World Premier International Research Center Initiative (WPI)
Executive Summary (For Interim Evaluation)

Host Institution	The University of Tokyo	Host Institution Head	Teruo Fujii
Research Center	International Research Center for Neurointelligence (IRCN)		
Center Director	Takao Hensch	Administrative Director	Nobukazu Toge

Instruction:
Summarize the Self-Evaluation Report for Interim Evaluation (**within 4 pages** including this page).

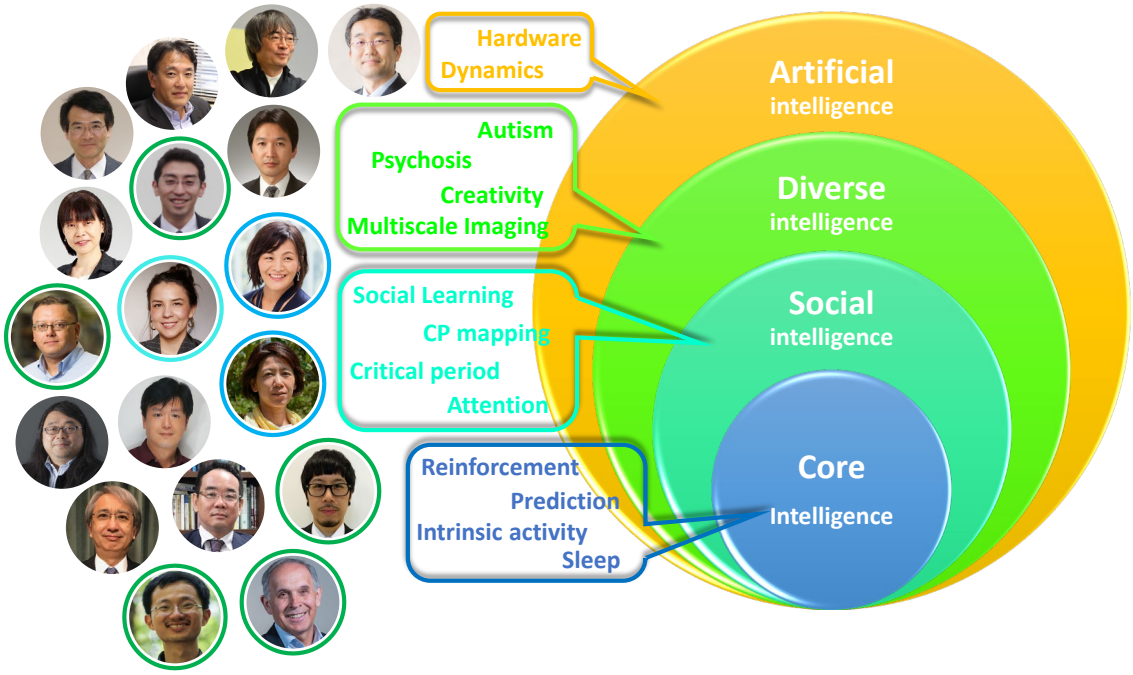
I. Summary

How does human intelligence (HI) arise? IRCN seeks 1) an understanding of the principles of brain development that underpin the emergence of HI, which in turn will 2) illuminate the etiology and treatment of cognitive disorders, and 3) inspire next-generation artificial intelligence (AI). The Center attained a well-balanced membership across gender, nationality and discipline, including neurobiology, human/clinical neuroscience, and computation. Just 3.5 years since its inception, the first seeds of IRCN's interdisciplinary fusion research are already bearing fruit as published products. Overall, IRCN is well-poised to build a visible and sustainable future that impacts society in the second half of its WPI term.

II. Items

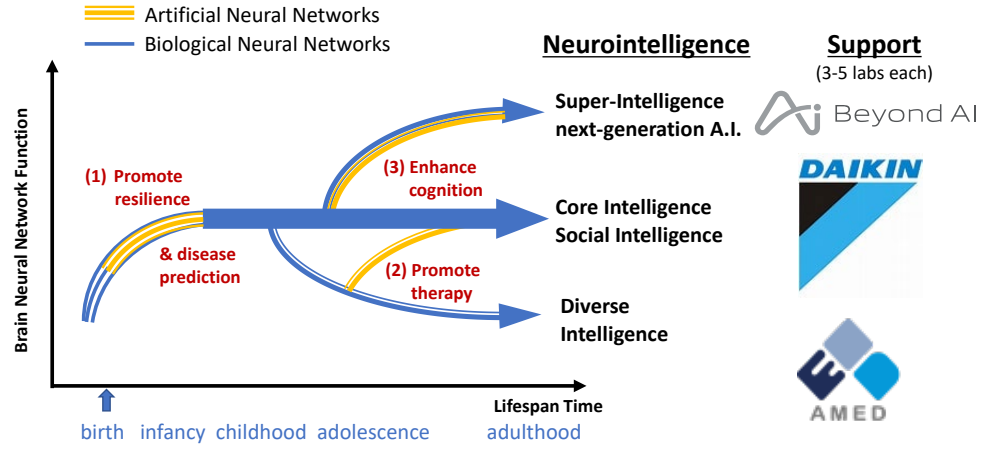
1. Overall Image of Your Center

We take the view that HI is composed of multiple intelligences – one that is informed by brain evolution. At its "core", each brain must be capable of learning (reinforcement), predicting and intrinsic activity/sleep. Collections of brains can then interact to yield a "social" intelligence that is shaped by attention, critical periods of shared experience and social learning. While aspects of core and social intelligence may be seen across species, further flexibility gives rise to "diverse" intelligence uniquely characteristic of humans, spanning a spectrum from creativity to mental disorders (autism, psychosis). Ultimately, AI inspired by these neurobiological insights will expand the capacity of HI, synergistically shaping our own future world. To answer "how does human intelligence arise", IRCN Team Science now addresses all four intelligences and how they are interrelated.



This IRCN vision of HI arising from nested intelligences has attracted 18 talented PIs at UTokyo from diverse disciplines, gender and nationalities (indicated in colored circles). An additional ~30 international Affiliated Faculty (AF) and dozens of postdoctoral or Associate Research Fellows (ARF) have joined the IRCN mission. By taking a brain development perspective, their fusion research has further focused the IRCN roadmap and milestones on

three major deliverables: 1) promote resilience & disease prediction early in life, 2) promote therapeutic strategies to redirect or reopen plasticity later in life, 3) enhance performance of HI in harmony with novel AI. These goals have been rewarded with competitive funding in FY2020, including collaborations with corporate sponsors like Softbank (BeyondAI) and Daikin, and leadership roles in JST, MEXT, and AMED grants, as indicated below.



文部科学省 科学研究費補助金 学術変革領域研究(A)
脳の若返りによる生涯可塑性誘導ーiPlasticity
臨界期生物学

2. Center's Research Activities

Research progress at IRCN has been vigorous since launching in Oct 2017. Capturing our fusion approach of uncovering novel principles of brain development, applying them toward novel computational psychiatry, and launching a more neuro-inspired AI are 10 examples:

I. NOVEL PRINCIPLES OF BRAIN DEVELOPMENT
- [1] Neuronal Mechanisms of Schizophrenia
- [2] Modeling Autism Spectrum Disorder
- [3] Organizing Principles of Auditory Circuits
- [4] Early Language/Song Development

II. NOVEL COMPUTATIONAL PSYCHIATRY
- [5] Machine Learning in Psychiatry
- [6] Large-Scale Analyses of Psychiatric Disorders
- [7] Dynamic Disease Prediction Algorithms

III. NOVEL ARTIFICIAL INTELLIGENCE
- [8] Deep Learning for Cellular Imaging
- [9] Reservoir Computing-Based AI
- [10] Novel AI Architectures

For example, collaboration between the labs of PI Haruo Kasai, a neurobiologist, and AF Shin Ishii, a computer scientist, generated multiple high impact papers in the last few years that promise even greater outcomes in the near future. Their seminal work, Iino et al (*Nature*, 2020), describes novel principles of brain circuits for reward learning that separate dopaminergic circuits to generalization (D1) and discrimination (D2). This yielded a novel computational AI framework built on reinforcement learning that makes robust hypotheses about the nature of psychotic hallucinations and the efficacy of D2 receptor antipsychotic drugs. A second example, from PI Kenichi Ohki, further illustrates how biological principles may guide computer vision. Utilizing cellular-scale imaging and modeling of neuronal responses in visual cortex, his lab found that partially overlapping receptive fields of neurons promote optimal image decoding against stochastic firing of neurons (*Nat Comms*, 2020), which may enhance the development of deep network AI.

Disease prediction is quickly becoming a powerful product of IRCN fusion research. The work of IRCN Deputy Director (DD) Kazuyuki Aihara, a computational scientist, provides new insights into the measurement and mathematical theory of the pre-disease state. His Dynamical Network Biomarkers theory shows great promise for detecting neurological conditions before they become irrecoverable. For this effort, he was chosen to lead a new JST Moonshot Program. In turn, principles of critical period biology have been revealed by the work at IRCN, which may enable a therapeutic reopening of brain plasticity (iPlasticity) in adulthood. This approach was recently awarded a major MEXT grant-in-aid program project (led by DD Masanobu Kano and involving several IRCN PIs) with UTokyo as a hub

supporting multiple labs across Japan. Clinical psychiatry research is also undergoing a revolution in methodology driven by the analysis and modeling of larger datasets, including the use of machine learning and deep neural networks to facilitate translation from animal models to rare patient populations. Both the Boston Children's Hospital Satellite (led by Director Hensch) and an AMED program project grant led by PI Kiyoto Kasai produced predictive biomarkers of neurodevelopmental disorders arising in infancy and adolescence, respectively (*PNAS*; *Mol Psych*; *Transl Psych,* 2020).

