 2025). **Toda** created a 3D culture platform to study tissue morphogenesis via engineered cell-cell signaling (*EMBO*

**Rep 2024**) and controlled adhesion strength through cytoskeletal regulation (*ACS Synth Biol* 2024). **Miyanari** identified TFDP1 as a chromatin accessibility regulator (*Nat Genet* 2024) and developed tools for studying epigenetic regulation, including genome editing reagents and nanobodies (*BioRxiv* 2024b). **Nakajima** developed ADAR-targeting DNA aptamers for cancer therapy, including an aptamer-based PROTAC that suppressed tumor growth and an electrochemical sensor for ADAR detection (*Biosens Bioelectron X* 2024). **Sato** advanced the application of AFM for RNA visualization, with a particular focus on RNA-mediated LLPS formation. Additionally, they employed single-molecule RNA imaging technology (*Nat Rev Genet* 2024) to investigate gene regulation dynamics during the cellular heat-shock response.

**Cancer research: Oshima** studied metastatic colon cancer, revealing clonal selection mechanisms (*J Biochem* 2024) and showing mutant p53 transactivates Wnt signaling (*Cancer Res Commun* 2025). **Hirao** uncovered drug tolerance mechanisms in brain tumors, linking lysosomal function to amino acid metabolism (*Nat Commun* 2025) and developing a cancer metabolic biomarker sensor (*Anal Chem* 2024). **Yano** demonstrated that WEE1 inhibitors enhance apoptosis in KRAS-mutant lung cancer, improving efficacy when combined with KRAS-G12C inhibitors (*Cell Rep Med* 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), **Ando** succeeded in the mass production of a spoon-shaped small cantilever and improved dynamic PID controller, enabling detection of a transient intermediate state of F<sub>1</sub>-ATPase. **Kodera** developed a theory to quantify the force applied to the sample during HS-AFM imaging (*Phys Rev Appl* 2025). For SICM, **Watanabe** improved the S/N ratio of current detection in SICM by filling a nanopipette with high-dielectric solution, thus reducing disturbance to the cells during imaging. **Takahashi** developed an AI-based automatic organelle collection system for subsequent mass spectroscopy analysis. For FM/3D-AFM, **Fukuma** applied the concept of localization microscopy to the analysis of 2D/3D high-speed FM-AFM images, enabling super-resolution imaging of 3D hydration structures.

**Nanoprobe studies on various life phenomena:** To lead the development of the Nanoprobe Life Science field, we established various transdisciplinary collaborations among the four major disciplines: nanometrology, life science, supramolecular chemistry and computational science. The published examples include Bio-SPM studies of cell property changes induced by particulate matter (*Environ Sci Technol* 2024), 3D carbon nanotube structures (*Small Methods* 2024), hemin-peptide catalytic systems (*ACS Nano* 2025), Influenza A virus ribonucleoproteins (*ACS Nano* 2024), a nanoactuator for neuronal optoporation (*ACS Nano* 2024), lipid channel TMEM16F (*Nat Commun* 2024), propionic acid glutamate receptors (*ACS Nano* 2024), and AI-based automatic on-surface molecular synthesis (*JACS* 2024).

## 2. Generating Fused Disciplines

Both the top-down and bottom-up Transdisciplinary Research Promotion Grants were continuously provided for the promotion of fused disciplines. The new top-down research themes were set up and have been executed since FY2024.

## 3. Realizing an International Research Environment

The total number of papers by 86 NanoLSI researchers in FY2024 was 206. Of these, 75 (36.4%) papers were internationally co-authored. Various measures have been executed for internationalization, such as outreach programs for external researchers, support for young foreign researchers to acquire research funds, and mobility and career paths of young researchers. In addition, the conclusion of the MOU with the International Centre for Interdisciplinary Science and Education (ICISE), Vietnam was reported.

## 4. Making Organizational Reforms

NanoLSI, as a WPI center developed successfully, led to the ripple effects on the host institution in terms of advancement of internationality, establishment of other world-level research centers, and cross-sectional deployment of research support personnel. NanoLSI has been steadily implementing the gender balance improvement plan that was submitted to the WPI Program Committee in June 2024.

## 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. External funding secured by 86 NanoLSI researchers in FY2024 amounts to 1,347 million yen (1,301 million yen in FY2023). In addition, fostering and securing of next-generation researchers by the Division of Nano Life Science of the Graduate School was reported including career paths.

## 6. Others

Major awards received by Prof. Ando, Prof. Oshima and Assoc. Prof. Okuda in FY2024 were reported. Particular outreach activities to both external researchers and high school students were highlighted.

- \* 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 2024.

\* 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 last year, we worked on the three projects shown in Fig. 1.

**(1)** We have been developing Bio-SPM technologies for visualizing the structures, dynamics and chemical distribution inside and at the surfaces of living cells. This year, while continuing to improve the performance and functionality of the methods, we focused on promising applications that may provide new insights that cannot be obtained by other existing methods, such as the study of nuclear envelopathy by Nanoendoscopy AFM and database construction by high-speed SICM. We also started to explore various applications of chemical mapping techniques.

**(2)** We have been investigating nanoscale mechanisms of cellular functions and diseases such as cancer and virus infection using existing and newly developed Bio-SPMs. These efforts continued to produce impactful publications, including HS-AFM analyses of Influenza A virus ribonucleoprotein complexes (*ACS Nano* 2024a), nanoactuator for neuronal optoporation (*ACS Nano* 2024b), lipid channel TMEM16F (*Nat Commun* 2024a) and propionic acid glutamate receptors (*ACS Nano* 2024c), and SICM analysis of the impact of environmental nanoparticles on cellular properties (*Environ Sci Technol* 2024). With an outlook toward developments beyond the 11th year, broader research at the molecular and cellular level, including diseases other than cancer, is advancing.

**(3)** We aim to establish the "Nanoprobe Life Science" field by creating a world-leading center for Bio-SPM collaborations. Continuing from last year, we organized various symposia, seminars and a summer school, through which many researchers visited NanoLSI from all over the world and worked on Bio-SPM Collaborative Research. For the summer school, we started to accept financial support from two SPM manufacturers, aiming for sustainable organization of this event in the future. To continue to lead the Bio-SPM research community, we have been working on extending the capabilities of our world-leading Bio-SPM techniques. Examples include development of 100 fps HS-AFM and 3D localization technique for high-speed 3D-AFM.

Achievements in FY2024 are summarized as follows.

- Papers: 206 (36.4 % internationally co-authored; 49 with an IF > 10; 74 with an IF > 7),
- Invited talks in international meetings:82,
- Funding: 1,346,953,144 yen overall (33 grants > 10,000,000 yen).

These achievements are at the highest global level for an institute with 86 researchers (as of March 2025).

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

#### (Development of nano-imaging techniques)

##### •Measurement of nanodynamics on cell surfaces:

Following their study from last year, Watanabe *et al.* analyzed the dynamic behavior of subcellular edge structures in migrating breast cancer cells, including filopodia, lamellipodia, and cytoskeleton-

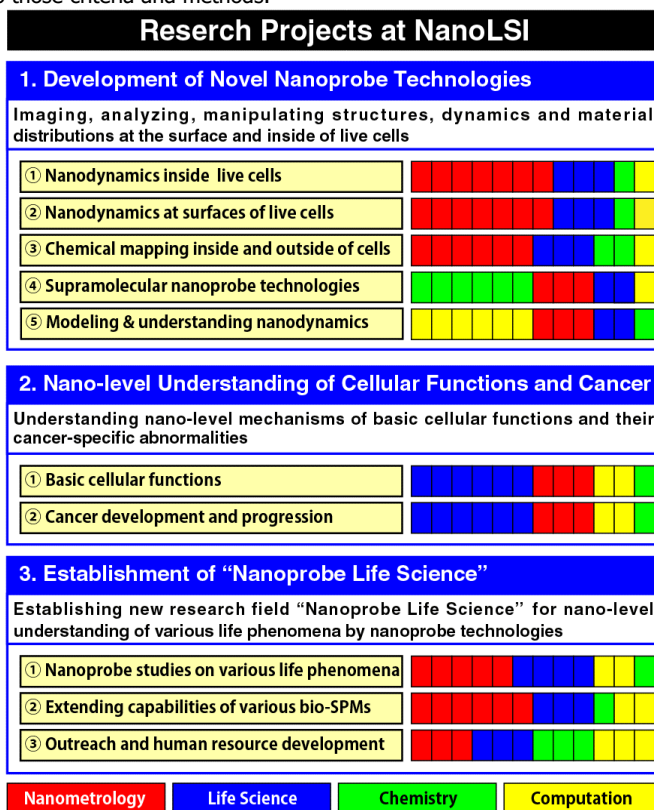


Fig. 1: Research projects at NanoLSI and contributions from the four major disciplines to each project.

related nano- and micro-structures. HS-SICM images identified three key features of local cell movement: (1) dynamic edges with abundant filopodia, (2) an inverse relationship between local cell migration rate and lamellipodia thickness, and (3) alterations in the length and distance between cytoskeleton-filament-related structures following a Poisson process (**Nanoscale 2025b**). They also investigated how small-sized particulate matter modulates the physical properties of cells using HS-SICM (**Environ Sci Technol 2024**).

Ichikawa *et al.* have been working on developing a method to label specific molecules using DNA origami in AFM imaging. So far, they have successfully designed a multi-layered, triangle-shaped DNA origami structure. However, this structure was not stable on the cell membrane. To solve this problem, they redesigned the DNA origami from scratch this year, incorporating strands that can be modified with cholesterol. Each origami structure has four extended strands, which can be modified with cholesterol. They confirmed that the redesigned origami was successfully fabricated on mica. They are currently testing whether this origami exhibits improved stability on the cell membrane. Furthermore, they have been developing a new technique to attach a FRET biosensor molecule, which is capable of detecting ATP,  $\text{Ca}^{2+}$ , and other functional molecules, to the tip of the cantilever, allowing functional molecule imaging at AFM resolution. In 2024 they established a method for selectively binding proteins to the cantilever tip using Celltak, a chemical reagent commonly used for immobilizing cell migration. Using this technique, they successfully attached the FRET biosensor jGCaMP8f, which detects  $\text{Ca}^{2+}$ , to the cantilever tip. They are currently working on estimating whether the FRET biosensor on the cantilever tip can detect local  $\text{Ca}^{2+}$  on the cell or organelle surface.

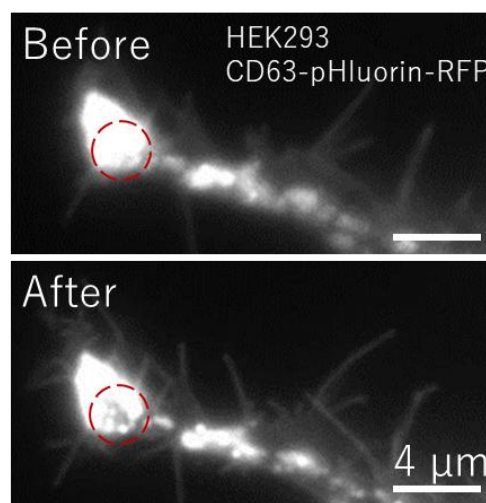
#### •Visualization of intracellular nanodynamics (nano-endoscopic observation):

**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**). This year, they refined the needle probe fabrication method and insertion conditions and successfully reduced cell disturbance and improved the imaging quality (**Nanoscale 2025**). In addition, they clarified the imaging mechanism and optimal conditions for 3D-AFM imaging of suspended nanofibers by detailed comparison between experiments and simulation (**Small Methods 2024**). With NE-AFM, they found that nuclear elasticity increases with serum depletion and decreases with subsequent TGF- $\beta$  treatment (i.e., EMT), demonstrating close correlation between nuclear elasticity and chromatin compaction level. They also succeeded in 3D NE-AFM imaging of nanostructures associated with cell-cell junctions at the interface between overlapped cells. Other NanoLSI researchers also continued their efforts in NE-AFM developments and applications. Kodera *et al.* developed HS-NE-AFM and visualized dynamics of actin fibers in a live cell. Okuda *et al.* used NE-AFM to visualize 3D intracellular structures of interacting neurons. Miyata *et al.* have been developing intracellular temperature mapping technique by combining NE-AFM with a nanodiamond sensor. Shimi *et al.* have been developing optically controlled nanomanipulator probes for local pulling or collection of intra-cellular structures.

### (Development of nano-endoscopic analysis and manipulation techniques)

#### •Injection and sampling of substances using a nanopipette

The SICM nanopipette enables the direct sampling of intracellular organelles. Exosomes, which are involved in intercellular communication, present challenges for isolation techniques and can only be obtained after they have been released. To address this, a nanopipette was inserted directly into the cell to collect multivesicular bodies, allowing for an evaluation of differences in exosome-containing contents (**Nano Lett 2025**). However, conventional nanopipettes with an aperture diameter of 100–250 nm have difficulty collecting small volumes using pressure alone. Therefore, they achieved femtoliter-level volume collection by controlling liquid-liquid interfacial tension via voltage. Additionally, by integrating distance control techniques developed through confocal microscopy and scanning ion conductance microscopy, they successfully collected intracellular structures with high spatial resolution. **Fig. 2** illustrates the collection of multivesicular bodies using a nanopipette. The localization of CD63-pHluorin-RFP in the multivesicular bodies was observed within the nanopipette. Furthermore, RT-qPCR analysis was performed to evaluate multiple microRNAs in the

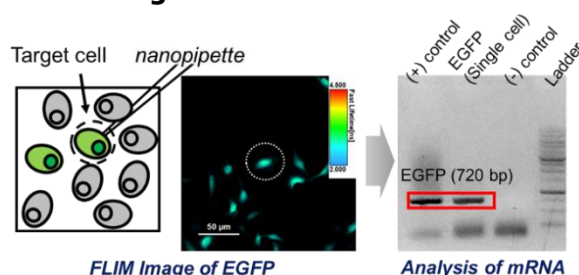


**Fig.2:** Fluorescence images during direct extraction of MVBs.

collected contents, identifying a subset containing hsa-miR-145-5p, which was predominantly collected from multivesicular bodies. This method of intracellular contents collection and analysis using nanopipettes allows for the assessment of intracellular components without averaging their contents.

#### •Analysis of nano-distribution of physical properties using a molecular sensor

Arai *et al.* have been developing fluorescence lifetime imaging (FLIM)-based biosensors for quantifying signaling molecules and metabolites at the single cell level. Starting with the development of intracellular ATP sensors, the variety of FLIM biosensors has been expanded to include citrate, glucose, and cAMP (***Cell Reports Methods* 2024**). While FLIM biosensor platforms provide valuable insights into cellular states, Arai *et al.* have broadened their analytical capabilities by collaborating with Takahashi to integrate nanopipette technology. Coupling FLIM with nanopipette technology enables spatiotemporal metabolomics and transcriptomics at the single cellular level. For preliminary tests, the collaborative team successfully identified a target cell using FLIM, picked it up with a nanopipette, and subsequently analyzed the mRNA of interest (**Fig.3**). Maeda & Zhang *et al.* established a highly reproducible method for preparing a SICM glass-pipette filled with a polymer conjugate of the carboxylate-modified pillar[6]arene that can specifically detect 1-MNA (1-methylnicotinamide), which is an oncometabolite, with a very high-sensitivity. Furthermore, Hirao, Ogoshi and Maeda *et al.* have developed new pillar[n]arene-based 1-MNA supramolecular biosensors that improves sensitivity to 1-MNA in urine by orders of magnitude without the need for sample purification (***Anal Chem* 2024**).



**Fig.3:** Microscopic tool to couple with FLIM and nano-pipette.

#### •Nano-manipulation using molecular machines

Arai *et al.* developed near-infrared (NIR) light-modulated molecular machinery composed of nano-sized lipid nanoparticles, enabling the creation of a local jump in the concentration of the neurotransmitter acetylcholine within targeted areas (***bioRxiv* 2024a**). This approach has been further extended to a drug delivery system (DDS) for targeted delivery of anticancer drugs to tumors. MacLachlan *et al.* developed rotaxanes containing platinum complexes threaded onto an axle molecule (***Angew Chem Int Ed* 2025**). These metal complexes could be used to sense oxidant species, which resulted in molecular changes that impacted the dynamics and optical properties of the complexes. 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 (***ACS Appl Nano Mat* 2024**). By combining different metal complexes in the system, they could create uniform fibers with controllable lengths. Moreover, MacLachlan *et al.* developed a series of platinum complexes with emissive properties that could be tuned across the visible spectrum and into the IR (***Chem Sci* 2024**). These complexes demonstrated unique coordination environments for the platinum centers and they may be useful in chemical sensing. MacLachlan and Akine developed several artificial peptides containing a disulfide-based staple. The reversible redox reaction of the disulfide staple efficiently controlled the helix inversion motions between the dynamic and quasi-static states (***Chem Eur J* 2024a**). Akine found that a helical Co<sub>3</sub> complex undergoes a unique chirality inversion motion on SiO<sub>2</sub> surface (***Chem Commun* 2024**). Akine also established molecular machinery systems based on metal-containing rotaxane structures (***Commun Chem* 2024**) and stacked macrocyclic structures (***Chem Eur J* 2024b**). Maeda *et al.* developed a new helical polymer-based molecular machinery system capable of showing helicity inversion, whose inversion speed can be controlled by external stimuli including solvents and temperature (***Chem Commun* 2024b, Chem Eur J 2025**). They also found that water-soluble poly(diphenylacetylene)s bearing amide pendants function as photocatalysts that rapidly break DNA upon visible light irradiation, which potentially can be used as a tool for cutting DNA independent of its base sequence by combining the SICM technology. Ogoshi *et al.* have developed a new pillar[n]arene-based chiral supramolecular machinery system based on a novel functionalization approach (***Angew Chem Int Ed* 2024a**), a fluorescent pillar[n]arene system (***JACS* 2024a, Angew Chem Int Ed 2024b**), silicone-bridged pillar[n]arenes (***JACS* 2024b**), supramolecular polymers (***JACS* 2024c**), and diastereoselective polypseudorotaxane formation (***Angew Chem Int Edit* 2024c**).

### (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 Foster group performed simulations to explore AFM of water-solid interfaces (*Nanoscale* 2024, *ACS Nano* 2024d, *Nano Lett* 2024), understanding the complex hydrogen bond networks dominating structure. They also expanded the use of machine learning tools in analysis of biomolecular systems (*J Chem Theory Comput* 2024, *JACS* 2025), developing tools for the rapid discovery of global minima in complex molecular structures and validating them with simulated AFM images (Fig.4). In a further step towards autonomous molecular design, they established a method to reliably dissociate a single chemical bond from hundreds of adsorbed organic molecules (*JACS* 2024d).

### •Elucidation of the underlying mechanism in AFM imaging of soft molecules (Sumikama)

Sumikama *et al.* published a paper elucidating the imaging mechanism of a flexible carbon nanotube (CNT) fiber in 3D-AFM (*Small Methods* 2024). To compare with experimental images, they developed a supra-coarse-grained probe model with a tapering shape. The simulated image agreed well with the experimental one (Fig.5). Analysis of the simulation results showed that the probe pushes flexible CNT fibers away during the approach and drags the fibers down after reaching them. Another paper revealed the cluster formation mechanism of AMPA receptors (*ACS Nano* 2024c). HS-AFM movies showed that dimers in the N-terminal domains of AMPA receptors split and exchange interaction partners between adjacent receptors to form clusters. Sumikama *et al.* built a simulation system and calculated the free energy profile for the dimer exchange using all-atom molecular dynamics simulations. As a result, the dimer exchange state was found to be metastable, supporting the HS-AFM observation.

### •Data assimilation for atomistic understanding of HS-AFM observations (Flechsigg)

Flechsigg *et al.* developed the computational framework for fully automated molecule recognition and large-scale quantitative analysis of HS-AFM imaging topographic data. An important achievement was the software implementation of flexible fitting (collaboration with WPI Nagoya Univ.) allowing inference at atomic level precision of biomolecular dynamics from resolution-limited HS-AFM imaging (Fig.6, *under review*). Furthermore, machine learning methods were applied towards further automation and scalability of analysis methods. 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) AMPA receptors vital for brain communication (*ACS Nano* 2024c), 2) MET receptors involved in cancer progression (*ACS Nano*, *under revision*), and 3) Myosin V molecular motor (*Nat Commun*, *under revision*). A topical review was published (*Annu Rev Biophys* 2024).

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

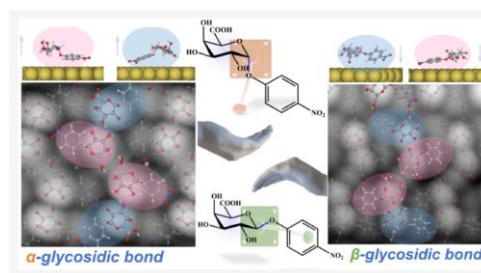


Fig.4: Comparison of images and predicted structure of two carbohydrate anomers on Au(111) – the stereochemistry of the glycosidic bond regulates on-surface chiral selection in carbohydrate self-assemblies.

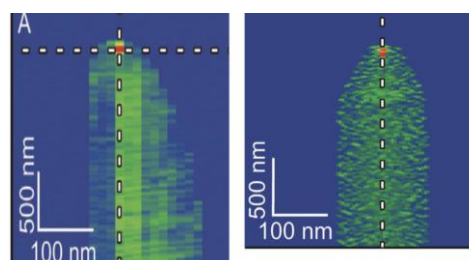


Fig.5: XY-slices of 3D-AFM images of suspended carbon nanotube fiber. (left) Experiment. (right) Simulation.

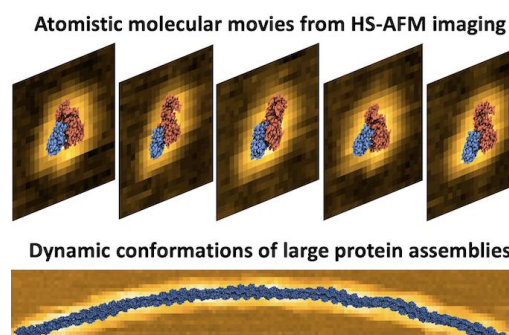
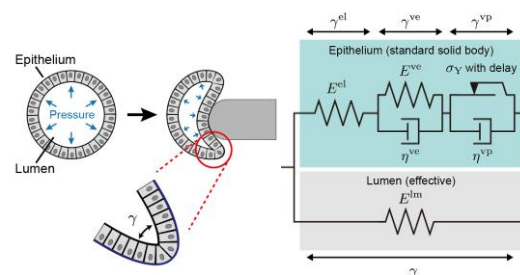


Fig.6: Flexible fitting to infer atomistic-precision dynamics from HS-AFM imaging.

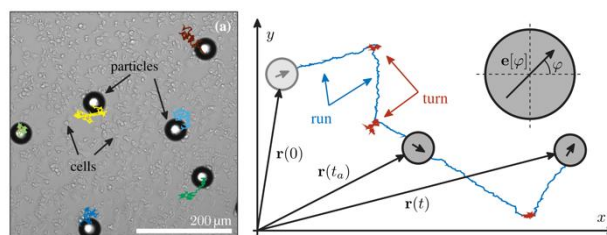
The Okuda Laboratory proposed new mathematical models that describe the 3D multicellular dynamics combined with experimental data. To estimate molecular penetration into the brain, they developed a diffusivity inference method and clarified the roles of brain structures (**Nat Commun 2024b**). Moreover, by combining mechanical tests with simple modelling, they revealed elastoplastic transition of epithelial folding (**Fig. 7, Nat Commun 2024c**). Furthermore, they developed a SIM-AFM to reveal the stiffness map with molecular distributions within 3D tissues (**Acta Biomater 2024**). Overall, they developed mathematical and measurement technologies to bridge the gap between microscopic molecular dynamics and macroscopic cell and tissue dynamics.



**Fig. 7:** A mathematical model of epithelial tissues exhibiting the elastoplastic bending property

### •Cell motility: from nano-scale dynamics to locomotion (Beta)

The Beta Laboratory relies on a combined experimental and theoretical approach to study various aspects of cell motility. A recent focus has been the interaction of ensembles of motile cells with passive micro-particles, revealing non-Gaussian statistics due to heterogeneities in the diffusive properties of the colloidal particles (**Phys Rev Lett 2024**). They have also studied how surface curvature may guide the directional migration of amoeboid cells (**PNAS 2024**).



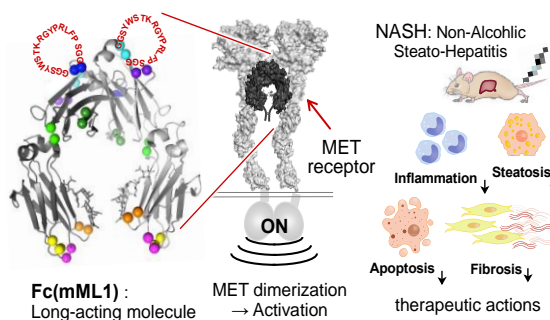
**Fig. 8:** Colloidal beads transported by a carpet of motile cells (left) and active particle model to mimic the trajectories of self-propelled objects (right).

Current efforts to obtain high-resolution AFM-images of the actin cytoskeleton in motile *Dictyostelium discoideum* cells complements this line of research. Besides adherent eukaryotic cells, a second focus of interest has been the locomotion of bacterial swimmers, with an emphasis on bundling instabilities of the lophotrichous soil bacterium *Pseudomonas putida* (**Phys Fluids 2024**) and a corresponding modeling framework, based on the concept of intermittently self-propelled particles (**Phys Rev Res 2024**). The particle tracking algorithms developed here are currently being adapted to extract the trajectories of mobile protein complexes from high-speed AFM images (**Fig. 8**).

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

### •Cell membrane receptor engineering and therapeutics (Matsumoto)

Based on the activation and dimerization mechanism for MET hepatocyte growth factor receptor, the Matsumoto group created MET-activating protein Fc(mML1), immunoglobulin Fc capable of inducing MET dimerization by grafting MET binding peptides (**Fig. 9**). Fc(mML1) induced dimerization and activation of MET in culture and showed long-stable pharmacodynamics in mice. In a mouse model of NASH (Non-Alcoholic Steato-Hepatitis), a common chronic liver disease, Fc(mML1) administration showed therapeutic action, reducing steatosis, inflammation, and fibrosis (**iScience 2024**). This peptide-grafting molecular engineering approach allows the creation of therapeutic biologics.



**Fig. 9.** Cell membrane MET receptor activation by Fc(mML1), peptide-grafted Fc and NASH improvement by Fc(mML1)

### •Intracellular trafficking (Wong)

The control of intracellular trafficking is critical for cell growth and differentiation. Nuclear pore complexes (NPCs) are multi-protein turnstiles that regulate nucleocytoplasmic trafficking. Recently, Wong *et al.* reported that NUP153, a component of the NPC, anchors super-enhancers (SEs) to the NPC and enhances TP63 expression by maximizing mRNA export. This anchoring is mediated through protein-protein interaction between the intrinsically disordered regions (IDRs) of NUP153 and the coactivator BRD4 (*Cell Chem Biol* 2024). They also developed an efficient method for isolating and purifying nuclei from mouse brain for single-molecule imaging using HS-AFM (*Cells* 2024). They also applied a machine learning stacking method to assess viral survival or decay in nanoscopic AFM scans. Future research may integrate these approaches with AFM techniques to enhance their understanding of viral states (*Cell Rep Phys Sci* 2024). Upon infection, HIV-1 releases its cone-shaped capsid into the cytoplasm, where it engages FG-repeat nucleoporins (FG-Nups) to enter the NPC. They speculated that the capsid mimics karyopherin interactions, enabling it to penetrate nucleoporin condensates. This model explained how HIV-1, despite its large size, non-destructively breaches the nuclear envelope (*Cell Host Microbes* 2024).

**•Cell communications via extracellular vesicles (Hanayama)**

The Hanayama Group has made progress in both understanding the biological functions of exosomes and advancing their manipulation. They elucidated the mechanism by which exosomes protect epithelial cells from silica nanoparticle-induced damage (*Arch Biochem Biophys* 2024). Additionally, they identified Rubicon—a molecule that increases with aging—as a key regulator that enhances the secretion of exosomes enriched with microRNAs that promote cellular senescence, leading to the discovery of novel aging markers and potential aging control strategies (*Nat Cell Biol* 2024). Further advancing exosome engineering, the group developed "designer exosomes" capable of simultaneously expressing three immune-regulatory molecules, establishing a novel therapeutic approach that induces cancer antigen-specific immune responses (*J Extracell Vesicles* 2025). Moreover, by integrating SICM, electrochemical syringes, and confocal microscopy, they successfully extracted and analyzed exosomes directly from living cells before their secretion, offering unprecedented insights into exosome biology (Fig. 10, *Nano Lett* 2025).

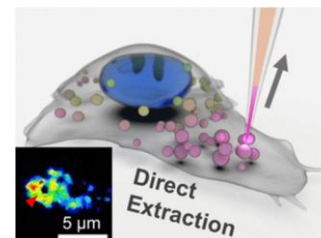


Fig. 10: Direct extraction and evaluation of exosomes inside a cell by SICM.

**•Morphogenesis — a bottom up & mechanical approach (Toda)**

The Toda group has been working on the mechanisms of how interacting cells organize tissue morphologies. In FY2024, they developed a 3D culture platform to explore how cell-cell communication can generate tissue patterns by engineering new cell-cell signaling between spheroids through the secretion of signaling proteins and the cellular responses to them. They have demonstrated the robust formation of tissue domains with sharp boundary by the interplay of diffusible signaling proteins and cell adhesion control (*EMBO Rep* 2024). They have also shown that the strength of cell adhesion can be controlled by engineering the intracellular cytoskeletal activity of cell adhesion molecules (*ACS Synth Biol* 2024).

**•Transcriptional regulation & epigenetics (Miyanari)**

The Miyanari group has been studying roles for chromatin dynamics in transcriptional regulation, which is crucial for cell lineage allocation in mammalian development. They discovered TFDP1 as a novel factor regulating chromatin accessibility and applied their results to manipulate chromatin plasticity (Fig. 11, *Nat Genet* 2024). They developed tools for studying epigenetic regulations such as proaerolysin, a negative selection reagent for genome editing (*BioRxiv* 2024b) and anti-Survivin nanobodies (*BioRxiv* 2024c, *Chem Biomed Imaging* 2024). They also contributed to a work regarding focal adhesion disassembly via myosin-driven contractility (*J Cell Sci* 2024).

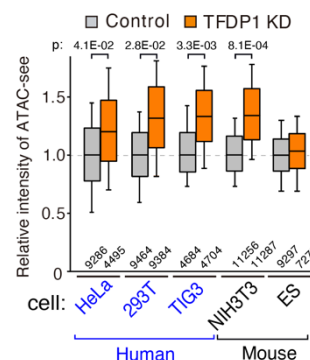


Fig. 11: Knockdown of TFDP1 leads to global elevation of chromatin accessibility.

## •Development of DNA aptamers as anti-cancer molecules and probes for detecting ADAR (Nakajima)

Nakajima *et al.* have successfully developed DNA aptamer molecules targeting ADAR, an enzyme that catalyzes RNA editing and whose abnormal expression is associated with cancer development. In collaboration with the Kodera group, they elucidated the molecular dynamics of ADAR oligomerization, its binding to RNA substrates, and the binding of DNA aptamer to ADAR using HS-AFM. Furthermore, they developed an aptamer-based PROTAC (Proteolysis Targeting Chimera) capable of degrading ADAR in cancer cells. This aptamer-based PROTAC significantly suppressed the proliferation of cancer cells. Additionally, they successfully developed a novel aptamer-antibody sandwich electrochemical sensor for detecting ADAR in complex biological samples (Fig. 12, *Biosens Bioelectron X 2024*).

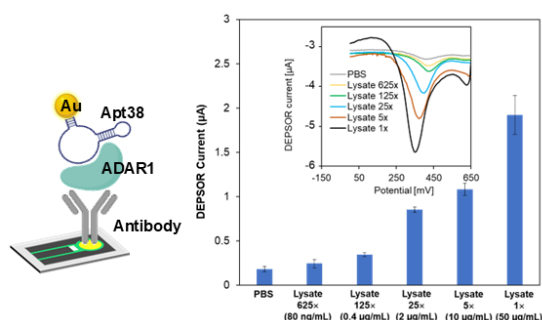


Fig. 12: Aptamer-antibody sandwich electrochemical sensor for detecting ADAR in complex biological samples.

## •RNA therapeutics for nonsense-associated genetic disorders & development of single-molecule imaging application (Sato)

The Sato group has been studying the roles of RNA regulation. In recent years, they have expanded the application of AFM to novel RNA-regulated mechanisms, such as RNA-mediated LLPS and mRNA decay. They are also developing a novel RNA therapeutic approach targeting nonsense-associated mRNA and NMD using a unique single-cell NMD reporter, identifying small compounds as potential drug candidates. Additionally, they have initiated a collaborative project to investigate gene regulation under heat-shock stress using single-molecule mRNA imaging, an area in which they have specialized expertise and technology (*Nat Rev Genet 2024*).

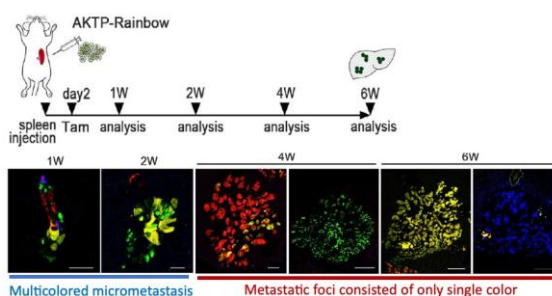


Fig. 13: Tumor cells were randomly labeled after spleen transplantation. While multicolored tumors were found at early stage, most metastatic foci consisted of single color cells, indicating clonal selection during metastasis.

## •Oncogenes and cancer cell dynamics (Oshima)

The Oshima group investigated the clonal evolution of metastatic colon cancer using randomly labeled patient-derived organoids with four fluorescent colors (*J Biochem 2024*). Interestingly, they observed a gradual reduction in heterogeneity within metastatic foci, ultimately leading to the dominance of a single subclone in established metastatic tumors. These findings suggest that cancer cells undergo clonal selection through a neutral mechanism during metastatic tumor progression (Fig. 13). Additionally, they explored the impact of tumor cell heterogeneity on oncogenic function. Notably, their study revealed that mutant p53 transactivates Wnt signaling in surrounding tumor cells through the COX-2/PGE2 pathway (*Cancer Res Commun 2025*). These discoveries provide valuable insights into the clonal evolution and heterogeneity of cancer.

## •Development of diagnostic and therapeutic technologies (Hirao)

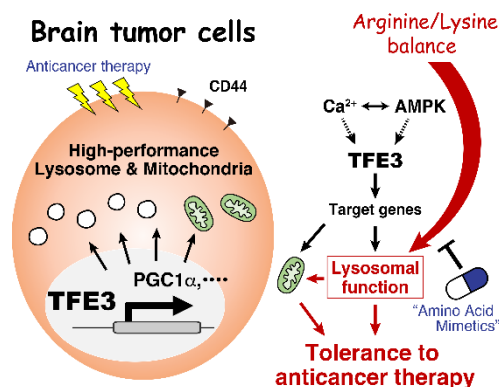


Fig. 14: Amino acid imbalance overcomes therapeutic tolerance in brain tumor.

The Hirao group has recently elucidated the molecular mechanisms underlying drug tolerance in brain tumors (*Nat Commun* 2025). Their research revealed that cells resistant to anti-cancer therapy exhibited high-performance lysosomes and mitochondria (Fig. 14), which are controlled by TFE3. In addition, they found that lysosomal functions are supported by amino acid metabolism, particularly the balance between lysine and arginine. An imbalance in lysine and arginine, induced by amino acid mimetics like homoarginine, inhibited lysosomal function, resulting in the sensitization of tumor cells to anti-cancer therapy. Furthermore, their efforts to advance innovative imaging technology led to the development of a novel sensor for detecting 1-MNA (*Anal Chem* 2024). These discoveries are expected to drive the development of nano-pipette imaging technology, as well as a diagnostic tool for cancer-associated metabolic abnormalities.

### •Development of a therapeutic approach to lung cancer (Yano)

*KRAS* mutations are prevalent genetic alterations in cancers, including lung cancer. Though *KRAS* G12C selective inhibitors were developed, the therapeutic efficacy of these drugs is not sufficient. Yano *et al.* show that WEE1 inhibitors enhance apoptosis in *KRAS*-mutant lung cancer with *TP53* mutations, triggering G2/M transition and disrupting CHK2-mediated DNA repair. Combined use of WEE1 kinase and *KRAS*-G12C inhibitors nearly eradicates *KRAS*-mutant NSCLC with *TP53* mutations in mouse models (*Cell Rep Med* 2024). This approach disrupts the DNA repair mechanisms of cancer cells (Fig. 15), offering an innovative therapeutic strategy for this challenging cancer type.