3. Feeding Research Outcomes Back into Society

Machine learning is a promising data-driven approach for analyzing / predicting dynamical phenomena in complex adaptive systems, such as in the brain, society and infrastructure. Several Social Collaborative Programs (SCP) have been established. DD Aihara leads the Intelligent Mobility Society Design with Toyota Central R&D Laboratories at UTokyo AI center, that proposed a mathematical method to infer nonlinear causality from time series data (S. Leng et al., *Nature Communications*, 2020) and analyzed real-world data, such as resting-state fMRI from monkeys or crowd flow at large sporting events. They also applied quantum annealing to large-scale traffic signal optimization to explore the potential of quantum computing (D. Inoue et al., *Sci. Rep.*, 2021).

DD Aihara also established an SCP for Brain-Morphic AI with NEC at the UTokyo Institute of Industrial Science on the mathematical modeling of dynamical neural networks and neuromorphic hardware implementation (Y. Sakemi et al., *Sci. Rep.*, 2020) and applied for several patents. DD Aihara has also collaborated with NTT and KKE (Kozo Keikaku Engineering), respectively, on developing photonic spiking neural networks (T. Inagaki et al., Nature Communications, 2021) and a practical system, RiverCast, for flood forecasting as an application of prediction with high-dimensional data (H. Ma et al., PNAS, 2018; S. Okuno et al., Sci. Rep.,2020; P. Chen et al., Nature Communications, 2020; S. Okuno et al., Water Resources Research, 2021) on the basis of his patent with KKE.

Through the Beyond AI joint project at UTokyo (SoftBank), PIs Ohki, Nagai, Tsuji, AF Nakayama and DD Aihara are working toward the development of highly reliable AI that utilizes brain activity data, insights from human infant learning or computational neuro-science for systematic understanding of cognitive individuality. Likewise, IRCN established an SCP (Chao, Daikoku, Miyamoto) with Daikin for research on "Neurocreativity" to identify novel biomarkers (EEG, microbiome, sleep) that facilitate the design of more creative and healthy environments for work and education. IRCN further aims to establish an SCP with NTTRI for Neuromorphic and Physics Inspired Energy-Efficient Information Processing.

Finally, the excitement of "Neurointelligence" research is reaching the general public, as a showcase, hands-on exhibit at the Miraikan science museum now through spring 2022. Nurturing next generation scientists with a stimulating global and interdisciplinary vision for society promises to be the lasting legacy of IRCN.

4. Generating Fused Disciplines

IRCN created a three-office structure to promote research "Synergy", "Community" and "Sustainability". Led by Deputy Directors (DD), these subgroups meet regularly to create a vibrant and inclusive research ecosystem. Synergy Office, in particular, has set aside seed funding to launch a "Team Science" approach to promote collaborative and inter-disciplinary research and selected twelve themes. These themes and collaborations are fundamentally proposed bottom-up, highlighting the strengths of our PIs. While they span very large conceptual and methodological spaces, the Teams nicely cover the four intelligences constituting HI (see item 1 above). Given limited resources and personnel, Teams are evaluated semi-annually by the Synergy Office which established criteria to narrow down and focus the Center's scope on the most successful fusions.

The Community Office engages Center members in various collective opportunities, such as graduate teaching, outreach planning, and support for international scientists. The Sustainability Office actively seeks funding opportunities to bridge IRCN research disciplines, such as domestic and international grants, potential donors, or corporate sponsors. To brainstorm new areas of fusion research, a weekly Science Salon, featuring one PI, AF or international partner, and Annual Retreat offer regular interactions.

5. Realizing an International Research Environment

Through open calls and targeted recruitment, IRCN now has ~30% foreign PIs (Konnerth, Hensch, Tsuji, Chao, Cai). For all PIs, IRCN directly supports one foreign postdoctoral fellow, as well as Team Science postdocs who are co-mentored across disciplines. Approximately 80% of the administrative staff is fluent in English to help researchers from overseas lead

comfortable research lives at IRCN. Announcements and communications are made in English and Japanese with a minimum time lag, and a portal site for internal use by IRCN members shares information in English on both research and daily life matters (eg. housing, home utilities, banking). Professionally managed core facilities enable foreign visitors to engage in research immediately upon arrival at UTokyo, including human fMRI; state-of-the-art cellular imaging for anatomy (STED, light sheet, confocal) or physiology (2P virtual reality, widefield 2P, functional ultrasound, mouse MRI); ES-mouse / Virus Core; Data Science analysis and modeling; Science Writing mentorship and editing support.

To further complement research domains represented at IRCN, the Director has made great efforts to establish a rich international network of ~20 partners, starting with Boston Children's Hospital satellite. Representative contingents from these sites regularly visit IRCN for symposia, workshops, teaching or research collaborations. This effort seeded a level of familiarity which has kept the Center in virtual contact with the rest of the world during the ongoing pandemic. Once travel is allowed, trainee exchange will be intensified. Notably, funds have been set aside for the Director's Globalization Award (DGA) to cover travel and stipend for incoming and outgoing interns. IRCN regularly hosts undergraduate summer interns from the Harvard Reischauer Institute, MIT, Europe or UC Berkeley, and runs a popular international "neuro-inspired computation" course.

6. Making Organizational Reforms

IRCN has expanded University reforms as follows: aggressive recruitment of a diversified ensemble of talented scientists (gender, nationality, discipline) at the Hongo Medical campus; assistance by bilingual administrative staff and regular use of English for Center activities; stimulating joint (split) appointments across departments; facilitating fusion research involving researchers from many faculties, laboratories, institutes and global partners; active involvement in the MEXT FoPM graduate training program that facilitates education spanning faculties; active trainee exchange from abroad.

7. Future Prospects

The pursuit of HI will continue at IRCN driven by Team Science in each of the four intelligences. Early examples above from 'Core' (Reinforcement, Prediction) and 'Diverse' Intelligences (Psychosis Risk, Autism) can further incorporate developmental aspects and interventions. The 'Social' Intelligence group has validated critical period timing mechanisms across species (mouse, zebrafinch, human) and a powerful role for attention in this plasticity (neuromodulation). Such neurobiological solutions have evolved over millenia and can now be introduced into computational models and developmental robots. Promising Multiscale Imaging and Critical Period Mapping tools are also anticipated. Eventually, the number of Teams will be reduced as a natural consequence of overlap and refinement, focusing on 1-2 topics for each of the 4 intelligence groupings in the post-WPI phase.

Most of the growth in the next 5 years of IRCN is expected in the outer ring of 'AI'. Team Science will be built around neuromorphic hardware and software architectures that more closely mimic brain processes. These are also opportunities to build SCPs with industry, like reservoir computing with Toyota Central R&D Labs or novel neuromorphic hardware designs with NTTRI and NTT. The fruits of the Moonshot Project for disease prediction are also expected to translate into applications or prophylactic treatments including wearable sensors that could interface with pharmaceutical or biofeedback companies. Applied IRCN science can contribute to the sustainability of the Center beyond the 10-year WPI period.

8. Host Institution's Concrete Plan toward Achieving the Center's Independence over the Next 5 Years (from its sixth year)

Support extended to IRCN from UTokyo is extensive and wide-ranging: occupancy of a large portion of Medical Building 1 to realize a nearly complete under-one-roof collection of labs; partial financial support of the human fMRI rental expenses; partial salaries for research and administration and partial research funding. IRCN PIs have been selected for University SCP (SoftBank, Daikin), attaining a substantial amount of outside funding. Four junior PIs receive salary and startup funds as UTokyo Excellent Young Scientists (Todai Takuetsu). In 2020, UTokyo announced it will issue corporate finance-type university bonds in order to finance part of its long-term operation. Together with IRCN fundraising, UTokyo will aggressively pave the way toward transforming IRCN into a permanent institution, increasing staff count and providing a new research building over the next ~10 years.

9. Others none

World Premier International Research Center Initiative (WPI)
Self-Evaluation Report for Interim Evaluation

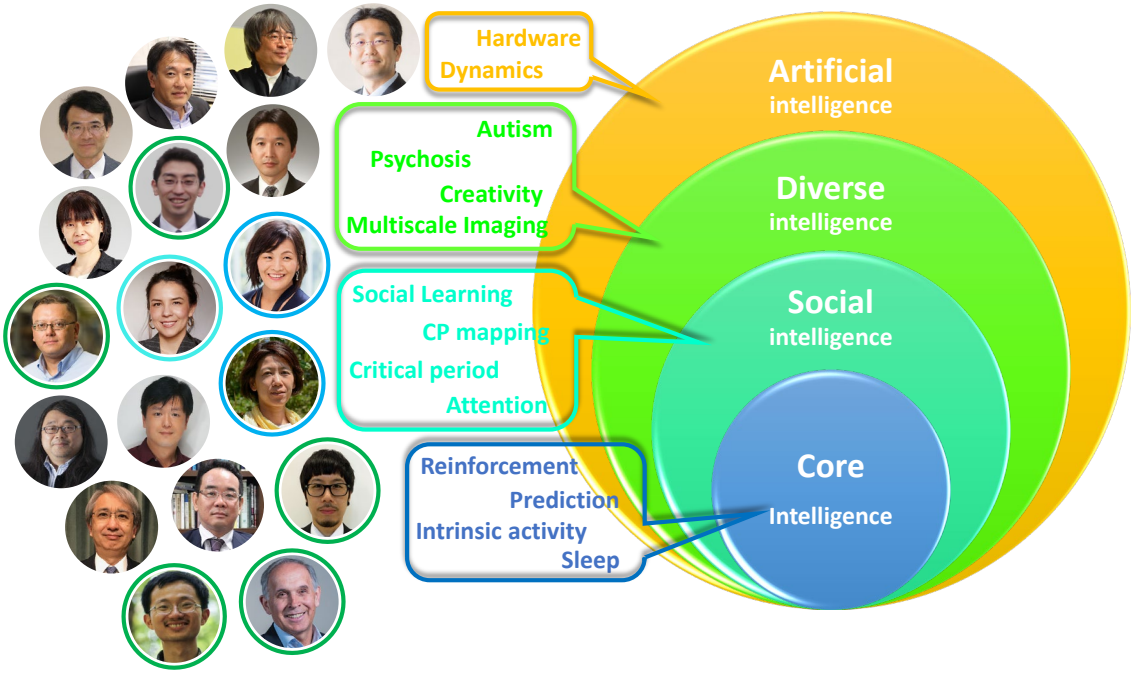
Host Institution	The University of Tokyo	Host Institution Head	Teruo Fujii
Research Center	International Research Center for Neurointelligence (IRCN)		
Center Director	Takao Hensch	Administrative Director	Nobukazu Toge

Common Instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2021) situation of your WPI center.
* As a rule, keep the length of your report within the specified number of pages. (The attached forms are not included to this page count.)
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

1. Overall Image of Your Center (write within 2 pages including this page)

Describe the Center's current identity and overall image.
- List the Principal Investigators in Appendix 2, and enter the number of center personnel in Appendix 3-1, 3-2, diagram the center's management system in Appendix 3-3, draw a campus map in Appendix 3-4, and enter project funding in Appendix 3-5, 3-6.