### (3) Establishment of a new research field: Nanoprobe Life Science

#### (Further improvement of Bio-SPM technologies)

#### •HS-AFM technology

The development of a faster high-speed AFM system is nearing completion. In collaboration with a cantilever manufacturer, Fukuda and Ando succeeded in mass production of tiny spoon-shaped cantilevers. They have high resonant frequencies (around 2 MHz and 6 MHz in water) and small spring constants (0.2 and 0.6 N/m). The natural resonant frequency of ~2 MHz was able to be increased to 3 MHz by using a mass control method established last year. This high resonant frequency, together with the Only Trace Imaging (OTI) mode capable of increasing the imaging rate by ~2.5 times and the dynamic PID (dPID) controller, enabled the detection of a transient intermediate state of F<sub>1</sub>-ATPase that could not be detected with previous HS-AFM systems. The optical beam deflection detector is now being modified for the 6 MHz cantilevers. They have already noticed that the combination of the OTI mode with the dPID controller can reduce tip perturbations on the sample. They modified the dPID controller for precise parameter setting. Using microtubules (MTs) oriented along the y-axis, which are much more susceptible to large tip forces than those oriented along the x-axis, we measured the probability of a MT not being broken within 10 sec while imaging at different frame rates. The results showed that this combination resulted in a 3-10 fold reduction in breakage probability at high frame rates compared to the case without dynamic gain tuning of the feedback control. Thus, the imaging rate is now increased by more than 7.5 times. In addition, Umeda and Kodera succeeded in developing a theory for estimating the tip-sample interaction force at arbitrary driving frequency in amplitude modulation AFM, including high-speed AFM (*Phys Rev Appl* 2025). This theory would be a critical toolset for accurate yet easy-to-use force quantification, enhancing the reliability of practical high-speed AFM application.

#### •Scanning ion conductance microscopy (SICM)

In high-speed SICM operation, the signal-to-noise ratio (SNR) of ion current detection remains a critical limitation. Enhancing the ion current signal by applying a large bias voltage to the nanopipette probe introduces strong electroosmotic flow, often resulting in notable deformation of soft biological samples. Watanabe *et al.* addressed this issue by filling the nanopipette with a high-dielectric solution to suppress the electroosmotic flow. The reduction in fluidic force under high bias was quantitatively confirmed using a cantilever positioned near the nanopipette tip. This approach enabled high-SNR SICM imaging of living cells with a small mechanical deformation, even at ion current levels an order of magnitude higher than those typically used in standard SICM protocols.

The relationship between the location of organelles and metabolites is crucial for understanding

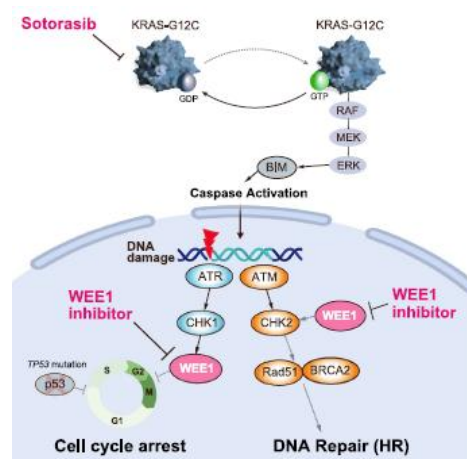


Fig. 15: Targeting WEE1 enhances the antitumor effect of *KRAS*-mutated lung cancer harboring *TP53* mutations.

cellular functions. However, unlike genes, metabolites cannot be amplified, making it difficult to obtain their spatial information. To address this, Takahashi *et al.* utilized a machine learning-based organelle collection method using a nanopipette. Furthermore, they are currently conducting mass spectrometry analysis of the collected organelle metabolites in collaboration with Professor Atsushi Hirayama and his group at Keio University. The collection time for organelles is approximately one second per organelle. To collect roughly 10,000 organelles required for mass spectrometry within 30 minutes, the collection speed needs to be improved to approximately 150 milliseconds per organelle. For this reason, they are also working to speed up the collection process from both software and hardware perspectives.

### •Development of 3D localization AFM

Recently, a super-resolution technique, originally developed for localization fluorescent microscopy, was adapted to 2D high-speed AFM image analysis. Meanwhile, Fukuma *et al.* developed high-speed 3D-AFM, allowing 1 s/volume atomic-resolution imaging. This year, they combined them to develop 3D localization AFM. A preliminary result has demonstrated that 3D localization image shows a much sharper contrast than the original or averaged image.

### (Nanoprobe studies on various life phenomena)

#### i) Characterizing Chemical, Environmental, and Stimulated Subcellular Physical Characteristics of Size-Fractionated PMs Down to PM<sub>0.1</sub> (*Environ Sci Technol* 2024, Furusho, Yurtsever, Watanabe, Sun, IF: 10.8)

Particulate matter (PM) poses serious risks to human health, affecting respiratory and organ systems and leading to severe diseases. Most studies focus on PM<sub>2.5</sub> components, sizes, and toxicities. However, the subcellular physical characteristics of size-fractionated PMs, particularly PM<sub>0.1</sub> nanoparticles, remain unexplored. This study examines the chemical composition of size-fractionated PMs, including PM<sub>0.1</sub>, collected during a biomass-burning event. PM size and distribution (PM<sub>0.1</sub>, PM<sub>0.5-0.1</sub>, PM<sub>1.0-0.5</sub>, and PM<sub>2.5-1.0</sub>) were analyzed using scanning electron microscopy and a Zeta sizer. Cytotoxicity experiments were conducted on HeLa and Cos7 cells, and respiratory-related cell lines, revealing the impact of particle sizes and concentration. High-speed scanning ion conductance microscopy assessed subcellular physical characteristics changes, including surface roughness (SR) and elastic modulus (*E*). SR showed distinct patterns across particle sizes and cell types, while *E* decreased. These findings provide a comprehensive understanding of the chemical and cellular effects of size-fractionated PMs and highlight the need to control exposure to small PMs.

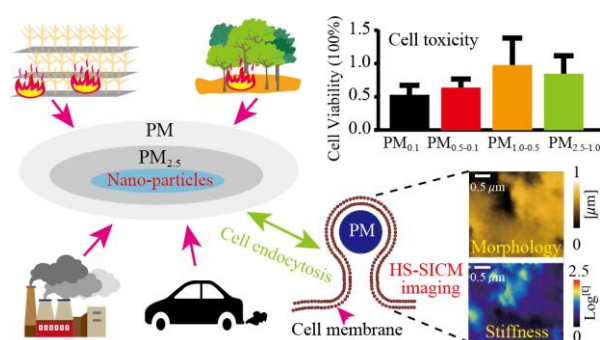


Fig. 16: Chemical, Environmental, and Stimulated Subcellular Physical Characteristics of Particulate matter.

#### ii) Revealing the Mechanism Underlying 3D-AFM Imaging of Suspended Structures by Experiments and Simulations (*Small Methods* 2024, Penedo, Sumikama, Miyazawa, Fukuma, IF: 10.7)

Recently, 3D-AFM technology has been widely applied to soft and flexible molecules including biomolecules. However, the imaging mechanism was not fully understood. In this study, they imaged a single carbon nanotube fiber (CNT) suspended between platinum pillars. The image obtained by 3D-AFM was in good agreement with the simulated one using a developed supra-coarse-grained CNT simulation. It was found that the probe pushes flexible CNT fibers away during the approach and drags the fibers down for a while after reaching the fibers. Based on the revealed imaging mechanism, the image was processed to construct a 3D image of the fiber (Fig. 17). Thus, it was demonstrated that the structure of flexible molecules can indeed be visualized by 3D-AFM, and the procedure of image processing was established.

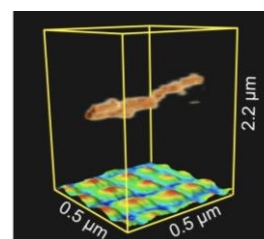


Fig. 17: A 3D image of a CNT fiber measured by 3D-AFM.

#### iii) Hierarchical Assembly of Hemin-Peptide Catalytic Systems on Graphite Surfaces (*ACS Nano* 2025, Yurtsever, Fukuma, IF:15.8)

Recent studies have demonstrated the formation of molecular hybrid systems comprising cofactors and peptides on graphite electrodes. The design of peptide sequences is crucial for forming robust catalytic molecular systems on electrodes. In this study, they employed peptides with simple dipeptide repeats, which effectively immobilize hemin, to construct a stable catalytic system and investigated the molecular basis of their self-assembly and catalytic activity by varying the sequence (Fig. 18). Frequency modulation atomic force microscopy (FM-AFM) revealed well-ordered peptide structures on graphite electrodes at the molecular scale. Electrochemical characterizations quantified hemin surface density and catalytic activity in the presence of H<sub>2</sub>O<sub>2</sub>. Strong peptide-peptide and peptide-hemin interactions, facilitated by  $\pi$ - $\pi$  interactions of tyrosine residues, contribute to system stability and efficiency. The dipeptide repeats serve as a useful platform to investigate the role of important amino acids, beyond histidine, in stably immobilizing cofactors. These results highlight the potential for developing durable and efficient catalytic interfaces in electrochemical applications.

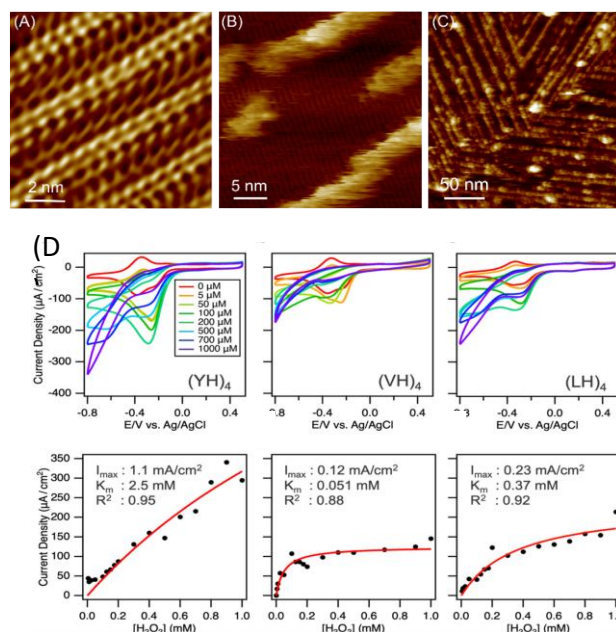


Fig. 18: (A-C) Peptide self-assembly and subsequent hemin adsorption on graphite substrate. (D) Cyclic voltammetry (CV) results for hemin-peptide electrodes at varying H<sub>2</sub>O<sub>2</sub> concentrations.

#### iv) Conformational Dynamics of Influenza A Virus Ribonucleoprotein Complexes during RNA Synthesis (*ACS Nano* 2024a, Fukuda, Ando, IF: 15.8)

Influenza A is a global health risk responsible for local epidemics and deadly pandemics. As such, the mechanism by which the virus replicates itself has attracted significant interest.

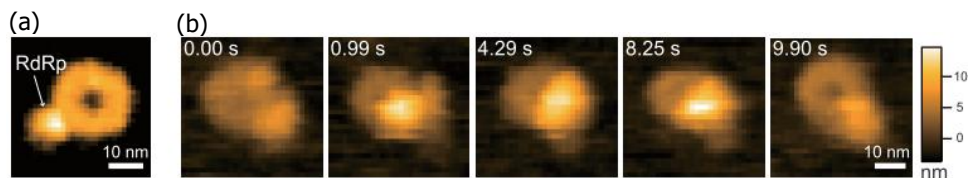
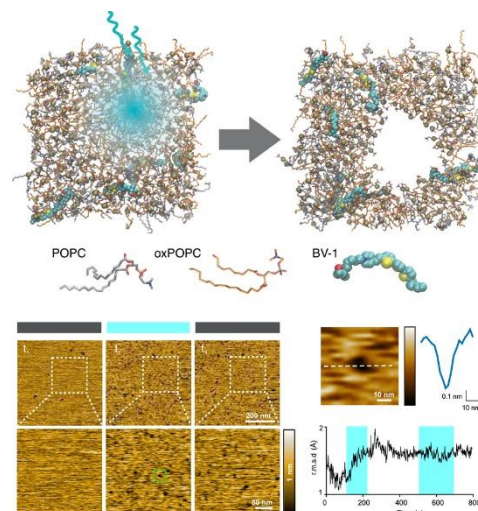


Fig. 19: (a) HS-AFM image of rRNP without NTPs. (b) HS-AFM images of rRNP with NTPs, showing the RNA synthesis process. Frame rate, 3.3 frames/seconds.

The influenza A virus (IAV) RNA-dependent RNA polymerase (RdRp) catalyzes RNA synthesis within the context of viral ribonucleoproteins (vRNPs) where genomic viral RNA (vRNA) is packaged by the viral nucleoprotein (NP). Although structural and biochemical studies have been extensively performed, these have provided snapshots regarding the vRNA synthesis, lacking information about dynamics underlying viral transcription and replication. Here, we used high-speed atomic force microscopy (HS-AFM) to visualize the dynamic processes of RNA synthesis performed by recombinant vRNP (rRNP) that forms a characteristic annular shape (Fig. 19a). This organization allows to identify the RdRp within the vRNP and visualize the RNA synthesis processes by HS-AFM. Our HS-AFM movies show that the rRNPs undergo a well-defined conformational cycle during RNA synthesis (Fig. 19b). We also provide estimations of the average RNA synthesis rate within the rRNP. Furthermore, we provide first evidence, to our knowledge, that rRNPs can perform consecutive cycles of RNA synthesis, accounting for their ability to recycle and generate multiple copies of RNA.

**v) Nanoactuator for Neuronal Optoporation (*ACS Nano*, 2024b, Marchesi, Franz, IF: 15.8)**

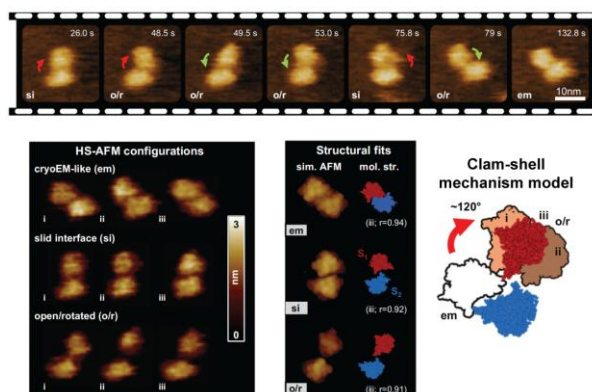
Light-driven modulation of neuronal activity at high spatial-temporal resolution is becoming of high interest in neuroscience. Here, a photoswitchable conjugated compound (BV-1) was engineered that spontaneously partitions into neuronal membranes and undergoes a charge transfer upon light stimulation (Fig. 20). Millisecond light pulses of cyan light then induce a decrease in membrane resistance, progressive depolarization and action potential firing. It was found that illumination of BV-1 induces oxidation of membrane phospholipids, which is necessary for the observed electrophysiological effects. Moreover, high-speed AFM and molecular dynamics simulations revealed that the underlying mechanism is a light-driven formation of pore-like structures across the plasma membrane. BV-1 thus represents a versatile new molecular nanomachine whose properties can be exploited for spatially controlled photostimulation and cell membrane poration.



**Fig. 20:** A photoswitchable compound (BV-1) permits light-driven formation of pore-like structures in lipid bilayers.

**vi) Structural heterogeneity of the ion and lipid channel TMEM16F (*Nat Commun* 2024a, Puppulin, Flechsig, Franz, Marchesi, IF: 14.7)**

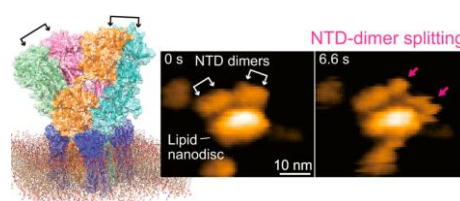
Understanding membrane remodeling activity by the dimeric TMEM16F channel involved in physiological processes of blood coagulation, bone development and viral entry has so far been limited by static structural information. HS-AFM observations now provide unprecedented insights into functional conformational dynamics, revealing significant structural flexibility under physiological conditions. Integrative modelling to infer atomistic-level models from imaging data shows that the large-scale motions observed under AFM microscopy consist in relative domain motions at the dimer interface of the channel, facilitating passive transport of phospholipids. Based on the combination of AFM experiments with modelling a new mechanistic model for the function of TMEM16F channel is provided.



**Fig. 21:** HS-AFM imaging of TMEM16F channel conformational dynamics and proposed mechanistic model.

**vii) High-Speed Atomic Force Microscopy Reveals Fluctuations and Dimer Splitting of the N-Terminal Domain of GluA2 Ionotropic Glutamate Receptor-Auxiliary Subunit Complex (*ACS Nano* 2024c, Sumino, Sumikama, Flechsig, Umeda, Kodera, Konno, Shibata, IF: 15.8)**

$\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazole propionic acid glutamate receptors (AMPA receptors) mediate rapid excitatory synaptic transmission by localizing at the postsynaptic spines. AMPARs have extracellular N-terminal domains (NTDs), which are essential for their clustering at synaptic sites, however, the molecular mechanisms of the clustering remain unsolved. In this study, we visualized the conformational dynamics of NTDs in the GluA2 subunit by HS-AFM. We found that NTD dimers fluctuated in both the resting and activated/open states. In contrast, in the desensitized/closed state, the NTD dimers adopted a more separate conformation with reduced fluctuation. Interestingly, individual NTD dimers were transitioned into monomers, with the monomeric state being prolonged in the activated/open state (Fig. 22). This NTD-dimer separation promoted subunit exchange between receptors and increased the number of interaction sites with the synaptic protein neuronal pentraxin 1 (NP1). Furthermore, HS-AFM revealed that NP1 forms a ring-shaped octamer and binds to the NTD. These findings suggest a molecular mechanism in which NP1, after forming an octamer, is secreted into the synaptic region and anchors



**Fig. 22:** HS-AFM snapshots showing NTD dimers and its splitting form.

to the GluA2 NTD tips, facilitating AMPAR bridging and clustering.

### viii) Precise Large-Scale Chemical Transformations on Surfaces: Deep Learning Meets Scanning Probe Microscopy with Interpretability (JACS 2024d, Foster, IF: 14.4)

Scanning probe microscopy (SPM) techniques have shown great potential in fabricating designer nanoscale structures through various manipulations of atoms and molecules. However, precise control requires extensive domain knowledge, which is not necessarily transferable to new systems and cannot be readily extended to large-scale operations. Therefore, efficient and autonomous SPM techniques are needed to learn optimal strategies for new systems, in particular for the challenge of controlling chemical reactions. In this work, we developed a machine learning infrastructure that autonomously identifies hundreds of individual molecules on a surface and successfully dissociates a single bond in each molecule with 80% accuracy (Fig. 23).

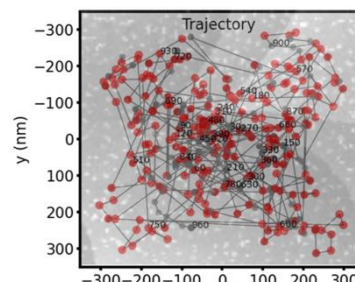


Fig. 23: trajectory of the autonomous SPM tip showing successful (red) and unsuccessful (grey) manipulation events at targeted molecules on the surface.

## 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 approach

The second phase (FY2024-FY2026) of priority interdisciplinary research has begun, as defined by the NanoLSI Future Planning Board and the NanoLSI Faculty Board.

The priority interdisciplinary research themes are described below. These reflect the recommendations made in the discussion and report of the Site Visit of the WPI Program Committee and will reinforce our efforts in the priority research themes. It should be noted that top-down Transdisciplinary Research Promotion Grant (TDRP-G) of up to a maximum of 10 million yen was provided for each priority interdisciplinary research theme.

1. 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 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-level 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 approach

Since the approval of our application to the WPI program, a bottom-up Transdisciplinary Research Promotion Grant (TDRP-G) has been established to support interdisciplinary research by groups consisting of young researchers. Through proposals from young researchers affiliated with NanoLSI and doctoral students in the Division of Nano Life Science, followed by review by NanoLSI PIs, a total of 29.5 million yen was provided for 17 research projects. Of the 17 research projects supported, four are research projects, each led by a graduate student in the Doctoral Level Section of Division of Nano Life Science. For each research project, the PI corresponding to the research project acts as a supervisor. At the beginning of the fiscal year following provision of the support, a research report meeting attended by all PIs is held to give advice on future research development.

## T-meeting

Among research groups individually led by 16 PIs, 2 Jr. PIs, one associate PI, 4 professors and 3 associate professors, two groups from different research domains were combined to give a research presentation session (T-meeting) in an organized manner. The T-meetings were held a total of 26 times in FY2024. Of these, 9 T-meetings were carried out by a combination of a research group led by an overseas PI and a research group based at 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)

The total number of papers in 2024 by 86 NanoLSI researchers was 206. Of these, 75 papers (36.4%) were internationally co-authored. Of the total 206 papers, 3 (1.5%) were in the top 1% and 33 (16%) 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, 19 (9.2%).

During the 8 years from 2017, when NanoLSI was established, to 2024, the total number of papers by NanoLSI researchers was 1,220. Of these, 507 (41.6%) were internationally co-authored. Of the total 1,220 papers, 32 (2.6%) were in the top 1% and 284 (23.3%) in the top 10% in terms of citations. The number of top 1% papers based on field-weighted Citation Impact corrections was 8 (0.66%), and the number of top 10% papers, 161 (13.2%).

The total number of papers in 2024 by 16 PIs was 123. Of these, 50 papers (40.1%) were internationally co-authored. Of the total 123 papers, 1 (0.8%) were in the top 1% and 18 (14.6%) in the top 10% in terms of citations. The number of top 1% papers based on field-weighted Citation Impact corrections was 1 (0.8%), and the number of top 10% papers, 11 (8.9%).

During the 8 years from 2017, when NanoLSI was established, to 2024, the total number of papers by 16 PIs was 893. Of these, 398 (44.6%) were internationally co-authored. Of the total 893 papers, 27 (3.0%) were in the top 1% and 224 (25.1%) in the top 10% in terms of citations. The number of top 1% papers based on field-weighted Citation Impact corrections was 8 (0.9%), and the number of top 10% papers, 131 (14.7%).

### Number of co-authored papers with overseas PIs in 2017-2024

The total number of papers co-authored by one of the four overseas PIs together with resident researchers in NanoLSI was 5 in 2024 alone: 3 with Prof. Yuri Korchev (nanometrology) of Imperial College London, UK, an overseas satellite, 1 with Prof. Mark MacLachlan (supramolecular chemistry), University of British Columbia, Canada, also an overseas satellite, 1 with Prof. Adam Foster (computational science) of Aalto University, Finland.

The total number of papers co-authored by one of the four overseas PIs together with resident researchers in NanoLSI was 31 in the 8 years from 2017 to 2024. Of these 31 papers, 13 were published with Prof. Korchev, and 6 with Prof. MacLachlan (2 co-authored by MacLachlan, Foster and Fukuma). In addition, 13 papers were published with Prof. Foster, and 1 with Prof. Alexander Mikhailov (former overseas PI, computational science) of the Fritz Haber Institute of the Max Planck Society, Germany or with his successor, Prof. Beta.

### Outreach programs for external researchers in FY2017-FY2024

The Bio-SPM Summer School and Bio-SPM Collaborative Research initiatives aim to invite external researchers to disseminate the scanning probe microscope (Bio-SPM) technology of NanoLSI, leading to joint research. In FY2024, the Bio-SPM Summer School was held at NanoLSI from August 5 (Mon) through August 10 (Sat) with 15 participants from 11 overseas countries. In addition, 14 researchers from Japan participated; the total number of participants was 29. It should be noted that the number of applicants was 38 from 22 overseas countries and 20 from Japan, i.e. a total of 58. In the Bio-SPM Collaborative Research, 9 joint research projects with overseas researchers from 8 countries were conducted in FY2024. In addition, in the same program, 22 joint research projects with domestic researchers were conducted.

Cumulatively, from FY2017 to FY2024, a total of 60 overseas researchers from 23 countries participated in the Bio-SPM Summer School. In addition, 100 researchers participated from Japan, so the total number of participants was 160. It should be noted that, in FY2020 and FY2021, overseas researchers were not invited due to COVID-19. In the Bio-SPM Collaborative Research, 44 collaborative research projects with overseas researchers from 17 countries were conducted from FY2017 to FY2024. In addition, 131 collaborative research projects were conducted with domestic researchers, so the total number of the Bio-SPM Collaborative Research projects is 175.

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 a cooperative organizational relationship between NanoLSI and the relevant research institutions. In FY2024, a review was conducted on the results and implementation methods of the Program, and the invitation of fellows was put on hold. We are currently calling for applications for Visiting Fellows including domestic researchers. In total, 4 research groups were invited from FY2017 to FY2024.

#### **Support for overseas researchers to acquire research funds in FY2017-FY2024**

With individual support from the URA, 23 overseas researchers have acquired a total of 34 KAKENHI grants from FY2017 to FY2024. As a result, in FY2024 alone, overseas researchers affiliated with NanoLSI submitted 23 new applications for KAKENHI, of which 8 were approved. This includes those whose budgetary support starts in FY2025.

#### **Mobility of and career path for young researchers**

As of the end of FY2024, the number of postdoctoral researchers (including fixed-term assistant professors) is 31 out of a total of 86 researchers at NanoLSI; 23 out of 31 (74%) are overseas researchers.

Four full-time postdoctoral researchers left NanoLSI during FY2024. Regarding their career paths, one has acquired a tenured associate professorship, and one has acquired a postdoctoral research fellow position. The other two researchers have acquired research and engineering positions at private companies. (For details, refer to Appendix 3.1, FY2024 Records of Center Activities 1.1 Special mention)

#### **Results of overseas researcher visits in FY2024**

The number of overseas researchers visiting NanoLSI in FY2024 was a total of 66 researchers from 21 countries for 775 person-days.

#### **Memorandum of Understanding signed with ICISE, Vietnam**

Several NanoLSI researchers were invited to participate in two international symposia hosted in FY2023 and FY2024 by the International Centre for Interdisciplinary Science and Education (ICISE), a partner academic organization of the United Nations agency UNESCO and the Ministry of Science and Technology of Vietnam. Through these exchanges, a memorandum of understanding for mutual cooperation, "Memorandum of Understanding between the International Centre for Interdisciplinary Science and Education (ICISE) and WPI Nano Life Science Institute (WPI-NanoLSI)," is to be signed between ICISE and NanoLSI in April 2025. Its aims are to promote Bio-SPM technology in the Southeast Asian region and to recruit excellent Vietnamese graduate students.

## **4. Making Organizational Reforms**

- \* Describe the system reforms made to the center's research operation and administrative organization, along with their background and results.
- \* Describe the measures you've taken and results achieved in implementing the center's gender-balance plan. Describe also your measures/results for fostering researchers with a view to achieving your gender plans and for conducting domestic and international promotion activities to attract female researchers to the center.
- \* 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. (Include measures taken by the host institution to provide a support system and to work toward improving the environment for achieving gender balance.)

NanoLSI was evaluated in the FY2024 Follow-up report of the WPI Program Committee as "NanoLSI and Kanazawa University have already made significant reforms in research and education systems." These successful cases of system reform include research professorships that allow concentration on research, a rigorous evaluation-based salary system, a tenure-track junior PI program, integrated management of NanoLSI and the Graduate School "Division of Nano Life Science," English-based administration, planning and organizing various research meetings in cooperation with researchers and administrative staff to foster interdisciplinary research, outreach programs to promote collaborative research with external researchers, and implementing the PDCA cycle based on external evaluation (WPI Program Committee evaluation). We continued implementing these successful cases in FY2024.

#### **Ripple effect on the host institution**

NanoLSI, as an international and outstanding institute for research and education, led to the following ripple effects on the host institution:

- Advancement of internationality: the proportion of international students in the Division of Nano Life Science (60% as of April 2025) is considered to be a successful example, and the host institution has set a target of 30% international students in undergraduate programs and 40% in graduate programs. This has been accepted by the "Multicultural Campus Project Toward Social Impact" by MEXT. The aim is to create an international "learning together" environment for domestic and international students;

- Establishment of a world-level research center: since the establishment of NanoLSI as a WPI Center and the commitment of its host institution were highly evaluated, the University was selected by J-PEAKS, the Program for Forming Japan's Peak Research Universities. We aim to create new world-level research centers that combine sciences, medicine and the liberal arts. We also aim to strengthen the fostering of young researchers through international brain circulation;
- Cross-sectional deployment of research support personnel: the URA who was working at NanoLSI to support foreign researchers in acquiring research funding has been transferred to the University Headquarters as a URA and is now responsible for supporting foreign researchers across the University and facilitating international brain circulation. Administrative staff who worked at NanoLSI are also quite active in other departments.

### **NanoLSI gender balance improvement plan**

We are steadily implementing the NanoLSI gender balance improvement plan that was submitted to the WPI Program Committee in June 2024. The results for FY2024 are as follows:

- Appointment of a new female PI: Due to the transfer of a PI in the cancer research field, Prof. Isozaki, a female researcher in the same field, was appointed as a NanoLSI PI as of April 1, 2025;
- Recruiting female Jr. PIs in the field of nanometrology: After the final selection procedure, a female Jr. PI was scheduled to take up the position in April 2025, but declined the position. NanoLSI is once again calling for international applications with a deadline of June 30, 2025;
- Appointment of a female professor as Deputy Administrative Director: As a leading candidate for the next Administrative Director, Prof. Goto, a female researcher in the field of pharmaceutical sciences, was appointed as Deputy Administrative Director as of September 1, 2024;
- Installation of a lounge for women: A lounge has been installed within the NanoLSI research building where female faculty, staff, and students affiliated with NanoLSI can take a break to manage their health, breastfeed their infants, and so on;
- Support system to hire a research assistant for researchers during pregnancy, childcare, or elderly care: one female researcher affiliated with NanoLSI used this system;
- "Cancer Research Early Exposure Program" for high school students: 38 female high school students participated (total number of participants was 61);
- STELLA Senior Program: 23 female high school students participated (total participants, 56);
- Proportion of female researchers affiliated with NanoLSI: 24% as of the end of FY2024 (21 female researchers out of a total of 86 researchers).

To improve gender balance, we will achieve a proportion of female researchers of 25% or more by the end of FY2026 through systematic personnel planning. In addition, we will steadily implement improvement plans, such as providing support for the personnel cost of hiring a research assistant, financial support for hiring a babysitter, and science awareness activities and research experience activities for elementary, junior and senior high school students, with a priority given to the participation of female students.

## **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 achieving gender balance; 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.

### **Securing external funds and revenues**

External funding secured by 86 NanoLSI researchers in FY2024 amounts to 1,347 million yen (1,301 million yen in FY2023). (For details, refer to Appendix 3-1 5. "Securing external research funding")

### **Prospect for securing permanent positions**

Based on the 22 tenured researcher positions currently deployed at NanoLSI, it was announced in the President's report at the 2024 WPI Program Committee meeting that 12 positions would be made permanent given priority to steadily secure nanometrology researchers who form the core of NanoLSI research. Under this policy and through position adjustments across the host institution,

permanent positions for NanoLSI researchers will be secured in the mid- to long-term.

### **Fostering and securing of next-generation researchers**

In the graduate school, the Division of Nano Life Science of the Graduate School of Frontier Science Initiative, which is managed in an integrated manner with NanoLSI, there are 14 students at the Master's Level Section of Integrated Course (including 5 international students; including 2 female students, of which 1 are also internationals) and 33 students at the Doctoral Level Section of Integrated Course (including 23 international students; including 18 female students, of which 16 are also internationals), i.e. a total of 47 students (including 28 international students; including 20 female students, of which 17 are also internationals) being enrolled as of April 2025.

From April 2024 to March 2025, 10 students graduated from the Doctoral Level Section, Division of Nano Life Science (3 Japanese and 7 international students). Concerning career paths after graduation, three Japanese students were appointed as researchers by companies (Sony Semiconductor Solutions Corporation, Shibuya Corporation, Shin-Etsu Chemical Co., Ltd.). In addition, of the seven international graduates, two were appointed as university faculty overseas, one as a researcher by a company (Micron Memory Japan, K.K.), one as a Research Associate at Osaka University, and the other three were appointed as postdoctoral researchers at Kanazawa University, Nagoya University, and the National Institute of Advanced Industrial Science and Technology.

### **Positioning NanoLSI within the host institution**

NanoLSI is positioned as an independent research institute equivalent to the departments in the statutes of Kanazawa University. In addition, in the university statutes, it is clearly stated that "special measures can be applied to the operation of the Nano Life Science Institute in order to promote the establishment of an independent research entity," and it is assured that NanoLSI is maintained and continued as a world-level research entity.

### **The host institution's commitment to NanoLSI after WPI grant ends**

In the report at the FY2024 WPI Program Committee Meeting, President Wada, Kanazawa University, announced that even after the end of the WPI subsidy period, for 10 years, almost the same commitment as now will continue regarding provision of budgets, preferential treatment on personnel affairs, and infrastructure maintenance and development.

## **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.

### **Toshio Ando, Distinguished Professor of Kanazawa University, awarded Leo Esaki Prize**

Prof. Ando's major research achievement, "Development of a high-speed atomic force microscope and its application to elucidation of the function and dynamics of protein molecules," is expected to explore new fields and is recognized as a research achievement with high recognition worldwide. Thus, Prof. Ando was awarded the 2024 Leo Esaki Prize.

### **Prof. Masanobu Oshima (NanoLSI PI) awarded the Tomizo Yoshida Prize**

The research achievement of Prof. Oshima on "Elucidating the mechanism of carcinogenesis and malignancy through genetic techniques" was recognized as having made a major contribution to understanding the mechanism of metastasis of gastrointestinal cancer. Thus, Prof. Oshima was awarded the 2024 (33rd) Tomizo Yoshida Prize. In addition, Prof. Oshima has been appointed to the position of President of the Japanese Cancer Association from March 2025.

### **Assoc. Prof. Satoru Okuda awarded the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology**

Assoc. Prof. Okuda received the Young Scientist Award in recognition of his research on the active mechanical properties and dynamics of multicellular tissues.

### **Press release of research outputs**

In FY2024, 31 press releases concerning research outcomes were issued, of which 15 appeared in English.

### **Outreach activities to external researchers**

In order to increase the visibility of NanoLSI among researchers both in Japan and overseas, the following three research meetings were held in FY2024:

- Big data and Machine Learning in Microscopy MLM24

This workshop was held in Kanazawa from September 17 to 19, 2024. Led by Prof. Adam Foster, one of the overseas PIs associated with NanoLSI, the event hosted 42 participants, 23 from 6 foreign countries and 19 from Japan.

- NanoBioCom2024

Led by The International Centre for Interdisciplinary Science and Education (ICISE), Vietnam in cooperation with NanoLSI, the Second International Symposium of Nano Life Science: Nano Biotechnology, Biophysics, Computation (NanoBioCoM2024) was held from September 25 to 27, 2024 at ICISE, Quy Nhon, Vietnam. The symposium received 88 abstracts for plenary, keynote, invited, oral and poster presentations from 19 countries.

- The 8<sup>th</sup> NanoLSI symposium

On November 27, 2024, the 8th NanoLSI Symposium was held in collaboration with the Okinawa Institute of Science and Technology (OIST), attracting 81 participants. On the next day, a guided tour showcased OIST's cutting-edge research facilities, including its core labs and individual research units, allowing for further exchange and networking.

### **Outreach activities to high school students**

Starting in 2022, NanoLSI has been continuing to promote exchanges between NanoLSI and the super science high schools as well as other high schools of Ishikawa Prefecture, providing high school students with opportunities to present their research and having NanoLSI researchers provide critiques and advice. Four meetings with this purpose were held in FY2024, with a total of 525 high school students participating.

Furthermore, starting from FY2022, NanoLSI and the Cancer Research Institute (CRI), Kanazawa University, have been jointly conducting an early experience program for cancer research, the Cancer Research Early Exposure Program, for high school students. This is a program that aims to allow excellent high school students who aspire to become researchers to experience seminars and receive training in experiments. Researchers from NanoLSI and CRI serve as instructors. In FY2024, a total of 61 high school students participated in the Program consisting of 11 elective events spanning 4 days. Of 61 students, 38 were female students. The implementation costs of this Program are covered by crowdfunding and donations. (For details, refer to Appendix 6. "FY2024 state of outreach activities") In addition, Kanazawa University implemented the STELLA Senior Program under the commission of the Science and Technology Challenge Program for Next Generation by JST, in which NanoLSI researchers offered a lecture titled "Idea-Based Course: Would you like to become a researcher? - We'll teach you all about research" to 32 outstanding senior high school students from across the country. Of 32 students, 14 were female students. Those students were also offered a research facility tour of NanoLSI.

## **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 "Continue further efforts to answer questions that are not easily addressed by methods other than Bio-SPM. Keep and strengthen interactions with expert researchers in cell biology."**

As we promised last year, we have been intensively working on promising biological applications of newly developed live cell SPMs as a part of a top-down Transdisciplinary Research Promotion Grant (TDRP-G) project. One application is the measurement of nuclear elasticity by nanoendoscopy AFM (NE-AFM). Fukuma *et al.* with the help of Shimi, an expert in nuclear envelopathy, have explored the dependence of nuclear elasticity on serum depletion, TGF- $\beta$  treatment, cell cycle, cardiomyopathy and substrate polarization. Through the summer school and Bio-SPM collaborative research programs, visiting researchers explored nuclear elasticity changes induced by inhibiting histone H3 methylation and shear stress. Some of the results have already been submitted for publication. Another subject is cell database construction by HS-SICM. Watanabe has been developing technology to extract various features from a HS-SICM movie. Together with Oshima, an expert in cancer research, they are applying these techniques to various cancer cells in an organoid.