Human intelligence (HI) may justifiably be considered as the compilation of multiple intelligences. This perspective has been fruitfully espoused by social scientists and educators, most notably in the eight categories made famous by Professor Howard Gardner (Harvard Univ.): spatial, logical-mathematical, linguistic, musical, bodily-kinesthetic, interpersonal, intrapersonal and naturalistic intelligences. Such cognitive classifications are practical and applied effectively in the classroom but lack mechanistic insights on how they might arise. IRCN, therefore, seeks 1) an understanding of the principles of brain development that underpin the emergence of HI, which would, in turn, illuminate 2) the etiology and treatment of cognitive disorders, and 3) inspire next-generation artificial intelligence (AI).



Here, we also take the view of HI composed of multiple intelligences – one that is informed by brain evolution. At its "core", each brain must be capable of learning (reinforcement), predicting and intrinsic activity/sleep. Collections of brains can then interact to yield a "social" intelligence that is shaped by attention, critical periods of shared experience and social learning. While aspects of core and social intelligence may be seen across species, further flexibility gives rise to "diverse" intelligence uniquely characteristic of humans, spanning a spectrum from creativity to mental disorders (autism, psychosis). Ultimately, AI inspired by these neurobiological insights will expand the capacity of HI, synergistically

shaping our own future world. To answer "how does human intelligence arise", IRCN Team Science now addresses all four intelligences and how they are interrelated.

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Barely 3.5 years since its inception, the first seeds of IRCN's interdisciplinary fusion research are already bearing fruit as published products. For example, collaboration between the labs of PI Haruo Kasai, a neurobiologist, and AF Shin Ishii, a computer scientist, generated multiple high impact papers in the last few years that promise even greater outcomes in the near future. Their seminal work, Iino et al (*Nature*, 2020), describes novel principles of brain circuits for reward learning that attribute separate dopaminergic circuits to generalization (D1) and discrimination (D2). This yielded a novel computational AI framework built on reinforcement learning that makes robust hypotheses about the nature of psychotic hallucinations and the efficacy of D2 receptor antipsychotic drugs. A second example, from PI Kenichi Ohki, further illustrates how biological principles may guide computer vision. Utilizing cellular-scale imaging and modeling of neuronal responses in visual cortex, his lab found that partially overlapping receptive fields of neurons promote optimal image decoding against stochastic firing of neurons (*Nat Comms*, 2020), which may enhance the development of deep network AI.

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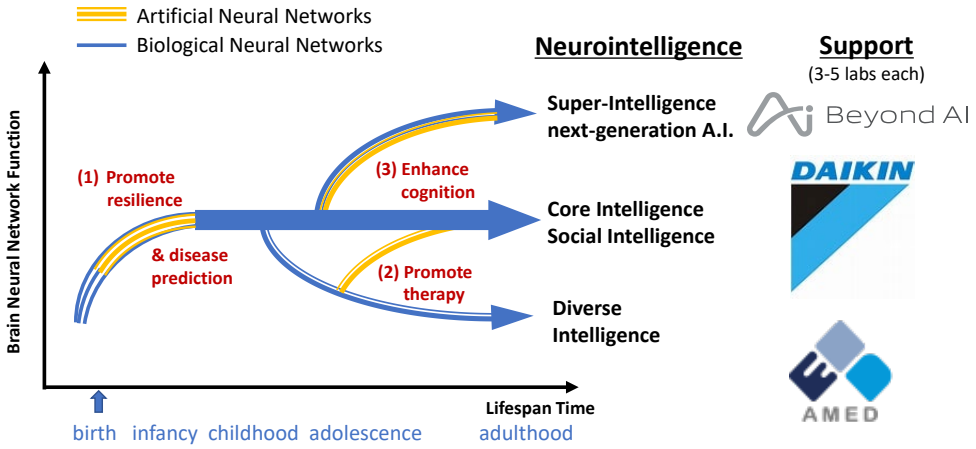


Overall, IRCN is well-poised to build a visible and sustainable future. The excitement of "Neurointelligence" research is reaching the general public, too, as a showcase, hands-on exhibit at the Miraikan science museum now through spring 2022. Nurturing the next generation of young scientists with a stimulating global and interdisciplinary vision for society promises to be the lasting legacy of IRCN.

MOONSHOT RESEARCH & DEVELOPMENT PROGRAM

文部科学省 科学研究費補助金 学術変革領域研究(A)
脳の若返りによる生涯可塑性誘導ーiPlasticity
臨界期生物学

2. Center's Research Activities (within 8 pages)

2-1. Research results to date

Give an overall picture of the Center's research activities. Select 10 representative research results achieved during the period from 2017 through March 2021. Number them [1] to [10] and provide a description of each.

- In Appendix 1-1, list the papers underscoring each research achievement (up to 20 papers) and provide a description of each of their significance. And in Appendix 1-4 list the center's research papers published in 2020.

Research progress at IRCN has been vigorous since its inception in October 2017. Below, we feature 10 areas that represent our fusion approach for uncovering novel principles of brain development, applying them toward novel computational psychiatry, and launching a more neuro-inspired A.I.

I. NOVEL PRINCIPLES OF BRAIN DEVELOPMENT

[1] Neuronal Mechanisms of Schizophrenia

a. Although symptoms first appear in adolescence and adulthood, the origins of the debilitating psychological disorder schizophrenia reside in the developing brain. The psychotic state of the schizophrenia brain, including hallucinations, delusions, and disordered thought and sociality, have largely eluded analysis at the level of neuronal mechanism. An interdisciplinary collaborative team of IRCN researchers hypothesized that psychosis involves defective neural signaling in a deep brain area called the ventral striatum. The researchers studied how mice predict future rewards in their environment, a behavior called reward learning that involves the release of dopamine onto neurons with a receptor called dopamine D1 receptor (D1R). Surprisingly, the team found that when the predicted reward fails to appear a second set of dopamine neurons is activated involving the dopamine D2 receptor (D2R), the major brain receptor for most antipsychotic medications. Reward omission triggers a sub-second signal in D2R neurons, called the dopamine dip, that facilitates discrimination learning and causes synaptic spines to expand and process signals in the D2R neurons. Using optogenetic technologies they artificially manipulated the dopamine dips and found that discrimination learning refines reward prediction and appears to go awry in psychosis.

b. A second study from a different IRCN collaborative team addressed the genetic basis of schizophrenia. Genetic risk factors for schizophrenia have been identified but their biological mechanisms remain largely unknown. The researchers explored the connection between a gene called Setd1a and impairments in synaptic function and behavior characteristic of schizophrenia. Setd1a is a histone methyltransferase that regulates the nuclear epigenome, and mutations in a human homolog have been identified in some schizophrenia patients resulting in increased disease risk. The team generated Setd1a mutant mice with a mutation found in a human patient and observed defects in behavior including sociality, working memory, and novel object recognition. Synaptic measurements revealed a deficit of synaptic transmission in the medial prefrontal cortex (mPFC) accompanied by reduced synaptic release and spine formation. RNA sequence profiling revealed changes in the levels of hundreds of genes including those related to synaptic functions, and developmental brain diseases and disorders. Further study of the Setd1a genetic network may help to understand the schizophrenia brain. Collectively, these results uncover novel principles of schizophrenia linking discrete neuronal mechanisms to the origins of mental illness and intelligence.

[2] Modeling Autism Spectrum Disorder

c. Autism Spectrum Disorder (ASD) is among the most common developmental brain disorders with a prevalence of 1 in 54 children in the US according to 2020 data from the Centers for Disease Control and Prevention. A scientific framework for one of the major overt symptoms of the disease, social impairment, remains lacking. Now, an IRCN collaboration has resulted in the identification of a synaptic mechanism shared by several ASD risk genes. The research team used a method called *in utero* electroporation to reduce gene expression levels of CNTNAP2 (contactin-associated protein-like 2) and AHI1 (Abelson helper integration site-1) in layer II/III pyramidal neurons of prefrontal cortex (PFC). They discovered a reduction in excitatory synaptic transmission in PFC neurons from both mutant mice. In behavioral tests, both strains showed impairments in social behavior and ultrasonic vocalizations similar to reduced social and communication abilities observed in ASD patients. Remarkably, social deficits in both mutant mice could be restored to normal levels with a drug called an ampakine (CX546) that enhances excitatory synaptic transmission. These findings suggest a common mechanism for social deficits in mice and potentially in patients, and that drugs such as CX546 may be candidate treatments, although they remain to be tested in the clinic.

d. ASD is characterized by a high degree of inter-subject variability in symptoms that computational models have been unable to explain. An IRCN team developed a novel computational model to examine how heterogeneity in ASD behavior might arise from continuous parameter modifications. They manipulated the parameters of a recurrent neural network corresponding to prediction ability, a cognitive mechanism thought to underlie atypical sensorimotor processing in ASD. Using a trajectory-learning task, they observed how network performance and its internal representation developed intrinsic variation and discovered two potential mechanisms for heterogeneity in ASD. Typical development and different forms of ASD showed opposite behavioral characteristics in the model, revealing a continuous process of prediction that is used during learning, and suggesting intrinsic cognitive variability in development. Behavioral performance and the quality of internal network representations in the model were not linearly correlated, thus better performance could not be predicted by better internal representations. These findings allow modeling of ASD aligned with experimental evidence of behavioral studies of ASD with important implications for promoting a stronger integration between behavioral and computational studies to account for ASD variability.