### **Comment 2 "Continue efforts to develop molecular sensors for practical use in nanoendoscopy."**

As we promised last year, we continued to promote this subject as a part of top-down TDRP-G. So far, we have developed a nanopipette sensor for detecting 1-MNA, a cancer-specific metabolite, with 10 nM sensitivity. However, this sensor was also sensitive to Ca<sup>2+</sup> and Mg<sup>2+</sup>, hindering its applications to NE-AFM. To overcome this problem, Ogoshi *et al.* improved the molecular sensor design to make it insensitive to the cations, and Maeda *et al.* established the method for synthesizing polymer gel with integrated sensors. Yanjun (the Korchev group is now trying to integrate it into a nanopipette and plans to use it for chemical mapping around and inside a live cell. Meanwhile, Akine *et al.* continued to improve the specificity and sensitivity of his originally designed lactate sensor.

**Comment 3 "Continue to grow global presence and increase awareness of the NanoLSI activities."**

To enhance our international visibility, we organized a NanoLSI-OIST joint international symposium in Okinawa, a workshop on machine learning in microscopy in Kanazawa, and five open seminars at NanoLSI. We also played a key role in organizing NanoBioCom conference in Vietnam to help them launch the Vietnamese Biophysical Society. In addition, we have been running open facility programs such as the Bio-SPM Summer School, the Bio-SPM Collaborative Research and the NanoLSI Visiting Fellows Program, through which we hosted 12 visitors from 4 countries. This year, we newly launched the "Bio-SPM forum" consisting of a mailing list to exchange information on events and recruitments between the previous participants to our open facility programs and a web site to exchange technical information and software on Bio-SPM.

**Comment 4 "Continue to better the gender balance and carry out the strategy as planned."**

As we promised last year, we aim to achieve female participation of over 25% at the end of WPI grant period by following the strategic plans set for different levels. At the management level, we newly appointed a female assistant administrative director, Prof. Goto. At the PI level, we newly appointed a female PI, Prof. Isozaki in the cancer research area in exchange for Prof. Matsumoto retiring at the end of FY2024 from his PI position. At the young researcher level, we newly appointed a female assistant professor, Dr. Kiya in the neuroscience research area. We will continue these efforts to achieve the final goal.

**Comment 5 "Start earnest discussions for the future plan of NanoLSI beyond the 11th year."**

We have been intensively discussing the future plan beyond the 11<sup>th</sup> year. So far, the director had annual meetings with individual PIs separately. This year, we divided PIs, Jr. PIs and Associate PIs into several groups to organize group meetings, where we not only share the progress of this fiscal year but also discussed future plans. Through these discussions we clarified research targets to be addressed after the 10<sup>th</sup> year. In addition, we have been discussing management plans in the future planning board, faculty board and other small meetings. We will summarize these plans in documents submitted to MEXT at the end of June.

# Appendix 1 FY 2024 List of Center's Research Results and Main Awards

## 1. Refereed Papers

- List only the Center's papers published in 2024. (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 (1-124)

1. Kaneda M, Zhang W, Liu Z, Gao Y, Maruyama M, Nakanishi Y, Nakajo H, Aoki S, Honda K, Ogawa T, Hashimoto K, Endo T, Aso K, Chen T, Oshima Y, Yamada-Takamura Y, Takahashi Y, Okada S, Kato T, Miyata Y. Nanoscrolls of Janus Monolayer Transition Metal Dichalcogenides. *ACS Nano*. 2024;18(4)2772-2781
2. Großmann R, Bort LS, Moldenhawer T, Stange M, Panah SS, Metzler R, Beta C. Non-Gaussian Displacements in Active Transport on a Carpet of Motile Cells. *Physical Review Letters*. 2024;132(8)88301
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8. Ishibashi K, Ichinose T, Kadokawa R, Mizutani R, Iwabuchi S, Togi S, Ura H, Tange S, Shinjo K, Nakayama J, Nanjo S, Niida Y, Kondo Y, Hashimoto S, Sahai E, Yano S, Nakada M, Hirata E. Astrocyte-induced mGluR1 activates human lung cancer brain metastasis via glutamate-dependent stabilization of EGFR. *Developmental Cell*. 2024;59(5)579-594.e6
9. Ishii S, Kakizuka T, Park S-J, Tagawa A, Sanbo C, Tanabe H, Ohkawa Y, Nakanishi M, Nakai K, Miyanari Y. Genome-wide ATAC-seq screening identifies TFDP1 as a modulator of global chromatin accessibility. *Nature Genetics*. 2024;56(3)473-482
10. Wang D, Nakayama M, Hong CP, Oshima H, Oshima M. Gain-of-Function p53 Mutation Acts as a Genetic Switch for TGF $\beta$  Signaling-Induced Epithelial-to-Mesenchymal Transition in Intestinal Tumors. *Cancer Research*. 2024;84(1)56-68
11. Mohammed TO, Lin Y-R, Akter L, Weissenbruch K, Ngo KX, Zhang Y, Kodera N, Bastmeyer M, Miyanari Y, Taoka A, Franz CM. S100A11 promotes focal adhesion disassembly via myosin II-driven contractility and Piezo1-mediated Ca<sup>2+</sup> entry. *Journal of Cell Science*. 2024;137(2) jcs261492.
12. Fukuda K, Takeuchi S, Arai S, Nanjo S, Sato S, Kotani H, Kita K, Nishiyama A, Sakaguchi H, Ohtsubo K, Yano S. Targeting WEE1 enhances the antitumor effect of KRAS-mutated non-small cell lung cancer harboring TP53 mutations. *Cell Reports Medicine*. 2024;5(6)101578
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16. Pirabul K, Pan Z-Z, Kanamaru K, Horiguchi Y, Takahashi Y, Kumatani A, Nishihara H. Probing non-Faradaic process during elastic deformation in a single sphere of extremely soft mesoporous carbon. *Carbon*. 2024;228, 119376
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## 2. Review articles (204)

204. Liu D, Zhao J, Zhao X, Shi S, Li S, Wang Y, Song Q, Cheng X, Zhang W. Chiral polymer micro/nano-objects: evolving preparation strategies in heterogeneous polymerization. *Science China-Chemistry*. 10.1007/s11426-024-2443-0

## 3. Proceedings

None

## 3. Other English articles (205-206)

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206. Hara R, Watanabe S, Terada N, Kase K, Muto A, Hamaguchi Y, Matsushita T, Ikeda H, Tanaka T, Yano S. The lung as a site for the generation of anti-MDA5 antibody in clinically amyopathic dermatomyositis. *Rheumatology*. 2024;63(12)e336-e338

## (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 2024 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
March 10, 2025	Atsushi Hirao	Critical roles of metabolic and immune responses in hematopoietic stem cell homeostasis	THE 2025 US-Japan-Australia Meeting Hematologic Malignancies
November 20, 2024	Adam S. Foster	Keynotes "Machine learning in SPM"	The 32 <sup>nd</sup> International Colloquium on Scanning Probe Microscopy, ISPM, SPMonSPM
November 20, 2024	Yuri Korchev	Nanopipette biosensors for cell and single molecule analyses: Scanning Ion Conductance Microscopy	The 32 <sup>nd</sup> International Colloquium on Scanning Probe Microscopy, ISPM, SPMonSPM
November 12, 2024	Masanobu Oshima	Tumor and stroma signaling interactions for invasion and metastasis	The 52 <sup>nd</sup> International Symposium of the Princess Takamatsu Cancer Research Fund
September 16, 2024	Miki Nakajima	Unraveling post-transcriptional regulation of drug-metabolizing enzymes and foundational drug metabolism research for drug development and pharmacotherapy.	26 <sup>th</sup> North American ISSX and 39 <sup>th</sup> JSSX Meeting
August 29, 2024	Tomoki Ogoshi	Keynote, "Chiral Supramolecular Assemblies Based on Planar-Chiral Pillar[n]arenes"	34 <sup>th</sup> International Symposium on Chirality
August 28, 2024	Mark MacLachlan	Keynote, "Responsive Photonic Materials from the Chiral Assembly of Cellulose Nanocrystals"	34 <sup>th</sup> International Symposium on Chirality

June 25, 2024	Toshio Ando	Plenary IUPAB Engstrom Lecture "Filming biomolecules in dynamic action by high-speed AFM"	IUPAB 2024 Kyoto (21st IUPAB & 62nd BSJ Joint Congress)
April 19, 2024	Takeshi Fukuma	Keynote, "Biomaterial Interfaces and Intracellular Phenomena Investigated by 3D Atomic Force Microscopy"	Nano in Bio 2024
April 15, 2024	Satoru Okuda	Epithelial folding irreversibility is controlled by elastoplastic transition via mechanosensitive actin bracket formation	EMBO   EMBL Symposium The mechanics of life: from development to disease

### 3. Major Awards

- List up to 10 main awards received during FY 2024 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
March 26, 2025	Shigehisa Akine	Chemical Society of Japan Award for Creative Work for 2024
February 26, 2025	Toshio Ando	Leo Esaski Prize
September 23, 2024	Miki Nakajima	JSSX (The Japanese Society for the Study of Xenobiotics) Award
September 21, 2024	Masanobu Oshima	The Tomizo Yoshida Prize
August 28, 2024	Katsuhiko Maeda	Molecular Chirality Award
April 4, 2024	Satoru Okuda	The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology The Young Scientists' Award

## Appendix 2 FY 2024 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 FY2024>							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	48	Nano Life Science Institute, Kanazawa University	Doctor of Engineering, Electrical engineering, Nanometrology	90	October, 2017	usually stays at the institute	
Noriyuki Kodera	46	Nano Life Science Institute, Kanazawa University	Doctor of Science, Biophysics and Nano- Bioscience	90	April, 2022	usually stays at the institute	
<u>Yuri Korchev</u>	64	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	61	Nano Life Science Institute, Kanazawa University	Doctor of Medicine, Stem Cell Biology	90	October, 2017	usually stays at the institute	
Masanobu Oshima	63	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	59	University Hospital, Kanazawa University	MD, PhD, Medical Oncology, Circumvention of targeted drug resistance	50	October, 2017	usually stays at the institute	
Kunio Matsumoto ※1	66	Nano Life Science Institute, Kanazawa University	Doctor of Philosophy, Biological Chemistry, Tumor Biology	90	October, 2017	usually stays at the institute	

Rikinari Hanayama	50	Nano Life Science Institute, Kanazawa University	MD, PhD, Immunology, Cell Biology	90	October, 2017	usually stays at the institute	
Richard W. Wong	50	Nano Life Science Institute, Kanazawa University	Doctor of Medicine, Molecular cell biology	90	October, 2017	usually stays at the institute	
Miki Nakajima	55	Nano Life Science Institute, Kanazawa University	Doctor of Pharmaceutical Sciences, Drug Metabolism and Toxicology, Clinical Pharmacology	90	October, 2017	usually stays at the institute	
Shigehisa Akine	52	Nano Life Science Institute, Kanazawa University	Doctor of Science, Supramolecular chemistry, Coordination chemistry	90	October, 2017	usually stays at the institute	
Katsuhiko Maeda	54	Nano Life Science Institute, Kanazawa University	Doctor of Engineering, Polymer chemistry	90	October, 2017	usually stays at the institute	
Tomoki Ogoshi	48	Graduate School of Engineering, Kyoto University / Nano Life Science Institute, Kanazawa University	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.	
<u>Mark MacLachlan</u>	51	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 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
<u>Adam Stuart Foster</u>	49	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
<u>Carsten Beta</u>	50	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.

\*Percentage of time that the principal investigator devotes to working for the center vis-à-vis his/her total working hours.

※ 1 Upon Professor Matsumoto having reached retirement age, Professor Isozaki will replace him as a PI  
from April 2025 for generational shift to cover the remaining two years of the WPI grand period and beyond.

## Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

**Name (Age)** Hideko Isozaki (45)

**Affiliation and position** (Position title, department, organization, etc.)

Professor, WPI Nano Life Science Institute, Kanazawa University

**Academic degree and specialty**

Ph.D. in Medicine

**Effort** **50%**

\* Percentage of time that the principal investigator devote to working for the center vis-à-vis his/her total working hours.

**Research and education history**

(Education)

Mar. 2002 B. Sc. in Pharmacy, Setsunan University, Osaka, Japan

Jun. 2016 Ph.D. in Medicine, Okayama University, Okayama, Japan

(Research)

Apr. 2002 – Mar. 2005 Pharmacist, Department of Clinical Pharmacy, Okayama University Hospital

Apr. 2005 – Mar. 2007 Pharmacist, Pharmacy, Kousei Hospital

Apr. 2007 – Mar. 2014 Pharmacist, Department of Clinical Pharmacy, Okayama University Hospital

Apr. 2014 – Jan. 2017 Scientist, Department of Hematology, Respiratory and Oncology,  
Okayama University

Feb. 2017 – May. 2017 Research Coordinator, Biobank, Okayama University Hospital

Jun. 2017 – May. 2022 Research Fellow, Massachusetts General Hospital Cancer Center,  
Harvard Medical School

Jun. 2022 – Sep. 2024 Instructor, Massachusetts General Hospital Cancer Center, Harvard  
Medical School

Nov. 2024- Professor, Kanazawa University Cancer Research Institute

**Achievements and highlights of past research activities**

**1. Acquired Resistance Mechanisms:** I lead translational research programs aimed at uncovering the mechanistic basis of drug resistance in non-small cell lung cancer (NSCLC) and developing novel therapeutic strategies. My work primarily focuses on patients with genetic alterations such as EGFR mutations and ALK rearrangements (Cancer Discovery 2018, citation 365; Cancer Res. 2016, citation 125; Jpn. J. Clin. Oncol. 2014, citation 12; Cancers 2015, citation 66). Based on our findings, my colleagues and I have initiated clinical trials to evaluate the efficacy of these proposed therapies (Cancer Discovery 2018, citation 365; Clin. Lung Cancer 2016, citation 11; Thorac Cancer 2021, citation 9).

**2. Cancer Evolution During Therapy:** Understanding how resistant cancer clones evolve enables us to identify targetable vulnerabilities that may prevent acquired resistance. I recently

discovered that the mRNA-editing enzyme APOBEC3A acts as a driving force in cancer evolution during targeted therapy (Nature 2023, citation 54). In our clinical cohort, 70% of NSCLC patients exhibited an increased percentage of APOBEC-induced mutations in resistant tumors. Notably, gene deletion of APOBEC3A significantly delayed the onset of acquired resistance, providing proof-of-concept for a novel therapeutic paradigm.

## Achievements

**(1) International influence** \* Describe the kind of attributes listed below.

a) Recipient of international awards

2023 Publication Award, United Japanese researchers Around the world (UJA)

2020 Pilot Grant Program Award, Lung Cancer Research Foundation (LCRF)

2020 Postdoctoral Fellowship Award, MGH ECOR Fund for Medical Discovery (FMD)

2016 JCA Scholar-in-Training Award, AACR-JCA Joint Conference

2015 Travel Grant Award, European Society for Medical Oncology (ESMO) Asia

b) Member of a scholarly academy in a major country

2024 Faculty, International Association for the Study of Lung Cancer (IASLC) HTTR24

c) Guest speaker or chair of related international conference and/or director or honorary member of a major international academic society in the subject field

2024 Invited Speaker, International Association for the Study of Lung Cancer (IASLC) HTTR24

d) Editor of an international academic journal

e) Peer reviewer for an overseas competitive research program (etc.)

Grant Reviewer, Lung Cancer Research Foundation

**(2) Receipt of major large-scale competitive funds (over the past 5 years)**

1. Apr. 2025 – Mar. 2028 "Role of Innate-immunity in cancer evolution International", Joint Research Acceleration Fund, Japan Society for the promotion of science (JSPS), 500,00,000 JPY, PI

2. Apr. 2025 – Mar. 2027 "Impact of APOBEC in Hereditary Cancer Evolution", JIKOCHOKOKU PROJECT, Kanazawa University, 100,00,000 JPY, PI

3. Dec. 2020 – May. 2023 "Targeting APOBEC3A induction as a new therapeutic strategy to prevent acquired drug resistance in non-small cell lung cancer" Pilot Grant Program Award, Lung Cancer Research Foundation (LCRF), 150,000 USD, PI

4. Jan. 2020 – Dec. 2020 "Impact of Therapy-Induced APOBEC3A Mutagenesis on Genomic Instability and Evolution of Acquired Drug Resistance to Lung Cancer Target Therapies", MGH Fund for Medical Discovery Tosteson & Fund for Medical Discovery (FMD) Awards, 150,000 USD, PI

**(3) Major publications (Titles of major publications, year of publication, journal name, number of citations)**

1. Haratake N., Ozawa H., Morimoto Y., Yamashita N., Daimon T., Bhattacharya A., Wang K., Nakashoji A., **Isozaki H.**, ..., Mitsudomi T., Hata A.N., Kufe D., MUC1-C Is a Common Driver of Acquired Osimertinib Resistance in NSCLC, 2024, *J. Thorac. Oncol.*, citation **13**

2. **◆Isozaki H.**, Sakhtemani R., Abbasi A., Nikpour N., ..., Buisson R., **◆Lawrence M.S.**, **◆Hata A.N.**, Therapy-induced APOBEC3A drives evolution of persistent cancer cells, 2023, *Nature*, citation **54** (**◆co-corresponding author**)
3. Harada D. \*, **Isozaki H.**\*, Kozuki T., ..., Takigawa N., Hotta K., Kiura K., Crizotinib for recurring non-small-cell lung cancer with EML4-ALK fusion genes previously treated with alectinib: A phase II trial, 2021, *Thorac. Cancer*, citation **9** (\*co-first author)
4. Piotrowska Z. \*, **Isozaki H.**\*, Lennerz J.K., ..., Wolf B., Hata A.N., Sequist L.V., Landscape of acquired resistance to osimertinib in EGFR-mutant NSCLC and clinical validation of combined EGFR and RET inhibition with osimertinib and BLU-667 for acquired RET fusion, 2018, *Cancer Discov.*, citation **365** (\*co-first author)
5. **Isozaki H.**, Ichihara E., Takigawa N., ..., Sendo T., Tanimoto M., Kiura K., Non-small cell lung cancer cells acquire resistance to the ALK inhibitor alectinib by activating alternative receptor tyrosine kinases, 2016, *Cancer Res.*, citation **125**
6. Ochi N., **Isozaki H.**, Takeyama M., Singer J.W., Yamane H., Honda Y., Kiura K., Takigawa N., Synergistic effect of pacritinib with erlotinib on JAK2-mediated resistance in epidermal growth factor receptor mutation-positive non-small cell lung Cancer, 2016, *Exp. Cell Res.*, citation **12**
7. **Isozaki H.**, Hotta K., Ichihara E., ..., Sendo T., Tanimoto M., Kiura K., Protocol Design for the Bench to Bed Trial in Alectinib-Refractory Non-Small-Cell Lung Cancer Patients Harboring the EML4-ALK Fusion Gene (ALRIGHT/OLCSG1405), 2016, *Clin. Lung Cancer*, citation **11**
8. **Isozaki H.**, Takigawa N., Kiura K., Mechanisms of acquired resistance to ALK inhibitors and the rationale for treating ALK-positive lung cancer, 2015, *Cancers*, citation **66**
9. Minami D., Takigawa N., Kato Y., Kudo K., **Isozaki H.**, ..., Toyooka S., Tanimoto M., Kiura K., Downregulation of TBXAS1 in an iron-induced malignant mesothelioma model, 2015, *Cancer Sci.*, citation **16**
10. Yamane H., **Isozaki H.**, Takeyama M., ..., Kubo T., Kiura K., Takigawa N., Programmed cell death protein 1 and programmed death-ligand 1 are expressed on the surface of some small-cell lung cancer lines, 2015, *Am. J. Cancer Res.*, citation **32**
11. **Isozaki H.**, Yasugi M., Takigawa N., ..., Sendo T., Tanimoto M., Kiura K., A new human lung adenocarcinoma cell line harboring the EML4-ALK fusion gene, 2014, *Jpn. J. Clin. Oncol.*, citation **12**

**(4) Others (Other achievements indicative of the PI's qualification as a top-world researcher, if any.)**

2016 Young Investigator Award, Japanese Lung Cancer Society

2016 Okayama Medical Association Award, Okayama University

## Appendix 3-1 FY 2024 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 FY2024 is as shown in the table cited below.