[3] Organizing Principles of Auditory Circuits

e. The mammalian auditory cortex is a leading model for the discovery of developmental principles of neural circuit organization of sensory information processing underlying higher cognition like language learning, and for markers of disordered cognition such as mismatch negativity seen in schizophrenia. An IRCN team identified a novel microcircuit in the mouse auditory cortex that mediates inhibitory gating of auditory critical period plasticity, a developmental process required for perceptual and cognitive development. A unique population of Layer 1 interneurons was found to send feedback projections to Layer 4 PV+ neurons that, in turn, are essential for regulating the tonotopic map critical period. This L1 projection is well-positioned to regulate thalamic drive onto L4 PV+ cells, and thereby shape the plasticity of auditory map formation. Layer I cells also contain the serotonin receptor 5-HT3$_A$R and α4 nicotinic acetylcholine receptor indicating that both inhibitory and volume transmission in multiple neuromodulatory networks converge on the L1 to L4 projection for finely-tuned critical period control. Thalamocortical maps in LI are stable and may serve as a scaffold for plasticity. Together, these findings, representing novel principles of neural development, will be useful for understanding brain processing for language development and predictive coding.

f. The 6-layer cortical column is a canonical feature of the mammalian neocortex. Cortical micro-architecture is evolutionarily conserved from mice to humans, portending common functional principles of information processing by neural circuits underlying cognition. Moreover, the columnar organization is a consequence of brain development, and unlocking its circuit logic is believed to be important for brain-based AI. A limitation of current understanding of the cortical column is the lack of studies that enable labeling and recording of neuronal activity from all layers in a comprehensive and unbiased manner to allow a fair estimation of functional contingencies. A team of IRCN researchers tackled this problem in the mouse auditory cortex that contains a tonotopic map and has served as a model for critical period development. They developed and used a novel 2-photon calcium imaging method at single-cell resolution to conduct a serial functional mapping of all pyramidal cell layers. They found that narrow columns crossing all layers have the best frequency responsiveness with fuzzy boundaries and a bandwidth of one octave. Local heterogeneity and sparse coding also define columnar organization as a reflection of neurodevelopmental wiring.

[4] Early Language/Song Development

g. Infant learning of words is enhanced by social cues provided by parents or caregivers. However, on-screen learning is increasingly common as digital tools proliferate. An IRCN team explored the role of social and communicative cues in the absence of a human tutor for word learning. Recruiting Japanese 12-month old infants, the team conducted on-screen word-object learning in conjunction with eye tracking to measure gaze following. They introduced contextual or referential social cues and measured word learning in reference to gaze following of the cues. These findings point to the effective enhancement of both gaze and word learning by social-communicative cues, contingency and reference, in the virtual environment with a non-human tutor. While the mechanisms of enhanced social learning were not definitely resolved by the current study, the innovative experimental design will enable an assessment of potential factors in isolation in future studies. As children increasingly learn from screens, the findings provide a coherent road map for further

exploration of social-communicative cues and the relationship between attention and learning in improving word acquisition outcomes. Conversely, environments and factors that adversely impair on screen learning and overall healthy brain development can also be empirically assessed.

h. Developmental critical periods for language and vocal communication, like their simpler sensory counterparts, frame normal neural circuit development, but the brain principles that define these windows are poorly understood. In the juvenile zebra finch, the higher auditory caudomedial nidopallium (NCM) is thought to harbor learning and memory traces of tutor songs, information that is critical for subsequent song production in males and song discrimination in females. An IRCN team measured neural activity in the NCM and the maturation of neurophysiological properties in response to song experience. Whole-cell patch clamp recordings of NCM neurons in juvenile birds during the sensory learning period revealed that a majority of neurons showed spontaneous firing, bursting patterns, and a transient surge in the number of active neurons during the peak of the learning period. Auditory isolation, in contrast, extended the sensory period and altered firing properties. These findings establish the developmental principle that physiological properties and memory encoding in NCM neurons reflect auditory experience during the critical period for vocal communication. Furthermore, the results suggest that the development of a cognitive AI could incorporate a triad of properties: learning windows, spontaneous activity, and information content.

II. NOVEL COMPUTATIONAL PSYCHIATRY

[5] Machine Learning in Psychiatry

i. The early detection of developmental psychiatric disorders enables potential therapy before critical developmental periods close and render the brain less receptive to rescue. The IRCN Boston Satellite developed a novel early biomarker for autism spectrum disorder (ASD) based on spontaneous pupil fluctuations and heart rate, indicators of arousal mediated by the cholinergic modulation of brain circuits. Early cholinergic defects were observed before overt symptoms in mouse models of idiopathic (BTBR) or monogenic (CDKL5 and MeCP2) ASD and a deep neural network trained on pupillary data (ConvNetACh) could recognize the abnormalities with 97% accuracy. The team developed a human clinical algorithm called ConvNetPatients by retraining the final network layers with heart rate variation data from Rett syndrome (RTT) patients. This hybrid algorithm showed significant accuracy in distinguishing RTT patients, indicating that the AI could mediate cross-species transfer learning of the biomarker. The results highlight the utility of mouse models in training patient-directed deep networks based on common neurobiological mechanisms. Furthermore, the study is a direct demonstration of applying neurodevelopmental principles, here, the timing of cholinergic signaling in brain arousal, to engineer novel AI-based clinical applications.

j. Computational psychiatry aims to combine large data analyses and modeling for greater predictive or diagnostic power of heterogenous mental disorders, and decode the natural spectral overlap between patients and disorders from variability of expression in single patient symptoms. Endophenotypes based on brain imaging data can enable such prediction to augment traditional behavioral diagnoses. In a collaborative study, IRCN members of a clinical consortium subjected structural brain imaging data from patients with schizophrenia or ASD, and subjects at ultra-high risk for psychosis, to a group of machine learning classifiers, and the outputs were correlated with behavioral prognoses. Classifiers based on cortical thickness or subcortical volume performed better than those for surface area, and they had the ability to accurately define disorder type and related behavioral symptoms. The results advance the selection of machine learning classifiers and their training parameters to effectively distinguish schizophrenia, ASD, and other psychiatric disorders in patient populations. Moreover, the prediction of psychosis may be facilitated by such classification protocols. However, there remains space for improvement and these studies show that principles of brain development and novel AI will be necessary to achieve practical clinical disease modeling.

[6] Large-Scale Analyses of Psychiatric Disorders

k. Given the genetic complexity, phenotypic overlap and spectral properties of psychiatric disorders, the identification of reliable brain endophenotypes is critical for accurate diagnostic classification. Recently, the Enhancing Neuro-Imaging Genetics through Meta-Analysis (ENIGMA) consortium published a comprehensive diffusion tensor imaging DTI white matter meta-analysis of

schizophrenia showing clear differences from control brains. In parallel, IRCN researchers are playing key roles in a large Japanese consortium, the Cognitive Genetics Collaborative Research Organization (COCORO) that recently reported an important replication study of the ENIGMA results. COCORO went further to compare DTI-based white matter microstructural differences in large cohorts of healthy controls (HCS) and individuals with schizophrenia (SZ), bipolar disorder (BPD), autism spectrum disorder (ASD) and major depressive disorder (MDD). Specific brain areas such as the corpus callosum showed similar disordered patterns while other differences were disorder-unique, such as specific neocortical tracts in SZ. In general, white matter patterns in SZ and BPD were similar, while MDD was more closely associated with HCS. These results provide valuable brain insights that will facilitate future AI-based predictive modeling in the clinic.

l. Adolescent-stage learning of prosocial behavior is one of the hallmarks of healthy cognitive and brain development in the peripubertal period when extensive connections between social brain regions are peaking. In a large population neuroscience study, IRCN researchers found key connections that play a role in the development of prosocial behavior in pre-teen children and show how the brain's chemical balance assists this wiring. In a multi-institute consortium, the team focused on the adolescent brain with advanced neuroimaging techniques that leveraged a large-scale study, the "Tokyo TEEN Cohort" involving 3,171 early adolescents. The authors used resting-state functional magnetic resonance imaging (rs-fMRI) of a subset of subjects to identify brain regions and found changes in the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC) linking brain activity and neural network structure. Connection strengths between the right ACC and middle/posterior cingulate cortex (MCC/PCC) positively correlated with prosocial behavior. Magnetic resonance spectroscopy (MRS) demonstrated a negative relationship in the ACC between prosocial behavior and GABA levels. These findings pinpoint a novel circuit for prosocial functioning and reveal how critical the early adolescent period is for the development of higher social cognition.