	Name (M/F)	From which institution	Position at NanoLSI	How long	To which institution	Position
1	MAHMOUD IBRAHIM SHOULKAMY IBRAHIM (M)	Molecular and Cell Biology, Zoology Department, Faculty of Science, Minia University (Egypt)	Assistant professor (Fixed-term contract)	2 years and 4 months	Molecular and Cell Biology, Zoology Department, Faculty of Science, Minia University (Egypt)	Associate professor (Tenured position)
2	TAKESHI YOSHIDA (M)	Institute of Medical, Pharmaceutical and Health Sciences Faculty of Medicine, Kanazawa University (Japan)	Assistant professor (Fixed-term contract)	6 year and 5 months	Employment in a private company	
3	SAHO KITAGAWA (F)	Graduate School of Agricultural Science, Tohoku University (Japan)	Assistant professor (Fixed-term contract)	2 years and 6 months	Employment in a private company	
4	REI YAGASAKI (F)	Division of Biological Sciences, Graduate School of Science, Kyoto University (Japan)	Assistant professor (Fixed-term contract)	2 years	University of Michigan (United States)	Postdoctoral Research Fellow (No fixed-term contract)

#### 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

**1-3. Postdoctoral Positions through Open International Solicitations**

- In the columns "number of applications" and "number of selections," put the total number (upper) and the number and percentage of overseas researchers in the < > brackets (lower).

Fiscal year	Number of applications	Number of selections
	24	2
FY 2024	< 87.5 % >	< 50.0 % >

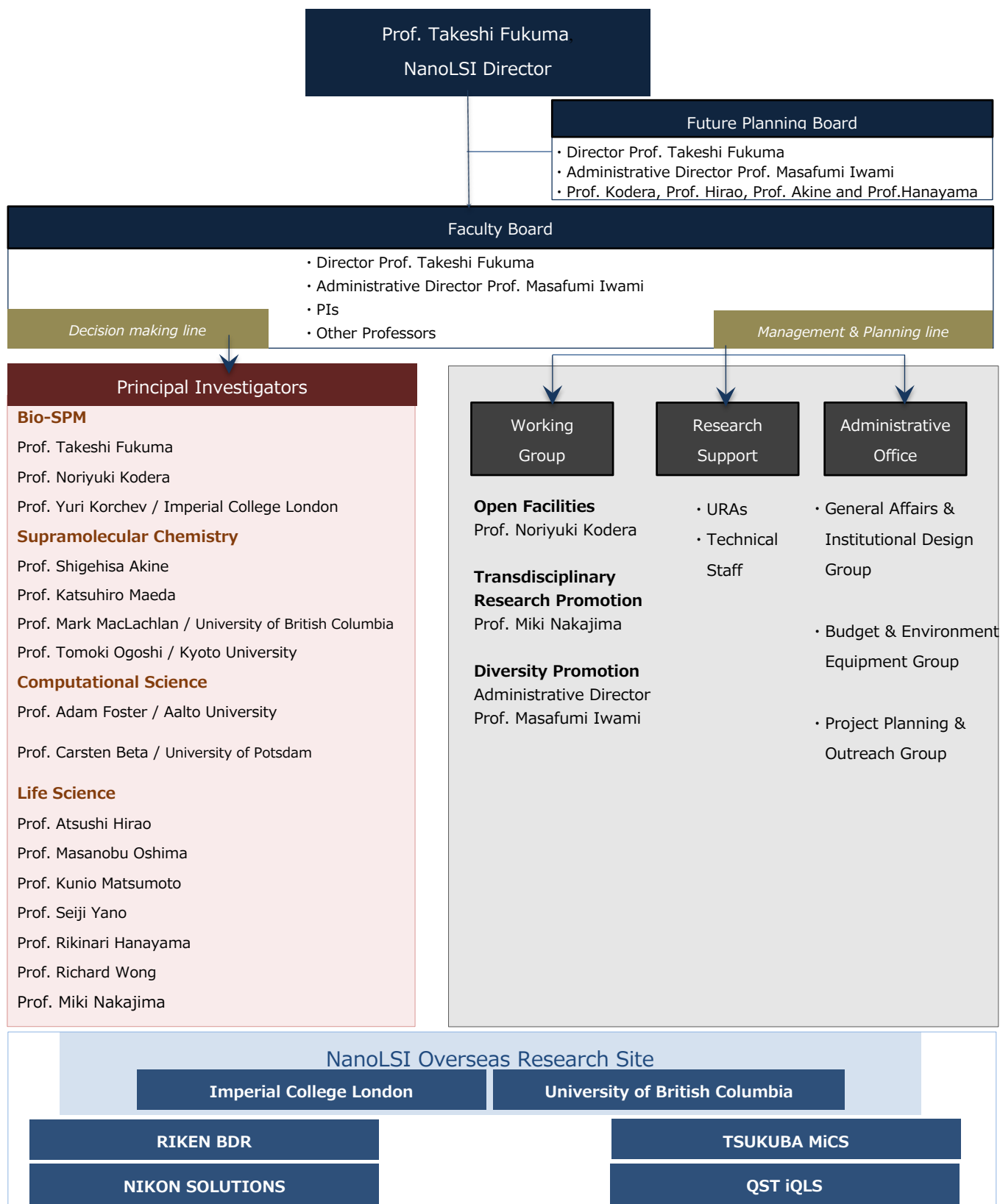
**2. Holding international research meetings**

- Indicate the number of international research conferences or symposiums held in FY2024 and give up to three examples of the most representative ones using the table below.

FY 2024: 4 meetings	
Major examples (meeting titles and places held)	Number of participants
Big Data and Machine Learning in Microscopy MLM24 Shiinoki Cultural Complex Ishikawa Prefecture, Kanazawa, Ishikawa	From domestic institutions: 19 From overseas institutions: 23
The 2nd International Symposium on Nano Life Science: NanoBiotechnology, Biophysics, and Computation (NanoBioCoM2024) The ICISE conference center, Quy Nhon, Vietnam	From domestic institutions: 14 From overseas institutions: 87
2025 Taiwan-Japan Joint Symposium on "Single-molecule dynamics" Nano Life Science Institute, Kanazawa, Ishikawa	From domestic institutions: 11 From overseas institutions: 6

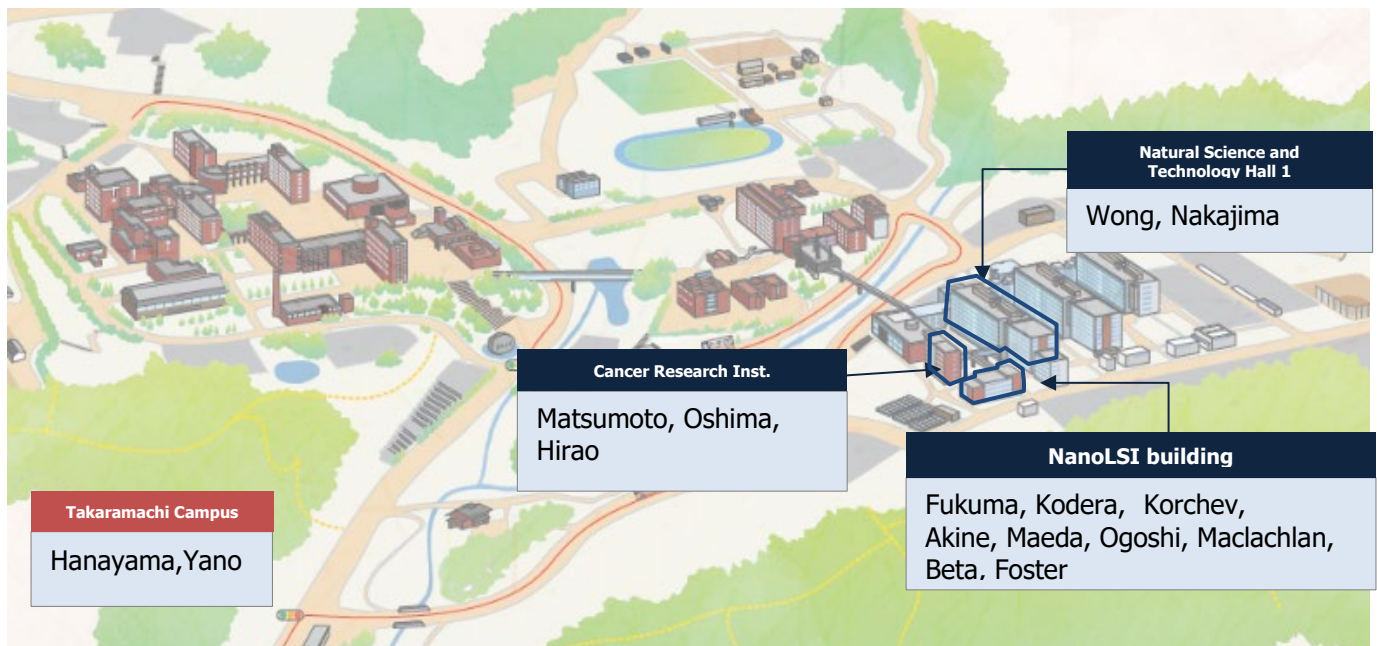
### 3. Diagram of management system

- 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 FY2024

NanoLSI External Research Funding Secured in FY2024 by type of funding source

CONFIDENTIAL

\* Including Indirect funding

	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)
■ Grants-in-Aid for Scientific Research										
Grant-in-Aid for Transformative Research Areas (A)	5	33,280,000			4	21,970,000			9	55,250,000
Grant-in-Aid for Transformative Research Areas (B)					2	9,165,000			2	9,165,000
Grant-in-Aid for Scientific Research (S)					1	6,337,500			1	6,337,500
Grant-in-Aid for Scientific Research (A)	8	56,875,000	2	10,179,000	4	13,520,000	4	1,430,000	18	82,004,000
Grant-in-Aid for Scientific Research (B)	9	31,148,572	2	910,000	14	33,410,000	10	30,745,000	35	96,213,572
Grant-in-Aid for Scientific Research (C)	1	187,114			8	10,678,243	11	12,965,982	20	23,831,339
Grant-in-Aid for Challenging Research (Pioneering)	1	14,300,000							1	14,300,000
Grant-in-Aid for Challenging Research (Exploratory)	6	11,378,737	1	1,079,260	4	11,152,540	4	6,240,000	15	29,850,537
Grant-in-Aid for Early-Career Scientists					4	8,320,000	1	2,170,957	5	10,490,957
Grant-in-Aid for Research Activity Start-up					6	8,888,682			6	8,888,682
Grant-in-Aid for Scientific Research on Innovative Areas			1	1,599,000					1	1,599,000
Fund for the Promotion of Joint International Research (Fostering Joint International Research (B))	1	260,000			2	4,523,939	2	6,155,214	5	10,939,153
Grant-in-Aid for JSPS Fellows	4	3,700,000							4	3,700,000
Total	35	151,129,423	6	13,767,260	49	127,965,904	32	59,707,153	122	352,569,740
■ Commissioned research projects										
AMED Advanced Research & Development Programs for Medical Innovation	1	8,450,000			1	6,240,000	1	18,532,800	3	33,222,800
AMED Cyclic Innovation for Clinical Empowerment	1	5,590,000							1	5,590,000
AMED Practical Research for Innovative Cancer Control	2	3,718,000					2	25,558,000	4	29,276,000
AMED Program for Promoting Platform of Genomics based Drug Discovery							1	2,600,000	1	2,600,000
AMED Project for Promotion of Cancer Research and Therapeutic Evolution	1	9,750,000					2	18,200,000	3	27,950,000
AMED Project of Translational and Clinical Research Core Centers	1	5,882,000							1	5,882,000
AMED Research and Development Program for Innovative Biologics	1	57,200,000							1	57,200,000
AMED Research on Development of New Drugs	1	26,000,000							1	26,000,000
AMED Research on Regulatory Science of Pharmaceuticals and Medical Devices	1	1,300,000							1	1,300,000
AMED The iD3 Booster	1	2,954,546							1	2,954,546
AMED Translational Research Programs	1	22,997,000			1	2,000,000			2	24,997,000
JSPS Bilateral Collaborations					1	1,500,000			1	1,500,000
JST Fusion Oriented Research for disruptive Science and Technology					4	33,772,271	2	13,000,000	6	46,772,271
JST Green Technologies of Excellence					1	19,500,000			1	19,500,000
JST New Industry Creation Fund for University Startups	1	15,600,000							1	15,600,000
JST Outline of the Program on Open Innovation Platforms for Industry-academia Co-creation (COI-NEXT)							1	4,586,807	1	4,586,807
JST Strategic Basic Research Programs (CREST)	4	36,724,004			5	37,662,896	1	3,900,000	10	78,286,900
JST Strategic Basic Research Programs (ERATO)					1	3,770,000			1	3,770,000
JST Strategic Basic Research Programs (SAKIGAKE)					3	38,481,894			3	38,481,894
Others	5	15,528,831			1	19,500,000	11	33,934,895	17	68,963,726
Total	21	211,694,381	0	0	18	162,427,061	21	120,312,502	60	494,433,944
■ Joint research projects										
Joint research projects (New)	15	53,201,191			7	9,559,034	6	41,191,400	28	103,951,625
Joint research projects (Carry-forward)	8	16,191,087			1	5,015,149	3	6,113,007	12	27,319,243
Total	23	69,392,278	0	0	8	14,574,183	9	47,304,407	40	131,270,868
■ Donations										
Donations (New)	11	13,580,000	9	38,500,000	12	57,796,078	20	26,650,000	52	136,526,078
Donations (Carry-forward)	21	173,937,324	3	5,219,255	15	19,439,645	21	33,556,290	60	232,152,514
Total	32	187,517,324	12	43,719,255	27	77,235,723	41	60,206,290	112	368,678,592

Securing external research funding

	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)
Total	111	619,733,406	18	57,486,515	102	382,202,871	103	287,530,352	334	1,346,953,144

Total: 1,346,953,144 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 2024 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 below.

\* 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 2024	Final goal (Date: March, 2027)
Researchers from within the host institution	12	11	12
Researchers invited from overseas	4	4	4
Researchers invited from other Japanese institutions	0	1	1
<b>Total principal investigators</b>	<b>16</b>	<b>16</b>	<b>17</b>

#### b) Total members

	At the beginning of project		At the end of FY 2024		Final goal (Date: March, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	49	/	86	/	81	/
Overseas researchers	8	16	30	35	31	38
Female researchers	6	12	21	24	20	25
Principal investigators	16	/	16	/	17	/
Overseas PIs	5	31	5	31	5	29
Female PIs	1	6	1	6	2	12
Other researchers	27	/	39	/	35	/
Overseas researchers	1	4	2	5	3	9
Female researchers	5	19	11	28	10	29
Postdocs	6	/	31	/	29	/
Overseas postdocs	2	33	23	74	23	79
Female postdocs	0	0	9	29	8	28
Research support staffs	8	/	26	/	29	/
Administrative staffs	13	/	19	/	18	/
<b>Total number of people who form the "core" of the research center</b>	<b>70</b>	<b>/</b>	<b>131</b>	<b>/</b>	<b>128</b>	<b>/</b>

	At the beginning of project		At the end of FY 2024		Final goal (Date: March, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Doctoral students	0	/	36	/	30	/
Employed	0	-	10	27.8	3	10.0

※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" column may be changed to coincide with the project's actual content.

(Million yens)

Costs (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	38.5	10.9
	Principal investigators (no. of persons):10	170.9	43.5
	Associate Principal investigators (no. of persons):1	11.0	11.0
	Junior Principal investigators (no. of persons):2	24.9	24.9
	Other researchers (no. of persons):65	344.6	222.7
	Research support staff (no. of persons):16	53.7	53.7
	Administrative staff (no. of persons):15	102.7	48.1
	Remuneration for RA(Research Assistant)	10.4	10.4
	Labor insurance premium adjustment amount	0.0	0.0
		Subtotal	756.7
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):3	4.3	4.3
	Research startup cost (no. of persons):9	30.5	30.5
	Cost of satellite organizations (no. of satellite organizations):2	28.3	28.6
	Cost of international symposiums (no. of symposiums):1	3.7	3.7
	Facility expenses	25.9	3.7
	Cost of consumables	13.4	13.4
	Cost of utilities	35.9	35.8
	Other costs	60.5	53.0
		Subtotal	202.5
Travel	Domestic travel costs	5.8	5.8
	Overseas travel costs	3.6	3.6
	Travel and accommodations cost for invited scientists (no. of domestic scientists):52 (no. of overseas scientists):36	3.3	3.3
		16.3	16.2
	Travel cost for scientists on transfer (no. of domestic scientists):2 (no. of overseas scientists):0	0.3	0.3
		0	0
	Subtotal	29.3	29.2
Equipment	Depreciation of buildings	0.5	0.5
	Depreciation of equipment	148.5	148.5
		Subtotal	149.0
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	133.2	0
	KAKENHI	205.9	0
	Commissioned research projects, etc.	198.9	0
	Joint research projects	45.3	0
	Others (donations, etc.)	39.3	0
	Subtotal	622.6	0
	Total	1,760.1	776.4

**WPI grant in FY 2024** 700

Costs of establishing and maintaining facilities 6.5

- Establishing new facilities 0.5
- Repairing facilities 2.3
- Others 3.7

Costs of equipment procured 148.5

- Confocal Microscope AX Upgrade Kit 1Set 17.8
- All-in-one fluorescence microscope 1Set 12.3
- Biomolecular Imaging Systems 1Set 12.3
- Others 106.1

\*1. Management Expenses Grants (including Mission Realization Acceleration Expenses, 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、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		
Project activities	Subtotal	2.7	2.7
Travel	Subtotal	0	0
Equipment	Subtotal	0	0
Research projects	Subtotal	0	0
Total		25.3	25.3

## Appendix 4 FY 2024 Status of Collaboration with Overseas Satellites

### 1. Coauthored Papers

- List the refereed papers published in FY 2024 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. 2025 and not described in Appendix 1.

#### Overseas Satellite 1 Imperial College London, UK (Total: three papers)

1) (3). Timoshenko RV, Gorelkin PV, Vaneev AN, Krasnovskaya OO, Akasov RA, Garanina AS, Khochenkov DA, Iakimova TM, Klyachko NL, Abakumova TO, Shashkovskaya VS, Chaprov KD, Makarov AA, Mitkevich VA, Takahashi Y, Edwards CRW, *Korchev YE*, Erofeev AS. Electrochemical Nanopipette Sensor for In Vitro/In Vivo Detection of Cu<sup>2+</sup> Ions. *Analytical Chemistry*. 2024;96(1)127-136

2) (14). Wang D, Woodcock E, Yang X, Nishikawa H, Sviderskaya EV, Oshima M, Edwards C, Zhang Y, *Korchev Y*. Exploration of individual colorectal cancer cell responses to H<sub>2</sub>O<sub>2</sub> eustress using hopping probe scanning ion conductance microscopy. *Science Bulletin*. 2024;69(12)1909-1919

3) (111). Vaneev AN, Gorelkin PV, Akasov RA, Timoshenko RV, Lopatukhina EV, Garanina AS, Abakumova TO, Aleksandrinn VV, Salikhov SV, Edwards CRW, Takahashi Y, Klyachko NL, *Korchev YE*, Erofeev AS. In vitro/In vivo oxygen electrochemical nanosensor for bioanalysis. *Journal of Electroanalytical Chemistry*. 2024;975, 118796

#### Overseas Satellite 2 University of British Columbia, Canada (Total: one papers)

1) (84). Ousaka N, *MacLachlan MJ*, Akine S. Redox-Triggered Reversible Switching between Dynamic and Quasi-static  $\alpha$ -Helical Peptides. *Chemistry-A European Journal*. 2024;30(56)e202402704

## 2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2024. 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
FY2024	0	0	0	0	0
	0	0	1	0	1

<From satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2024	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
FY2024	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
FY2024	0	2	0	0	2
	0	0	0	0	0

## Appendix 5 FY 2024 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: 66**

	Name	Age	Affiliation 所属		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	Satish Tripathi	-	President, University at Buffalo, the State University of New York	USA	Ph.D. Computer Science	Fellow of the American Academy of Arts and Sciences, 2024	2024/4/22	Discussion and observation of the research activities at NanoLSI
2	Nojin Kwak	-	Vice president, University at Buffalo, the State University of New York	USA	Ph.D. Mass Communication	Fellow, AIEA Leadership Academy for New SIOs, 2023	2024/4/22	Discussion and observation of the research activities at NanoLSI
3	Adam Rubin	-	Assistant Vice Provost and Director, University at Buffalo, the State University of New York	USA	M.A. East Asian Studies	-	2024/4/22	Discussion and observation of the research activities at NanoLSI
4	Zhao Zhixuan	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2024 Symposium
5	Xu Hexin	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2024 Symposium
6	Sheng Danqi	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2025 Symposium
7	Zhang Ziyi	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2026 Symposium
8	Shen Cheng	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2027 Symposium
9	Teng Xinyu	-	Student, Fudan University	China	-	-	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2028 Symposium
10	Motoyuki Hattori	-	Professor, Fudan University	China	Ph. D. School of Life Sciences	Early Carrer Award in Protein Science Society in Japan, 2008	2024/6/23~2024/6/28	Collaborative Research Participation in IUPAB2029 Symposium

11	Lekshmi Kailas	46	Experimental Officer in AFM, University of Leeds	UK	Ph. D., Physics	Surface architecture of endospores of the <i>Bacillus cereus</i> /anthracis/ <i>thuringiensis</i> family at the subnanometer scale. Proceedings of the National Academy of Sciences, 2011	2024/7/15~2024/7/19	Collaborative Research
12	Wang Wei	35	Research Fellow, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast	UK	Ph.D.	Butyrate and propionate are microbial danger signals that activate the NLRP3 inflammasome in human macrophages upon TLR stimulation, <i>Cell Reports</i> , 2024, 43(9), 114736	2024/7/15~2024/8/5	Collaborative Research
13	Marianti A. Manggau	-	Dean, Faculty of Pharmacy, Hasanuddin University	Indonesia	Ph. D., Molecular Pharmacology and Toxicology	•2022 Satyalancana Karya Satya XX •2019 Hasanuddin University Best Researcher	2024/7/18	Discussion and observation of the research activities at NanoLSI
14	Elly Wahyudin	-	Prof. the Faculty of Pharmacy, Hasanuddin University	Indonesia	DEA, Pharmacokinetics	Isolasi Bakteri Asam Laktat dari Air Susu Ibu, dan Potensinya dalam penurunan kadar kolesterol secara in vitro, <i>Majalah farmasi dan Farmakologi</i> , 2008	2024/7/18	Discussion and observation of the research activities at NanoLSI
15	Yulia Yusrini Djibir	-	Professor, Hasanuddin University	Indonesia	Ph.D. Pharmacology and Clinical Pharmacy	Asian swamp eel ( <i>Monopterus albus</i> ) oil and vitamin D3 emulsion as novel approach to improve lipid profiles and glycemic control in rat model, <i>Farmacia</i> , 2025	2024/7/18	Discussion and observation of the research activities at NanoLSI
16	Firzan Nainu	-	Prof. Pharmacy, Pharmaceutical Science and Technology, Hasanuddin University	Indonesia	Ph.D. Pharmaceutical Sciences	Pharmaceutical prospects of bee products: Special focus on anticancer, antibacterial, antiviral, and antiparasitic properties, <i>Antibiotics</i> , 2021	2024/7/18	Discussion and observation of the research activities at NanoLSI
17	Herlina Rante	-	Prof. Pharmacy, Pharmaceutical Science and Technology, Hasanuddin University	Indonesia	Ph.D. Pharmaceutical Microbiology	$\alpha$ -Glucosidase inhibitory activity of breadfruit leaf extract ( <i>Artocarpus altilis</i> (parkinson) fosberg), <i>Journal of Physics: Conference Series</i> , 2019	2024/7/18	Discussion and observation of the research activities at NanoLSI
18	Tran Thi Quynh	29	Postdoctoral Researcher, Institute of Physical Chemistry, Université Paris-Saclay	France	Postdoctoral Researcher, Physical Chemistry of Biological Systems	-	2024/7/31~2024/8/13	12th NanoLSI Bio-SPM Summer School
19	Dua Jayesh	28	PhD Student, Materials Science Department, University of Washington	USA	PhD Student, Materials Science Department	2024 CEI Graduate Fellowship	①2024/7/30~2024/8/20 ②2025/3/17~2025/3/29	①12th NanoLSI Bio-SPM Summer School ②Bio-SPM Collaborative Research Program

20	Kiss Balint	31	PostDoc, Philosophy Nanomechanics of viral infection processes, Semmelweis University	Hungary	PostDoc, Philosophy Nanomechanics of viral infection processes	Topography, spike dynamics and nanomechanics of individual native SARS-CoV-2 virions, Biophysical Journal 120 (3), 15a, 2021	①2024/8/1~2024/8/14 ②2025/3/6~2025/3/30	①12th NanoLSI Bio-SPM Summer School ②Bio-SPM Collaborative Research Program
21	Santamaria Andreas	30	Postdoctoral Researcher, Integrative Biophysics of Membranes (Pierre-Emmanuel Milhiet Lab), Center for Structural Biology	France	Postdoctoral Researcher, Integrative Biophysics of Membranes	Strikingly different roles of SARS-CoV-2 fusion peptides uncovered by neutron scattering, Journal of the American Chemical Society 144 (7), 2022	2024/8/1~2024/8/19	12th NanoLSI Bio-SPM Summer School
22	Mathew Lydia	25	D2, Indian Institute of Technology Bombay	India	D2, Department of Chemistry, Membrane Biophysics and Chemical Biology Lab	-	2024/8/3~2024/8/11	12th NanoLSI Bio-SPM Summer School
23	Bukhteeva Irina	28	PhD Student, Department of Physics and Astronomy, University of Waterloo	Canada	PhD Student, Physics and Astronomy	·2023 the WIN Nanofellowship ·2023 the best poster award at QUEBS	2024/8/3~2024/8/11	12th NanoLSI Bio-SPM Summer School
24	Svetic Ana	25	D1, Department of Physics, University of Trieste	Italy	D1, Nanotechnology, Nanoinnovation	-	2024/8/3~2024/8/11	12th NanoLSI Bio-SPM Summer School
25	Van Deventer Ruan	26	Graduate student, Department of Pharmaceutical Sciences, University of Nebraska Medical Center	USA	Graduate student, Pharmaceutical Sciences	-	2024/8/3~2024/8/15	12th NanoLSI Bio-SPM Summer School
26	Yvanoff Charlotte	34	PhD Student, Department of Bio-engineering Sciences, Vrije Universiteit Brussel	Belgium	PhD Student, Bio-engineering Sciences	Development of bone cell microarrays in microfluidic chips for studying osteocyte-osteoblast communication under fluid flow mechanical loading, IOP Publishing Biofabrication, 2022	2024/8/3~2024/8/16	12th NanoLSI Bio-SPM Summer School
27	Ruana Cardoso Lima	29	PhD Student, Department of Physics and Astronomy, Physics of LivingSystems, Wuite Lab Vrije Universiteit Amsterdam	Netherland	PhD Student, Physics and Astronomy, Physics of LivingSystems	Physical virology: how physics is enabling a better understanding of recent viral invaders, Biophysical Reviews, 2023	2024/8/3~2024/8/18	12th NanoLSI Bio-SPM Summer School
28	Knelissen Yari Katar	26	PhD Student, Zernike Institute for Advanced Materials, Molecular Biophysics, University of Groningen	Netherland	PhD Student, Advanced Materials, Molecular Biophysics	-	2024/8/3~2024/8/26	12th NanoLSI Bio-SPM Summer School

29	Chen Rongjing	23	D1, Laboratory of Soft Matter Physics, The Institute of Physics, Chinese Academy of Sciences	China	D1, Soft Matter Physics	-	2024/8/4~2024/8/11	12th NanoLSI Bio-SPM Summer School
30	Wang Meijiao	28	PhD Student, Department of Chemistry, Renmin University of China	China	PhD Student, Advanced Light Conversion Materials and Biophotonics	Single-nucleus multi-omic profiling of human placental syncytiotrophoblasts identifies cellular trajectories during pregnancy. Nat Genet, 2024	2024/8/4~2024/8/11	12th NanoLSI Bio-SPM Summer School
31	Zhang Yuge	28	PhD candidate, Interdisciplinary Nanoscience Center, Bio-SPM group, Aarhus University	Denmark	PhD candidate, Interdisciplinary Nanoscience	-	2024/8/4~2024/8/12	12th NanoLSI Bio-SPM Summer School
32	Divinagracia Gideon	25	Undergraduate Student, Bioprocess Engineering Laboratory, Department of Chemical Engineering, University of the Philippines Diliman	Philippines	Undergraduate Student, Bioprocess Engineering	-	2024/8/4~2024/8/13	12th NanoLSI Bio-SPM Summer School
33	Mark John Maclachlan	51	Professor, The University of British Columbia	Canada	Ph. D. Supramolecular Chemistry, Nanomaterials chemistry	<ul style="list-style-type: none"> <li>•2016 Award for Research Excellence in Materials Chemistry (Canadian Society for Chemistry)</li> <li>•2015-2022 Tier 1 Canada Research Chair in Supramolecular Materials</li> <li>•2014 Steacie Prize for Natural Sciences (E.W.R. Steacie Memorial Fund)</li> <li>•2014 Elected Fellow of the Royal Society of Canada (FRSC)</li> </ul>	<ul style="list-style-type: none"> <li>①2024/8/17~2024/9/1</li> <li>②2025/2/15~2025/2/22</li> </ul>	Participation as principal investigator
34	Jin jun Xiong	68	Director, Institute for Artificial Intelligence and Data Science, University at Buffalo, the State University of New York	USA	Ph.D. Electrical Engineering	the 2024 Best Paper Award from the International Institute of Electrical and Electronics Engineers (IEEE)	2024/8/21	Discussion and observation of the research activities at NanoLSI
35	Yuri Korchev	64	Professor, Imperial College London	United Kingdom	Ph. D. Biophysics	The 2024 Science and Technology Minister's Award (the Japanese Ministry of Education, Culture, Sports, Science and Technology)	<ul style="list-style-type: none"> <li>①2024/9/2~2024/9/14</li> <li>②2024/11/11~2024/11/21</li> </ul>	Participation as principal investigator
36	Adam Stuart Foster	49	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	<ul style="list-style-type: none"> <li>①2024/9/6~2024/9/29</li> <li>②2024/11/8~2024/11/22</li> </ul>	Participation as principal investigator

37	Fabio Priante	-	Postdoctoral Researcher, Aalto University	Finland	-	The 2020 ACS CELL Division Graduate Student Award	2024/9/10~2024/9/24	Participation in MLM24 Symposium
38	David Gao	-	Director, Nanolayers Research Computing LTD	UK	Ph. D. Philosophy	-	2024/9/13~2024/9/22	Participation in MLM24 Symposium
39	George Heath	-	University Academic Fellow, University of Leeds	UK	-	-	2024/9/14~2024/9/22	Participation in MLM24 Symposium
40	Jiali Li	-	Senior Research Fellow, National University of Singapore	Singapore	-	-	2024/9/14~2024/9/22	Participation in MLM24 Symposium
41	Maria K Chan	-	Scientist, Argonne National Laboratory	USA	Ph. D. Physics	a Fellow of the American Physical Society (APS), 2024	2024/9/15~2024/9/20	Participation in MLM24 Symposium
42	Christian Wagner	-	group leader SPM&AI, Forschungszentrum Jülich	Germany	-	-	2024/9/15~2024/9/20	Participation in MLM24 Symposium
43	Oliver Hofmann	-	Assoc. Prof., Institut für Festk örperphysik	Austria	-	-	2024/9/15~2024/9/23	Participation in MLM24 Symposium
44	Beta Carsten	50	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	①2024/9/19~2024/10/11 ②2024/11/12~2024/11/30	Participation as principal investigator
45	DAMDINDORJ Boldbaatar	-	President, The Mongolian National University of Medical Sciences	Mongolia	MD, Medicine	Exogenous and endogenous ghrelin counteracts GLP-1 action to stimulate cAMP signaling and insulin secretion in islet $\beta$ - cells, FEBS letters, 2012	2024/10/22	Discussion and observation of the research activities at NanoLSI
46	BATBAATAR Gunchin	58	Vice president for Academic Affairs, The Mongolian National University of Medical Sciences	Mongolia	Ph.D., Medicine	Effect of Mycoplasma hominis and cytomegalovirus infection on pregnancy outcome: A prospective study of 200 Mongolian women and their newborns, PLoS One 12 (3), e0173283, 2017	2024/10/22	Discussion and observation of the research activities at NanoLSI
47	BAYASGALAN Tumenbayar	-	Director of Institute of Postgraduate Training, The Mongolian National University of Medical Sciences	Mongolia	MD, Medicine	2017 University of California Davis Global Affairs Seed Grant Award for International Activities	2024/10/22	Discussion and observation of the research activities at NanoLSI
48	DAVAALKHAM Dambadarjaa	48	Dean of School of Public Health, The Mongolian National University of Medical Sciences	Mongolia	Ph.D., Medicine	2004 Best researcher and best lecturer by the Ministry of Health of Mongolia	2024/10/22	Discussion and observation of the research activities at NanoLSI

49	ADILSAIKHAN Mendjargal	-	Director of Mongolia Japan Hospital of MNUMS, The Mongolian National University of Medical Sciences	Mongolia	Ph.D.	The inhibitory effect of salidroside on RANKL-induced osteoclast formation via NFκB suppression, In Vitro Cellular & Developmental Biology - Animal 61(1), 2024	2024/10/22	Discussion and observation of the research activities at NanoLSI
50	OYUNTUGS Byambasukh	-	Head of Department of Endocrinology, School of Medicine, The Mongolian National University of Medical Sciences	Mongolia	Ph.D. Philosophy	Relation between leisure time, commuting, and occupational physical activity with blood pressure in 125 402 adults: the lifelines cohort, Journal of the American Heart Association 9 (4), e014313, 2020	2024/10/22	Discussion and observation of the research activities at NanoLSI
51	ENKHJARGAL Gombojav	-	Senior lecturer of Dept. of Environment and Occupational health, School of Medicine, The Mongolian National University of Medical Sciences	Mongolia	Ph.D., Environmental Health	-	2024/10/22	Discussion and observation of the research activities at NanoLSI
52	KHANDMAA Sukhbaatar	-	Director of Department of Undergraduate education policy and management, The Mongolian National University of Medical Sciences	Mongolia	-	-	2024/10/22	Discussion and observation of the research activities at NanoLSI
53	ULZIIMAA Daramragchaa	-	Director of Department of International Relations, The Mongolian National University of Medical Sciences	Mongolia	-	-	2024/10/22	Discussion and observation of the research activities at NanoLSI
54	Guy TRAN VAN NHIEU	61	Principal Investigator, I2BC – CNRS UMR9198 – INSERM U1280	France	Ph. D., Medical Microbiology	Actin-based confinement of calcium responses during Shigella invasion. Nature Communications. 2013 Mar 5	①2024/10/25-2024/11/3 ②2024/12/9-2024/12/13 ③2025/3/23-2025/3/29	Bio-SPM Collaborative Research Program
55	Yvanoff Charlotte	34	PhD Student, Department of Bio-engineering Sciences, Vrije Universiteit Brussel	Belgium	PhD Student, Bio-engineering Sciences	-	2024/10/30~2024/11/23	Collaborative Research
56	Fernando Calvo	-	Tenured Scientific Leader, the Institute of Biomedicine and Biotechnology of Cantabria	Spain	Ph. D. Biomedicine	· ERC Consolidator Grant,2021 · I3 Scientific Excellence Recognition, 2021	2024/11/6	Participation in International Symposium on Tumor Biology and Interdisciplinary Sciences in Kanazawa 2024
57	Sophie Acton	-	Faculty of Life Sciences, University College London	UK	Ph. D. Biochemistry	Horsnell et al. Lymph node homeostasis and adaptation to immune challenge resolved by fibroblast network mechanics. Nat Immunol. 2022 Aug;23(8):1169-1182	2024/11/6	Participation in International Symposium on Tumor Biology and Interdisciplinary Sciences in Kanazawa 2024