[7] Dynamic Disease Prediction Algorithms

m. The clinical diagnosis of a disease is traditionally based on a doctor's assessment after seeing a patient's overt symptoms and running confirmatory laboratory tests. However, the development of a disease obviously begins far earlier and novel methods to predict the so-called pre-disease state based on physiological measurements are of urgent medical and scientific interest. An IRCN team provided new insights into the measurement and mathematical theory of the pre-disease state. The current study employed a metabolic syndrome model, Tsuruma Suzuki Obese Diabetes (TSOD) mice. Using a mathematical theory called Dynamical Network Biomarkers (DNB) the researchers expected that a pre-disease state should precede a transition to overt disease. The team measured large-scale gene expression using DNA microarrays to capture the genetic signature of the pre-disease state before the emergence of symptoms. With the DNB theory they found that 147 genes alone could describe an animal's pre-disease state. The findings add to major diseases where the DNB theory has been shown to be useful in disease prediction. Future work will focus on psychiatric and other brain disorders for earlier interventions in these pervasive illnesses. More broadly, the DNB theory may be applied to any dynamic process to predict "tipping points" before they occur.

n. The pre-symptomatic prediction of clinical ASD critically depends on the identification of early biomarkers that combine an accurate link to pathophysiology and ease of detection. Brain oscillations measured by electroencephalography (EEG) are thought to be precise indicators of altered brain developmental trajectories captured in precise dynamical data. An interdisciplinary team based at the IRCN Boston Satellite used longitudinal EEG measurements in 3 to 36 month infants at low and high risk of ASD combined with data driven modeling of power trajectories to predict ASD clinical outcomes. Remarkably, EEG dynamics during the first postnatal year could best differentiate ASD diagnoses, particularly in the gamma and delta band range. A developmental shift across time scale to include high frequency power also predicted outcomes. The results introduce a powerful physiological tool and modeling approach for ASD diagnosis and provide insights on the specific dynamics and time course most useful for dissecting pathophysiology and classification of outcomes. Future work may extend this framework to other disorders of early postnatal brain development as well as to natural variations in normal cognitive functions and intelligence.

III. NOVEL ARTIFICIAL INTELLIGENCE

[8] Deep Learning for Cellular Imaging

o. An IRCN team investigated the historical problem of classification of the cell cycle, the backbone of eukaryotic development and regeneration. The researchers examined whether changes in cell biological features such as the nucleus, Golgi apparatus, and cytoskeleton tracked by a neural network trained on large numbers of cells can classify the cell cycle. They constructed convolutional neural networks (CNNs) and trained them with data from cells labeled with Hoechst (DNA), GM130 (Golgi) and EB1 (microtubule plus ends), targeting cell features that were known or presumed to show dynamic changes across the cell cycle. The results demonstrated that their CNNs could extract known cell features to classify the cell cycle phases of G1/S or G2. Combinations of features were even more effective at classification and a morphological analysis called Grad-CAM allowed them to identify pairs of features that were more effective in classification. The size and shape of the nucleus, for example, were identifiable classifiers. The results demonstrate that CNN models will become increasingly powerful classification tools for biological imaging. AI algorithms that can classify cell structure and dynamics with biological explainability will provide new insights on brain development for the enhancement of medical and pharmaceutical diagnostic applications.

p. AI-driven deep analysis of biological images promises to unlock large advances in understanding the structure and function of the brain's neuronal networks. However, a bottleneck in progress is the noise inherent in most images that prevents the acquisition of the type of clean, labelled images that deep networks require to better learn and predict new data. An IRCN team reported a new AI algorithm for the analysis of noisy pictures from 2-photon imaging microscopy. The team built a novel stacked-network architecture, with four U-nets arranged in tandem to process learning of images at coarse, medium, and fine scales, and termed Mu-net for "Multi-scale U-net". Data were collected from whole mouse brains virally-labelled with fluorescent indicators and made transparent with a tissue-clearing agent. To further enhance image quality, the researchers trained the Mu-net with another type of AI called a generative adversarial network (GAN) that enabled the images to become more robust to noise. Together, the Mu-net architecture with GAN training was successful in removing noise from images to a greater degree than other state of the art CNN-type models. Mu-net algorithms might become standards for the mapping of 3D brain structure and future work will focus on incorporating novel principles drawn from brain development and cognitive functions.

[9] Reservoir Computing-Based AI

q. Machine learning relies on training multilayer neural networks organized in a linear stack of pancake-like layers. Reservoir computing (RC), in contrast, replaces the layers with a nonlinear dynamical system of a recurrent neural network with fixed processing rules and training of only the connections to the output and are thought to be an intriguing contender for next generation AI. In a collaborative study, a team of researchers from IRCN and several partners including NEC, reported large improvements in RC efficiency after introducing key changes to the network's structure and internal parameters. The team achieved greater RC efficiency by redesigning internal connections in the standard reservoir model. Connections from past and/or drifting states in the time course of the computations were added to connect to the output layer. This change channeled the reservoir's useful state information to the output, while reducing the size of the reservoir without sacrificing computing efficiency. The type of network miniaturization achieved here is essential for the emergence of so-called edge computing, where data processing and cloud storage moves closer or even within end-user devices and sensors for local computing. The low power consumption of RC, unlike deep machine learning, may allow integration in embedded systems. Reservoir networks will also increasingly be explored for parallels in the human brain and various forms of intelligence.

r. Another limitation of current deep learning is that data from short time-series events with high dimensionality lack efficient and robust methods to predict future events. An international team of IRCN researchers sought to transform high-dimensional short time-series data through a neural network framework for the prediction of a target variable. They modified the network to generate the reservoir directly from the input spatial data and use it to generate a temporal output, making the network independent of external factors and enabling use of a data processing tool based on delay and non-delay embedding theory. They termed this framework an Auto-Reservoir Neural Network (ARNN), which can map spatial input data to future temporal values, a process called multi-step ahead prediction. Theoretical advantages of the method include improved prediction

accuracy, efficiency, and robustness, from relatively small, high-dimensional datasets. The model was tested on a wide range of real-world applications and was able to predict future outcomes based on relatively small datasets validating the utility of the method. One of the applications of ARNNs would be to use electrical brain activity and short-term behavioral data from humans or animals to predict future behavior and improve analysis or neurofeedback of human intelligence.

[10] Novel AI Architectures

s. One of the more remarkable talents of the mammalian brain is its ability to convert photons from visual scenes into interpretable patterns of neural signals in the visual and higher cortices. This conversion employs "sparse coding" where only small groups of highly active neurons are recruited to represent a visual scene. IRCN researchers employed cellular-scale imaging and reconstructive modeling of neuronal responses to show how the brain interprets sparse activity patterns. They found that optimal image decoding involved a high diversity of overlapping response properties for each cell, termed receptive fields, that provided full, redundant coverage of the range of visual features in the natural images. These properties allowed the visual cortex to remain robust to the stochastic firing of neurons, yet maintain reliable representation using only a few highly active neurons. These findings highlight the remarkable efficiency of the brain for information processing and may enhance AI development by introducing stochasticity to artificial neural networks (ANN). Indeed, the research team is finding that adding stochasticity to ANNs is helpful for the network to defend against adversarial examples, which is one of the most prominent limitations in current AI.

t. Beyond visual perception, human intelligence requires the exploitation or avoidance, respectively, of rewards and risks. An IRCN team developed a computational model of a novel form of AI called reinforcement learning in a multilayered neural network configuration called an extreme learning machine (ELM). The model, called OVaRLAP, contains computational elements similar to the D1 and D2 neurons that process respective positive or negative dopamine reward prediction error signals and drive two different patterns of reinforcement learning, generalization and discrimination. The team tested the performance of OVaRLAP in a computer game called the painful grid-world navigation task and observed high performance due to the fast generalization resulting from the D1- and D2-like elements in the network's final layer. However, when an impairment in the same discrimination learning by D2-like elements similar to human psychosis was applied to the ELM, the model surprisingly generated aberrant behavior that mimicked schizophrenia symptoms related to the dopamine reward system and its powerful generalization and discrimination capacity. Intriguingly, these results imply that future neuro-inspired AI might inherit both high cognitive capacities and mental disorders from their biological antecedents with implications for AI ethics.

2-2. Research environment including facilities and equipment

Describe the degree to which the Center has prepared a research environment appropriate for a world premier international research center, including facilities, equipment and support systems, and describe the functionality of that environment.

Most WPI Centers are launched with a new building designed for maximum research integration. In the absence of a new building on the crowded Hongo campus, IRCN has realized an "under-one-roof" research eco-system by renting and renovating space in the historical, 100 year-old Medical Building 1 immediately adjacent to and connected with the Faculty of Medicine Experimental Research Building. Together, they house all Core Facilities and most PIs and their laboratories. For example, to promote fusion research and daily interaction, one can find birdsong and mouse labs near a robotics and baby lab on the first floor. Small psychophysical testing rooms, a Collaboration Lounge and other common meeting spaces have been set up on the third floor, creating a casual and comfortable environment for daily exchange of research ideas, breakout discussions and small classroom instruction. The Human fMRI core includes small testing rooms, a mock scanner, global standard Siemens 3T Prisma scanner in the basement of the Experimental Research Building with a separate entrance for patients arriving from the clinic. A state-of-the-art cellular microscopy facility is on the third floor of the Medical Building 1, housing proprietary wide-field 2-Photon imaging (Nikon collaboration), functional Ultrasound (fUS) imaging of awake mice, homemade lightsheet microscope for cleared whole-brain tissue, 2P imaging with a virtual reality system, STED, confocal and light microscopes. The ES-mouse / Virus Core utilizes cutting-edge Genome editing and other bespoke technologies developed at IRCN to produce research reagents on demand. The Data Science core manages servers and data analysis and the Science Writing Core provides professional

editing and mentorship of the entire scientific writing and presenting process. All core facilities are led by expert managers at the Associate Professor level or above.

2-3. Competitive and other funding

Describe the results of the Center's researchers to date in securing competitive and other research funding.
・ In Appendix 3-6, describe the transition in acquiring research project funding.

IRCN faculty have been extraordinarily successful in obtaining extramural funds for collaborative research in 2020. Regarding funding from companies, SoftBank selected three PIs, Kenichi Ohki, Yukie Nagai, and Sho Tsuji (out of just 10 awarded) for their "The Beyond AI project" at UTokyo. Likewise, IRCN launched two Social Collaborative Programs (SCP, 社会連携講座) with Daikin, one of the largest companies to produce air conditioners, on creating work environments that promote efficiency and creativity. DD Kazuyuki Aihara established an SCP for Intelligent Mobility Society Design with Toyota Central R&D Laboratories at the AI center, UTokyo, in 2019.