58	Aki-Ogawa-Iio	-	Post-doctoral researcher, University of Cincinnati	USA	Ph. D., Internal Medicine	Expression analysis of protease-activated receptor-2 in cats, Veterinary immunology and immunopathology, Aug 31, 2020	2024/12/9~2024/12/11	Collaborative Research
59	Le Thi Phuong Ngan	32	Researcher, Vietnam National University Ho Chi Minh City	Vietnam	Ph. D. Microbiology	<ul style="list-style-type: none"> <li>•IUPAB Travel Award at The First International Symposium of Nano Life Science: Nanobiotechnology, Biosensor, Computation (NanoBioCoM2023)</li> <li>•Excellent Poster Presentation at the National Biotechnology Conference 2020, Institute of Biotechnology, Hue University, Vietnam</li> </ul>	2025/1/9~2025/2/9	Bio-SPM Collaborative Research Program
60	Antonio Jose Capezza	31	Senior Researcher, KTH Royal Institute of Technology	Sweden	Ph. D. Ph.D.Agricultural Science, Fiber and Polymer Technology	<ul style="list-style-type: none"> <li>•Best Innovation Award by Vattenfall AB at the Svergies Ingenjörsgdagen 2022</li> <li>•The Best Poster Award at the Seventh RIKEN-NCTU Symposium on Physical and Chemical Sciences in 2019</li> </ul>	2025/1/13~2025/1/30	Bio-SPM Collaborative Research Program
61	Christofer Lendel	47	Prof.KTH Royal Institute of Technology	Sweden	Ph. D. Structural and biophysical studies of molecular recognition mechanisms between protein molecules	Protein nanofibrils and their use as building blocks of sustainable materials, (Review Article) RSC Adv., 2021, 11, 39188-39215	2025/1/13~2025/1/30	Bio-SPM Collaborative Research Program
62	Rodrigo Sanches Pires	-	KTH Royal Institute of Technology	Sweden	Ph. D. student, Biophysical Chemistry	-	2025/1/13~2025/1/30	Bio-SPM Collaborative Research Program
63	Diego Carlero Carnero	32	Postdoctoral fellow, Centro Nacional Biotecnología	Spain	-	Conformational Dynamics of Influenza A Virus Ribonucleoprotein Complexes during RNA Synthesis, ACS Nano 18(30), July 2024	2025/2/2~2025/3/11	Bio-SPM Collaborative Research Program
64	Jaime Martin Benito Romero	58	Research Professor, Centro Nacional Biotecnología	Spain	Ph. D. Electron Microscopy Unit (Biochemistry)	Structural insights into the ability of nucleoplasmin to assemble and chaperone histone octamers for DNA deposition, Scientific Reports, Journal article, Part of ISSN: 2045-2322, 2019-12	2025/2/2~2025/3/11	Bio-SPM Collaborative Research Program
65	Rebeca Bocanegra	45	Research assistant, IMDEA Nanoscience	Spain	-	DNA replication machineries: Structural insights from crystallography and electron microscopy, In book: History of The Enzymes, Current Topics and Future Perspectives, July 2023	2025/2/14~2025/3/23	Bio-SPM Collaborative Research Program
66	Bui Nguyen Tram Anh	24	MSc. Student, Laboratory of Biosensors, University of Science, VNU-HCM	Vientam	MSc. Student, genomics and molecular biology	Best oral presentation in "International Workshop on Molecular Diagnostics in Microbiology and Diseases" conference held at ICISE, Quy Nhon city, Vietnam, Dec. 2023	2025/3/1~2025/3/9	Collaborative Research

## Appendix 6 FY2024 State of Outreach Activities

\* Fill in the numbers of activities and times held during FY2024 by each activity.

\* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2024 (number of activities, times held)
PR brochure, pamphlet	*NanoLSI Leaflet revised version (JP, EN) (3) *Open Facility Programs flyer revised version (EN) (1) *Bio-SPM Summer School flyer revised version (JP, EN) (1) *Bio-SPM Collaborative Research flyer revised version (JP, EN) (1) *Bio-SPM Visiting Fellows Program flyer revised version (JP, EN) (1) (Total: 7)
Lectures, seminars for general public	*NanoLSI Open Seminar (5) *Conference, Symposium including co-host (6) *Kanazawa University Open Lecture (1 by Hirao) (Total:12)
Teaching, experiments, training for elementary, secondary and high school students	*Lecture for Kanazawa Izumigaoka High School (4/10) *Feedbacks on research presentations for Kanazawa Izumigaoka High School (7/10, 7/17) *Cancer research Early Exposure Program (8/2, 8/5-7) *Feedbacks on research presentations for Nagano Senior High School (9/13) *Feedbacks on research presentations for Komatsu High School (11/2) *Annual Presentation Workshop of Ishikawa Super Science High Schools and Ishikawa New Super High School (1/22) (Total: 7)
Open houses	*Visit by Buffalo, The State University of New York (4/22) *Visits by MEXT (6/25, 7/22, 9/18, 3/18) *Provide hands-on training on NanoLSI Bio-SPM technology to International Union of Pure and Applied Physics (IUPAB) (7/1) *Visit by Hasanuddin University Faculty of Pharmacy, Makassar, Indonesia (7/18) *Visit by Institute for Artificial Intelligence and Data Science, University at Buffalo, the State University of New York (8/21) *Interview by The Japan Association of National Universities (9/3) *NanoLSI Facility Tour for the STELLA Program (Senior Course), Kanazawa University (9/23) *Visit by The Mongolian National University of Medical Sciences (MNUMS) (10/22) *Visit by Fukushima Institute for Research, Education and Innovation:F-REI (12/4) (Total: 12)
Participating, exhibiting in events	*13th WPI Science Symposium (11/16) (Total: 1)
Press releases	Hanayama/Yoshida (2), Shibata (2), Wang/Oshima/Zhang/Korchev, Kodera, Biyani, Fukuda/Takeuchi/Yano, Alam/Sumikama/Fukuma, Fukuda, Takahashi, Sakai, Ngo (2), Miyata, Ueno, Mizuno/Toda, Okuda, Arai, Okuda/Teranishi, Yurtsever/Fukuma/Asakawa, Kono/Shimi, Nakayama, Hirao, Konno, Yurtsever/Fukuma, Hanayama/Yamano/Lyu, Wong (2), Grant award, Call for Collaborative Research (Total: 31)
Others (TV program, Podcast)	*TV Program (5); NHK BS premium "Frontier", NHK BS "Frontier", NHK BS premium "Humanience: 4 Billion Years of Evolutionary Schemes", NHK BS "Humanience: 4 Billion Years of Evolutionary Schemes", BS-TBS "Hiroshi Sekiguchi: What's Going to Happen Next!?" *Podcast (10); Miyanari, Konno, Franz, Flechsig, Yurtsever, Shibata, Zhang, Biyani, Alam, Fukuda (Total: 15)

\*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 2024 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 00% 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 result of using OO to disseminate information, a 00% increase in inquiries from researchers was obtained over the previous year.
- As a result of vigorously carrying out OO outreach activity, ¥00 in external funding was acquired.

### I. Enhancing the visibility of NanoLSI's initiatives overseas

#### 1. Big Data and Machine Learning in Microscopy MLM24

The workshop "Big Data and Machine Learning in Microscopy MLM24" was held over three days from September 17 to 19, 2024, at the Shiinoki Cultural Complex, Ishikawa Prefecture (Hirosaka, Kanazawa City).

Led by Professor Adam Foster, one of the key overseas PIs at WPI-NanoLSI, the workshop was organized jointly by WPI-NanoLSI and the School of Science at Aalto University, with the theme of "Big Data and Machine Learning in Microscopy." The event hosted 42 participants from countries such as the United States, the United Kingdom, China, Canada, and Japan total 7 countries. In addition to a tutorial program aimed at early-career researchers, presentations and discussions were held on various topics, including data management in high-resolution microscopy and machine learning analysis methods, as well as the automation of microscopy observations.

#### 2. NanoBioCoM2024 in Quy Nhon, Vietnam

After the success of the first International Symposium of Nano Life Science: Nano Biotechnology, Biosensor, Computation (NanoBioCoM2023) held from 17-19 September 2023, we continued to organize the second symposium and focused more on the field of biophysics.

Biophysics is an interdisciplinary field that combines principles and methods from physics and biology to study the physical aspects of biological systems. The primary function of biophysics is to understand the underlying physical mechanisms and principles that govern the structure, dynamics, function, and behavior of biological molecules, cells, tissues, and organisms. Resolving differences between single molecule experiments and ensemble averaged experiments has fundamental importance in the area of the nano life sciences. The Second International Symposium of Nano Life Science: Nano Biotechnology, Biophysics, Computation (NanoBioCoM2024) is held from 25-27 September 2024 at ICISE, Quy Nhon, Binh Dinh province, Vietnam to provide participants a brilliant insight into new techniques and research trends in life science.

The main aim of this symposium is to introduce a wide range of experimental and computational methods relevant to modern nano life science that are able to comment on these differences. Vietnam, a developing country of nearly 100 million people, is actively creating research programs within the nano life sciences including nano biotechnology (nanomedicine, HS-AFM, FM-AFM, SICM), biophysics (biomolecular nanosystems, nanobio-hybrids, nanosized biostructures, nano-based biosensors), and computation and deep learning (artificial intelligence (AI) in biology). This symposium event is used to further stimulate these research programs by inviting a range of experts from both within Vietnam, and the world, to give structured talks on nano life science topics. The described computational methods range from coarse-grained simulation to molecular dynamic approaches.

The symposium has received 88 abstracts for plenary, keynote, invited, oral and poster presentations. There have been 50 abstracts assigned for oral and 38 abstracts assigned for posters. Presenters come from 19 countries such as Japan, France, Germany, Italy, Poland, USA, Canada, Taiwan, Thailand, Philippines, Malaysia, India, Pakistan, Kazakhstan, and Vietnam as well as 56 universities and research institutes. This symposium has awarded 40 scholarships for young researchers and excellent students to meet, learn and exchange academic topics with worldwide well-known scientists at NanoBioCoM2024.

### II. Enhancing collaboration with domestic research institutions

The 8th NanoLSI Symposium

On Wednesday, November 27, 2024, the 8th NanoLSI Symposium was held in collaboration with the Okinawa Institute of Science and Technology (OIST), attracting 81 participants.

OIST, an international educational and research institution, is renowned for drawing exceptional researchers and students from both Japan and abroad. With over 50% of its students and staff coming from outside Japan, OIST is a rare example of global diversity in the country. This joint symposium with OIST, which emphasizes interdisciplinary research and fosters advanced initiatives, provided an invaluable opportunity for learning and the exchange of ideas.

The symposium was organized by Professor Akihiro Kusumi from OIST and Professor Rikinari Hanayama from NanoLSI. Following the opening remarks by NanoLSI Director, Dr. Fukuma, the main session featured oral presentations from six researchers representing NanoLSI and OIST, sparking vibrant discussions among participants. Following this, the poster session included 26 presentations by young researchers from NanoLSI, OIST, and other institutions. The session maintained a lively and collegial atmosphere, enhanced by refreshments shared among attendees. After the sessions, some researchers discussed future collaboration, making the symposium a fruitful one.

On the next day, Thursday, November 28, a guided tour showcased OIST's cutting-edge research facilities, including its core labs and individual research units, allowing for further exchange and networking.

### III. Contribution to foster future young researchers

#### 1. The Cancer Research Early Exposure Program

The Cancer Research Early Exposure Program, especially for high school students, was organized by researchers from the NanoLSI and the Cancer Research Institute, Kanazawa University, following on from the previous year's program. The NanoLSI conducted six programs from 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, one researcher from the NanoLSI talked to high school students about her careers as a researcher 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.

No. of students: 45 in the research experience program and 34 in the seminar

Supported by: Hirao, Oshima, Shibata, Hirata, Nakayama, Arai, Watanabe, Sato, and Vu (9)

#### 2. 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.

In response to strong requests for support from Ishikawa Prefectural Kanazawa Izumigaoka High School, the following support from NanoLSI's researchers was provided in 2024 to the two-year research projects of the students of the Dept. of Science and Mathematics.

- ◇ 4/10: Lecture on how to start and key points for conducting research projects.  
No. of students: Second-year students 41  
Provided by: Sandhu (NanoLSI PR advisor)
- ◇ 7/10: Support for poster presentation (theme presentation) and advice from researchers (in Japanese).  
No. of students: Second-year students (presentation) 81, First-year students and Third-year students (audience) 119, total 200.  
Supported by: Konno, Arai, Sandhu (NanoLSI PR advisor), and several others.
- ◇ 7/17: Support for oral presentations of the research results and advice from researchers (in English).  
No. of students: Third-year students (presentation) 39, Second-year students and First-year students (audience) 81, total 120.  
Supported by: Sumino, Sumikama, Sandhu (NanoLSI PR advisor), and several others.
- ◇ 1/22: Ishikawa Super Science High School (SSH) Research Presentation and Ishikawa New Super High

School (NSH) Research Presentation (3 SSH schools and 5 NSH schools in Ishikawa have participated.)  
No. of students: Second year students (presentation) 164  
Supported by: Nakayama, Sandhu (NanoLSI PR advisor)

### 3. The Kanazawa University STELLA Program Junior Course

The Kanazawa University STELLA Program Junior Course, organized by Kanazawa University, is a program for elementary and junior high school students that aims to foster future scientists with a wide range of scientific knowledge and skills, as well as the ability to think independently and conduct their own research. The program emphasizes hands-on activities and group interaction, promotes individual research, and connects to the Kanazawa University STELLA Program Senior Courses (for high school students). The program is mainly open to elementary and junior high school students in Ishikawa, Toyama, and Fukui prefectures.

No. of students: 56\*

From FY2025, researchers from NanoLSI will also contribute to this program.

\*No. of students is expressed in cumulative total.

## Appendix 7 FY 2024 List of Project's Media Coverage

\* List and describe media coverage (e.g., articles published, programs aired) in FY2024.

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

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2024.4.19	Newspaper (1)	Award: Assoc. Prof. Satoru Okuda, The Minister of Education, Culture, Sports, Science and Technology Award for Young Scientists (Science News)
2	2024.5.24	Newspaper (1)	Research result: Asst. Prof. Koji Fukuda, Targeting WEE1 enhances the antitumor effect of KRAS-mutated non-small cell lung cancer harboring TP53 mutations (Hokkoku)
3	2024.6.21	Newspaper (1)	Others: Prof. Takeshi Fukuma, Column "Koyusho" (Nikkei)
4	2024.7.26-7.30	Newspaper (3)	Research result: Prof. Yasufumi Takahashi, Superatomic Layer of Cubic Mo4S4 Clusters Connected by Cl Cross-Linking (Nikkei, Kyodo PR Wire, Hokkoku)
5	2024.7.3	Newspaper (1)	Research result: Asst. Prof. Takashi Sumikama, Atomic force microscopy in 3D (Hokkoku)
6	2024.8.23	Newspaper (1)	Research result: Prof. Toshio Ando, PQBP3 prevents senescence by suppressing PSME3-mediated proteasomal Lamin B1 degradation (Science News)
7	2024.8.30	Newspaper (1)	Research result: Prof. Mikihiro Shibata, High-speed atomic force microscopy reveals dynamic behavior of brain receptors (Hokkoku)
8	2024.8.6	Newspaper (2)	Event report: Cancer research Early Exposure Program (Hokuriku Chunichi, Hokkoku)
9	2024.9.12	Newspaper (1)	Research result: Asst. Prof. Masaya Ueno, High sensitivity high throughput biosensor measures metabolite levels that indicate disease (Hokkoku)
10	2024.9.17-9.20	Newspaper (3)	Award: Assoc. Prof. Tatsuki Fukami, Assoc. Prof. Yusuke Miyanari, Assoc. Prof. Kyoko Nakagawa-Goto, Research grant by The Hokkoku Cancer Foundation (Hokkoku(3))
11	2024.9.18	Magazine (1)	Interview: Prof. Takeshi Fukuma, Interviewed article was published on the website. (Yotsuya Gakuin website)
12	2024.9.20	Newspaper (1)	Award: Prof. Masanobu Oshima, Received the Tomizo Yoshida Prize of the Japanese Cancer Association (Fukushima Minpo)
13	2024.11.8- 2025.2.27	Newspaper (9)	Award: Prof. Toshio Ando, Received the 2024 Leo Esaki Prize (Mainichi, Ibaraki(2), Asahi(2), Yomiuri, Tokyo Yomiuri(2), Nikkei(2), Nikkan Kogyo, Bunkyo News Flash)

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
14	2024.11.15-12.17	Newspaper (1), Magazine (1)	Research result: Assoc. Prof. Satoru Okuda, Stiffness distribution patterns in inner and outer tissue of the skin reversed during mouse growths (Science News, JST Science Japan)
15	2024.11.19-11.20	Newspaper (2)	Research result: Prof. Satoshi Arai, Development of fluorescence lifetime biosensors for ATP, cAMP, citrate, and glucose using the mTurquoise2-based platform (Nikkei, Nikkan Kogyo)
16	2024.12.5-12.25	Newspaper (8)	Research result: Assoc. Prof. Satoru Okuda, Evolutionary changes leading to efficient glymphatic circulation in the mammalian brain (Chunichi, Nikkei, To-o Nippo, Nishinippon, Hokkoku, Shizuoka, Nagasaki, Kahoku Shimpō)
17	2024.12.13-2.13	Newspaper (1), Magazine (1)	Research result: Assoc. Prof. Satoru Okuda, An actin bracket-induced elastoplastic transition determines epithelial folding irreversibility (Nikkei, JST Science Japan)
18	2024.12.16	Newspaper (1)	Event report: Prof. Masanobu Oshima, The 84th Annual Meeting of the Japanese Cancer Association will be held in Kanazawa in September, 2025. (Hokkoku)
19	2025.1.1	Newspaper (1)	Research result: Prof. Rikinari Hanayama, Development of an active targeting method using designer exosomes (Science News)
20	2025.1.23-2.15	Newspaper (3), Magazine (1)	Research result: Assoc. Prof. Takahiro Nakayama, Observing the shape changes in collagen fibers caused by ultraviolet rays and developing a new evaluation method (PR times, Livedoor, Jiji Medical, Cosmetic Science )
21	2025.2.25-3.11	Newspaper (3)	Award: Assoc. Prof. Yusuke Miyanari, Received a Specific Research Grant from Yazaki Memorial Foundation for Science and Technology (Nikkan Kogyo, Hokkoku, Nikkan Sangyo)
22	2025.3.3	Newspaper (1)	Others: Distinguished Professor Toshio Ando, Column "A Word on Management" (Nikkan Kogyo)
23	2025.3.24	Newspaper (1)	Research result: Prof. Richard Wong, Live imaging captures DNA folding in sperm cells for the first time (Nikkei)