At the governmental level, DD Kazuyuki Aihara was selected as Project Manager of the JST Moonshot Research and Development Program leading a project on "Comprehensive Mathematical Understanding of the Complex Control System between Organs and Challenge for Ultra-Early Precision Medicine". Another proposal by DD Masanobu Kano on "Biology of Critical Period" was selected as a Grant-in-Aid for Transformative Research Areas（A）（学術変革研究(A) (2020-2024). This large group grant will support many laboratories beyond IRCN, and includes Takao Hensch, Kenichi Ohki, Sho Tsuji and Kazuyuki Aihara as co-PIs. Yasushi Okada is head of the Grant-in-Aid for Scientific Research on Innovative Areas "Information Physics of Living Matters (2019-2023)". Kenichi Ohki (2021-2023) and AF Shinsuke Koike (2019-2023) are main PIs of the Brain/MINDS project by AMED while Kiyoto Kasai and Kazuyuki Aihara are main PIs of the Brain/MINDS Beyond project by AMED (2018-2022). Sho Yagishita (H. Kasai lab), Shinsuke Koike and Kiyoto Kasai were further awarded a Bruker animal MRI machine (JPY 4M) from Brain/MINDS AMED to be installed in IRCN. Yukie Nagai, Shoji Takeuchi and Yukiko Gotoh are lead PIs, respectively, of a JST-CREST "Cognitive Mirroring (2016-2021)", JST-CREST "Information Carriers and Innovative Devices (2020-2024)" and an AMED-CREST "Understanding of Biological Phenomena and Responses at the Early Life Stages to Improve the Quality of Health and Medical Care (2019-2014)".

In addition, PIs of IRCN have been very competitive in obtaining KAKENHI grants for their own studies. For example, Haruo Kasai, Kenichi Ohki, Yukiko Gotoh, Kazuyuki Aihara and Shoji Takeuchi obtained Grants-in-Aid for Scientific Research(S) （基盤研究(S)). The AFs of IRCN are also very successful in obtaining extramural funds for collaborative research related to IRCN. For example, Noboru Mizushima and Hiroki Ueda are leading, respectively, the JST-ERATO (MIZUSHIMA Intracellular Degradation) and JST-ERATO (UEDA Biological Timing) projects. AF Shigeo Okabe is the representative PI of the Grant-in-Aid for Transformative Research Areas（A）（学術変革研究(A)）"Glia Decode" (2020-2024) and also co-leading an AMED-CREST grant "Understanding of Biological Phenomena and Responses at the Early Life Stages to Improve the Quality of Health and Medical Care (2019-2014)", while AF Haruhiko Bito is leading the Grant-in-Aid for Scientific Research on Innovative Areas "Brain information dynamics underlying multi-area interconnectivity and parallel processing (2017-2021)". Also AF Reiko Mazuka leads a Specially Promoted Research grant entitled "Compensatory contribution of linguistic and social factors for early language acquisition: Cross-linguistic study between European and Asian languages (2020-2024).

2-4. State of joint research

Describe the results of joint research conducted with other research organizations both in and outside Japan.

Researchers of IRCN have been collaborating with many other research organizations both in and outside of Japan. The outcomes of such collaborative research are published as exemplified below:

(1) The international research group, led by Luonan Chen of the Chinese Academy of Sciences, Wei Lin of Fudan University and Kazuyuki Aihara of IRCN, used a method called randomly distributed embedding (RDE) to create a novel procedure for reducing high-dimensional data into simple lower dimensions that can more easily be transformed into statistical distributions for the generation of more accurate predictions (Proc. Natl. Acad. Sci. USA 115 (43): E9994-E10002, 2018).

(2) In collaboration with Haruo Kasai, a PI of IRCN, and Haruhiko Bito, an AF of IRCN, Conor Liston's group in the Feil Family Brain and Mind Research Institute and at Weill Cornell Medicine reveals that in mouse models of depression, a single dose of ketamine quickly reverses

depression-like behavior by promoting the growth of new synaptic connections (Science 364 (6436): eaat8078, 2019).

(3) In collaboration with Takao Hensch at IRCN, Michela Fagiolini and Charles A. Nelson, AFs of IRCN at Boston Children's Hospital, revealed that two simple, quantifiable measures — spontaneous fluctuations in pupil dilation or heart rate — could enable a much earlier diagnosis of Rett syndrome and possibly other disorders with autism-like features (Proc. Natl. Acad. Sci. USA 117(38):23298-23303, 2020).

(4) The COCORO consortium composed of Ryota Hashimoto of the National Center of Neurology and Psychiatry in Tokyo, Japan, Daisuke Koshiyama of the University of Tokyo School of Medicine, Naohiro Okada and Kiyoto Kasai at IRCN, and participating Japanese and international medical research institutions, used diffusion tensor imaging (DTI) to report complex patterns of microscopic changes in the brain's white matter across four major psychiatric disorders: schizophrenia, bipolar disorder, major depression, and autism spectrum disorder (Mol Psychiatry 25: 883–895, 2020).

(5) Together with Janet F. Werker's group in Canada (CIFAR), Takao Hensch at IRCN reported that synesthesia (共感覚) may result from incomplete pruning (剪定) of neural connections in the brain during infancy (Proc. Natl. Acad. Sci. USA 117(18): 10089-10096 2020).

(6) In collaboration with Masanobu Kano's group at IRCN, Masanori Sakaguchi, Masashi Yanagisawa and their colleagues at WPI-IIIS at the University of Tsukuba found that adult-born neurons in the dentate gyrus of the hippocampus are responsible for memory consolidation during rapid-eye-movement (REM) sleep (Neuron 107(3):552-565, 2020).

(7) An international team of researchers from the South China University of Technology (Pei Chen and Rui Liu), the Chinese Academy of Sciences (Luonan Chen), and IRCN (Kazuyuki Aihara) reported that a method for real world data analysis using a modification of a class of computing algorithms called reservoir neural networks showed surprising versatility and performance (Nature Communications 11(1):4568, 2020).

2-5. Appraisal by society and scientific organizations

Describe how society and/or scientific organizations in and outside Japan have recognized the Center's research achievements.

- To substantiate the above evaluation, list the main awards received and invitational/Keynote lectures given by the Center's researchers in Appendix 1-3.

Since the Center launched in October 2017, IRCN researchers have received many awards including highly prestigious commendations (see Appendix 1-3). For example, the Medal with Purple Ribbon from the Japanese Government was awarded to Haruo Kasai (2018), Yukiko Gotoh (2020) and AF Noboru Mizushima (2021); the Medical Award of the Japan Medical Association to Masanobu Kano (2018) and Noboru Mizushima (2020); the Inoue Prize for Science to Kenichi Ohki (2018), the Nakaakira Tsukahara Memorial Award to PI Yasushi Okada (2020), and the Naito Memorial Award for the Advancement of Science to AF Shigeo Okabe (2020). IRCN researchers are also regularly invited to various symposia and international conferences, including many Keynote or Plenary Lectures (see Appendix 1-3). These honors clearly reflect the global impact of IRCN PIs and AFs and their very high appraisal by scientific organizations and societies worldwide.

3. Feeding Research Outcomes Back into Society (within 2 pages)

3-1. Applications of research results

Describe the applications created from research results, their effect in spawning innovation, intellectual properties (IPs) obtained, and joint research activities conducted with corporations, etc.

DD Aihara established the Social Collaborative Program (SCP) for Intelligent Mobility Society Design with Toyota Central R&D Laboratories at the AI center, UTokyo in 2019. In this SCP, he performs the mathematical analysis of complex adaptive systems with IRCN Project Associate Professor Gouhei Tanaka, Dr. Yamashita, and researchers of Toyota Central R&D Laboratories. Machine learning is a promising data-driven approach for analyzing and predicting dynamical phenomena in complex adaptive systems. In fact, many systems in the real world are considered complex. The brain, social and infrastructure systems are all typical examples. To understand their structures, DD Aihara and colleagues proposed a mathematical method to infer nonlinear causality from time series data (S. Leng et al., *Nature Communications*, 2020) and analyzed real-world data, such as resting-state fMRI from monkeys or crowd flow data at large sporting events. They also applied quantum annealing to large-scale traffic signal optimization to explore the potential of quantum computing

(D. Inoue et al., *Sci. Rep.*, 2021).

In 2016, DD Aihara also established an SCP for Brain-Morphic AI with NEC at the UTokyo Institute of Industrial Science. He collaborated with IRCN AF Kohno, IRCN Project Associate Prof. Leleu and others on the mathematical modeling of dynamical neural networks and neuromorphic hardware implementation (Y. Sakemi et al., *Sci. Rep.*, 2020) and applied for several patents. IRCN is also collaborating with SoftBank through the Beyond AI joint project at UTokyo. Here, PIs Ohki, Nagai, Tsuji, AF Nakayama and DD Aihara are working toward the development of highly reliable AI that utilizes brain activity data and computational neuroscience for the systematic understanding of cognitive individuality and applied insights from human infant learning to AI.

As further activity on the application of research results, IRCN established in 2020 an SCP (Zenas Chao, Tatsuya Daikoku, Hiroyuki Miyamoto) with Daikin, Ltd. for research on "Neurocreativity" to identify novel biomarkers (EEG, microbiome, sleep) in order to facilitate the design of more creative and healthy environments for work and education. IRCN is further planning to establish an SCP with NTTRI for Neuromorphic and Physics Inspired Energy-Efficient Information Processing in 2021. DD Aihara has also collaborated with NTT and KKE (Kozo Keikaku Engineering), respectively, on developing photonic spiking neural networks (T. Inagaki et al., Nature Communications, 2021) and a practical system, RiverCast, for flood forecasting as an application of prediction with high-dimensional data (H. Ma et al., PNAS, 2018; S. Okuno et al., Sci. Rep.,2020; P. Chen et al., Nature Communications, 2020; S. Okuno et al., Water Resources Research, 2021) on the basis of his patent with KKE.

3-2. Achievements of Center's outreach activities

* Describe what was accomplished in the center's outreach activities during the period from 2017 through March 2021 and how the activities have contributed to enhancing the center's "globally visibility." In Appendix 5, describe the concrete contents of these outreach activities and media reports or coverage of the activities.

The portfolio of global outreach effort by IRCN includes numerous activities in the media, leaflets, presence in cyberspace, public exhibitions, face-to-face or virtual events and donation programs. While the COVID-19 situation in 2020 disrupted physical gatherings with a large number of participants, many virtual outreach activities were successfully maintained via the internet.

A large number of press releases were delivered between 2017 through 2020, most in both Japanese and in English. These are put forward on the IRCN website http://ircn.jp/ and http://ircn.jp/en/ carry the same information in both languages, and on social media via https://twitter.com/IRCN_UTokyo and https://www.facebook.com/University.of.Tokyo.IRCN that are also concurrently updated. Through these internet vehicles, IRCN has also been posting people, core facilities, collaboration and research activities, recruitment and events including International Symposia, Workshops, Computation Course, Opening Ceremony and monthly Science Salons. To emphasize IRCN's presence, English and Japanese version leaflets, pamphlets and novelty goods have been prepared, and are distributed to speakers and participants at IRCN-related events as well as to potential donors.

To intensively collaborate with other WPI institutes, IRCN co-sponsored an IPMU/ELSI/IRCN joint seminar and an IPMU/IRCN joint seminar, participated in a Super Science High School Event and the WPI science symposium. We also co-sponsored the UTokyo IIS/Riken AIP/IRCN joint symposium. IRCN has also hosted a special experiments program for high school students in 2018, 2019 and 2020. Open house events were successfully held in 2018 and 2019 with participation from local academic and general community members. We also contributed to a symposium and IRCN Core Facility Tour at The University of Tokyo Homecoming day and Festival. The annual Summer Student Internship Program and International Neuro-inspired Computational Course greatly raised the global visibility of WPI-IRCN.

At the Miraikan Science Museum in Tokyo, IRCN contributed to a public talk session in 2018, an Open Lab experiment in 2019, and has been holding a permanent exhibition since March 2021 to raise the interest of the general populace on the science of Neurointelligence that IRCN pursues.

4. Generating Fused Disciplines (within 3 pages)

4-1. State of strategic (or "top-down") undertakings toward creating new interdisciplinary domains

Describe the content of "top-down" measures taken by the Center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields.

In direct response to the 2019 WG comments, IRCN created a three-office structure to promote research, "Synergy", "Community" and "Sustainability". Led by each DD, these subgroups meet regularly to create a vibrant and inclusive research ecosystem. In FY2020, the Synergy Office, in particular, set aside seed funding to launch a "Team Science" approach to promote collaborative and inter-disciplinary research and selected twelve themes. As these collaborative Teams span very large conceptual and methodological spaces and not all will be equally successful, therefore, given limited resources and personnel, Teams are evaluated semi-annually by the Synergy Office which established criteria to narrow down and focus the Center's scope on the most successful fusions. Ultimately, each of the four intelligences constituting HI will be represented, as described in S01.

The Community Office engages Center members in various collective opportunities, such as graduate teaching, outreach planning, and support for international scientists. The Sustainability Office actively seeks funding opportunities to bridge IRCN research disciplines, such as domestic and international grants, potential donors, or corporate sponsors. The Executive Director also organizes a weekly Science Salon, featuring one PI, AF or international partner every Wednesday morning, and additional symposia. Finally, the Annual Retreat is used to brainstorm new areas of fusion research through interactive discussion and poster sessions.

4-2. State of "bottom-up" undertakings from the center's researchers toward creating new interdisciplinary domains

Describe the content of "bottom-up" measures taken by the Center to advance research by fusing disciplines. For example, measures that facilitate doing joint research by researchers in differing fields.

Team Science themes and collaborations are fundamentally proposed from the bottom up. This has generated 12 groupings that highlight the strengths of our PIs: Reinforcement learning, Prediction, Intrinsic Activity, Sleep, Critical Period Timing, Critical Period Mapping, Attention, Social Learning, Creativity, Psychosis Risk, Autism, Multiscale Imaging. Additional Teams are being planned for Chromatin Remodeling, and Novel AI Architectures (hardware) and Algorithms (software). The Synergy Office also supports an IRCN Program Committee (IPC, led by Masashi Sugiyama and Yoko Yazaki-Sugiyama) to solicit workshop and symposia ideas from PIs. The Community Office supports a grassroots organization, the IRCN Postdoctoral Advisory Committee (I-PAC, led by Sho Tsuji), that runs seminars on career development, scientific presentation, grant writing, etc. This has been very popular among foreign trainees who must quickly learn to navigate the Japanese research system and try to remain connected to the research communities in their home countries.

4-3. Results of research in fused research fields

Describe the Center's record and results by interdisciplinary research activities yielded by the measures described in 4-1 and 4-2.

- In Appendix 1-2, list up to 10 of the Center's main papers on interdisciplinary research that substantiate the above record of results, and describe their content.

The published outcomes from interdisciplinary fusion research are a work in progress due to the intrinsic multi-year publication timing of major studies, the necessary time required to develop cross-disciplinary knowledge and practical resources for fusion in a new center, and the slowdown of research during the COVID-19 pandemic. Nevertheless, current research results strongly validate the center's efforts toward creating a fused neurocomputation research field termed "neurointelligence" from a convergence of top-down management and bottom-up approaches.

A collaboration between the labs of Haruo Kasai, a neurobiologist, and Shin Ishii, a computer scientist, has yielded multiple high impact papers in the last few years, and promises even greater outcomes in the near future. The team's seminal work is Iino et al (2020) Nature describing novel principles of brain circuits for reward learning resulting in a novel computational AI framework built on reinforcement learning that is poised to fundamentally advance both fields of neurobiology and computer science as a fused discipline.

In Iino et al (2020) Nature, they investigated a poorly understood deep brain signaling system involving the dopamine D2 receptor (D2R), the major brain receptor for most antipsychotic medications. Reward omission in mice triggered a transient signal in D2R neurons called the dopamine dip, that facilitates discrimination learning. Using optogenetic technologies and pharmacology to control the dips they showed that aberrant discrimination learning causes a misappropriation of reward similar to that seen in psychosis.

A second study from the Kasai-Ishii collaboration, Fujita et al (2020), explored the computational significance of the D2R signaling system. They developed a computational model

based on D2R neurons as a novel form of reinforcement learning-type AI in a multilayered neural network configuration called an extreme learning machine (ELM). In a virtual navigation task the model showed powerful discrimination learning and performance but when the D2R element was removed they surprisingly observed psychosis-like behavior.

Finally, their third study, Lee et al (2020) is potentially the most important work of the three, in developing an AI for the analysis of noisy 3D images from 2-photon microscopy. Image noise prevents the acquisition of clean, labelled images that deep networks require to learn and predict new data. The team built a novel AI architecture termed Mu-net with generative adversarial network (GAN) training that enabled the images to become more robust to noise. AI-driven deep analysis of this type promises to decode the brain's neuronal networks.

Like the Kasai-Ishii collaboration, other IRCN publications show the emergent fusion of biology and AI disciplines. While these studies originated mainly in one lab, they illustrate the change in fundamental perspective toward the integration of data analysis and modeling with traditionally descriptive biological research with an eye toward novel AI; for now, machine learning, but soon involving more innovative architectures.

The lab of Yasushi Okada with Daisuke Takao created a novel AI for image analysis (Nagao et al (2020). They used the classification of cell cycle phase as a model system to test their algorithm, examining whether changes in cell features such as the nucleus, Golgi apparatus, and cytoskeleton could be tracked by a convolutional neural network. The results demonstrated that their CNNs could extract cell features to classify cell cycle phase and such AIs are already becoming powerful classification tools for brain/biological imaging.

Machine vision is one of the high-profile fields in AI, but can animal vision provide biological principles to guide its development? The lab of Kenichi Ohki (Yoshida et al, 2020) sought to understand a puzzling property of biological vision observed in neurons of the visual cortex where a small number of stochastic neurons can reliably represent complex natural scenes. Using cellular-scale imaging and modeling of neuronal responses, they found that sparse coding promotes optimal image decoding, yet achieves stable representation, a finding that may enhance AI development by introducing the concept of stochasticity to artificial neural networks.

Novel methods to predict pre-disease states based on physiological measurements are of urgent medical and scientific interest. Kazuyuki Aihara, a computational mathematician, and his group have an ongoing project to fuse the modeling of pre-disease states with applied clinical fields and provide new insights into the measurement and mathematical theory of the pre-disease state. A recent study, Koizumi et al (2019), Using a mathematical theory called Dynamical Network Biomarkers (DNB) to predict metabolic syndrome in an animal disease model. The interdisciplinary fusion of this framework is the basis of the Aihara Moonshot Project.

Clinical psychiatry research is undergoing a revolution in methodology driven by the analysis and modeling of larger datasets coupled with a more precise mechanistic underpinning of disorders based on biology, especially imaging. AI tools are an emergent part of this field and IRCN is centrally positioned to coordinate progress with key clinical researchers in Japan coupled to its biological and neurocomputational networks. The IRCN Boston Satellite is another node for clinical translation and fusion as recent studies demonstrate.

In a fusion of clinical and computer sciences, IRCN members analyzed structural brain imaging data from patient cohorts with schizophrenia or ASD, and subjects at ultra-high risk for psychosis, to a group of machine learning classifiers, and the outputs were correlated with behavioral prognoses (Yassin et al, 2020). The classifiers accurately predicted disorder type and behavioral symptoms, providing insight on the parameters for optimal machine learning classification and training for psychiatric disorder imaging data.

The IRCN Boston Satellite developed a novel early biomarker for autism spectrum disorder (ASD) based on spontaneous pupil fluctuations and heart rate, indicators of cholinergic modulation of nascent brain circuits (Artoni et al, 2019). A deep neural network trained on mouse pupillary data recognized cholinergic abnormalities with 97% accuracy and when retrained with human data (transfer learning) showed significant accuracy in identifying RTT patients. This product demonstrates the power of neurodevelopmental principles to inspire novel AI-based clinical applications, relying on abundant animal data to test and diagnose rare disorders in humans.

5. Realizing an International Research Environment **(within 4 pages)**

5-1. International Circulation of Best Brains

5-1-1. Center's record of attracting and retaining top-world researchers from abroad

Describe the participation of top-world researchers as PIs and their stays as joint researchers at the Center.

・ In Appendix 3-2, give the number of overseas researchers among all the Center's researchers, and the yearly transition in their numbers. In Appendix 4-2 give the achievements of overseas researchers staying at the center to substantiate this fact.

IRCN was launched with only two foreign PIs, Arthur Konnerth and Takao Hensch. Through an open call and targeted recruitment in FY2018, they were joined by three more human cognitive scientists, Sho Tsuji, Zenas Chao and Mingbo Cai. Over the same timeframe, IRCN made formal MOU agreements with several premier research institutes worldwide (see S5-1-3 below). This generated a consistent stream of faculty visitors until the pandemic shut down travel. IRCN also hosted two Professors from McGill University (Jon Sakata, Sarah Woolley) as part of the Tokyo College Program. Numerous non-PI faculty level members also participated in IRCN fusion research and events, including Affiliated Faculty (AF; senior) and Associate Research Fellows (ARF; junior).

5-1-2. Employment of young researchers at the Center and their job placement after leaving the Center

Describe the Center's employment of young researchers, including postdoctoral researchers, and the positions they acquire after leaving the Center.

・ Enter the following to substantiate the facts provided above:
- In Appendix 4-3, describe the Center's state of international recruitment of postdoctoral researchers, the applications received, and selections made.
- In Appendix 3-2, give the percentage of postdoctoral researchers employed from abroad
- In Appendix 4-4, describe the positions that postdoctoral researchers acquire upon leaving the Center.

IRCN directly supports one foreign postdoctoral fellow per PI lab as well as Team Science postdocs who are co-mentored across disciplines. While most fellows from abroad have yet to reach their first full 3-year term, some talented senior fellows from Japan have moved on to faculty positions from IRCN. These include Ayuko Hoshino (Tokyo Tech), Takashi Kanamaru (Kogakuen Univ.), Timothee Leleu (UTokyo), Yoshito Hirata (Tsukuba Univ.) and Mayumi Kimura (Deputy AD, WPI-IIIS).

5-1-3. Overseas satellites and other cooperative organizations

・ In Appendix 4-1, describe the state of cooperation with overseas satellites and other cooperative organizations. In Appendix 4-5, describe the state of the Center's agreements concluded with these organizations.

The IRCN satellite is located at Boston Children's Hospital (BCH), the largest pediatric hospital in the United States and consistently ranked number 1 in the country for Neurology (US News & World Report). BCH serves an unparalleled role bridging world class neurodevelopmental research in mouse models to clinical studies with human patients. Specifically, the work focuses on perinatal brain trajectories and critical period principles in the first years of life to complement the focus on adolescence at UTokyo IRCN. AFs include Michela Fagiolini (Neurology), Charles Berde and Laura Cornelissen (Anesthesiology), Charles Nelson (Developmental Medicine), David Hunter (Ophthalmology) and computational modelers Nancy Kopell and Michelle McCarthy (B.U.). Many have spoken at IRCN over the past few years in workshops, international symposia, and science salons. Three important translational research projects are currently underway: 1) impact of repeated neonatal anesthesia on brain development trajectories, 2) EEG biomarkers of excitatory-inhibitory circuit imbalance predictive of autism risk, and 3) recovery from amblyopia (lazy eye) by critical period reopening strategies. All are expected to alter clinical best practice following publication. Basic research studies have contributed directly toward establishing innovative whole-brain functional ultrasound imaging in the Multiscale Imaging Team, and alos the Critical Period Timing Team, Critical Period Mapping Team, Attention Team, Social Learning Team, and Autism Team Science. Other related faculty, including Gabriel Kreiman, Patrick Purdon, Laurel Gabard-Durnam, Hisashi Umemori and Chinfei Chen, also visited to foster collaboration with IRCN PIs.

To further complement research domains represented at IRCN, the Director made great efforts over the first 3 years to establish a rich international partner network. Representative contingents from each of these sites have already visited IRCN for symposia, workshops, teaching or research collaborations prior to the COVID-19 pandemic. This effort seeded a level of familiarity which has kept the Center in virtual contact with the rest of the world during the ongoing travel shutdown. Active collaborations were recently launched with A*Star (Singapore), CIFAR (U British Columbia), Ecole Normale Superieure (France), Univ Bielefeld (Germany), KTH (Sweden) and OIST (Japan).

5-2. Center's record of holding international symposia, workshops, research meetings, training meetings and others

- In Appendix 4-6, describe the main international research meetings held by the Center.

As summarized in Appendix 4-6, IRCN has hosted 48 mid- to large-scale symposia or major schools in years 2017 through 2020. The total number of participants exceeded 2,400, with approximately 40% from overseas. The subjects covered by these meetings include: Neurointelligence in general, Neuronal Circuits, Neuro-inspired Computation, and Deep Learning.

5-3. System for supporting the research activities of overseas researchers

Describe the Center's preparations to provide an environment conducive for overseas researchers to concentrate on their work, including for example living support in various languages or living support for their families.

The administrative group at IRCN consists of several teams in accordance with their areas of expertise: the general affairs team (gTeam) to manage general affairs, human resources, visas, benefits, regulations and orientations for living in Japan; the financial team (fTeam) to manage budget, procurement and facility; the research support team (rTeam) to help researchers access sources of external funds, prepare grant applications, research contracts and safety and compliance matters; the international team (iTeam) to support organizing international seminars and events. They are complemented by the public relations group (PR Group) and the networking / information technology group (IT Group), and the Science Writing Core, on their specialized matters, respectively. Approximately 80% of this staff is fluent in English to help IRCN researchers from overseas lead comfortable research lives at IRCN. Announcements and communications are made in English and Japanese with a minimum time lag, and a portal site for internal use by IRCN members has been in operation for sharing information in English on both research and daily life matters (eg. housing, home utilities, banking).

5-4. Others

Describe the Center's policy for sending Japanese researchers overseas to gain international experience, and give examples of how the Center is working to create career paths for its researchers within a global environment of researcher mobility.

Although COVID-19 has slowed the exchange of researchers across borders, IRCN remains fully engaged in globalization efforts by co-hosting virtual conferences on neuro-inspired A.I. and weekly salon seminars including speakers from the network of worldwide MOU partners (above) established prior to the pandemic. Once travel is permitted, extra effort will be made toward trainee exchange. Notably, funds have been set aside for the Director's Globalization Award (DGA) to cover

travel and stipend for incoming and outgoing interns. IRCN already has experience in hosting summer undergraduate research students from the Harvard Reischauer Institute, MIT, UC Berkeley and Europe. With such a research environment constantly populated with a number of researchers from abroad, young Japanese members of IRCN build social networks and gain working experience with researchers from diverse backgrounds. Appreciating how to aid colleagues from abroad, Team Science trainees from IRCN will be actively sent to partner institutions to foster collaboration and build career paths through the DGA mechanism. The Director has already begun placing UTokyo Medical Students at Harvard Medical School for spring internships during their free quarter.

6. Making Organizational Reforms (within 3 pages)

6-1. Decision–making system in the center

Describe the strong leadership that the director is giving on the Center's operation and its effect, and the division of roles and authority between the Center and its host institution.
- In Appendix 3-3, draw a concrete diagram of the Center's management system.

All Center decisions are finalized by the Director in weekly consultation with the Executive Board (EB) and approval by bi-monthly Steering Committee (SC) vote. The Center's decision-making bodies as of FY2020 are outlined in Appendix 3-3 and how they operate together is described in Appendix 6-1-2. Daily operational decisions and chores are made between the AD, GM and Director within the Center. Overall budget, PI-level hiring and enactment of bylaws are subject to approval by the University of Tokyo Institutes for Advanced Study (UTIAS). Long-range planning on institutional matters of the Center is the subject of semi-regular discussion by EB members, the Director of UTIAS and Directorate of UTokyo. To facilitate communication with the Medical School and UTokyo Headquarters, starting April, 2021, the AD and Director will be assisted by a new Special Advisor to the Director (SAD), Prof. Masamitsu Iino, formerly Vice Dean at UTokyo School of Medicine who is familiar with the infrastructure of University operations and Medical Building 1.

6-2. Arrangement of administrative support staff and effectiveness of support system

Describe the assignment of the Center's administrative support staff who have English language and other specialized skills, effort made in establishing the support system, and the system's effectiveness.

Section 5-3 has described IRCN's approach to this issue. The staff has turned over drastically in the past two years and is fully functional as of Spring 2020. One area of need is to replace URAs with research knowledge to support grant submission. With anticipated growth of research funds in the near future (Moonshot, MEXT program project grants, etc…) and the post-COVID-19 environment, continual monitoring of the whole capacity of the administrative staffing is considered mandatory.

6-3. System reforms advanced by WPI program and their ripple effects

Concisely itemize the system reforms made to the Center's research operation and administrative organization, and describe their background and results. Describe the ripple effects that these reforms have on the host institution. (If any describe the ripple effects on other institutions.)

IRCN has expanded University reforms in the style of Kavli IPMU in the following areas:
(1) Aggressive recruitment of a diversified ensemble of talented scientists (gender, nationality)
(2) Assistance by bilingual administrative staff and regular use of English for Center activities
(3) Stimulating joint (split) appointments across departments
(4) Promotion of fusion research involving researchers from many faculties, laboratories, institutes and global partners.
(5) Involvement in the MEXT FoPM graduate training program that facilitates education spanning faculties and enhances the presence of IRCN in the academic community of the University.
(6) Active trainee exchange from abroad and expected to work reciprocally post-COVID-19.

6-4. Support by Host Institution

The following two items concern the support that the host institution provides the Center. Describe the measures that the host institution has taken to sustain and advance the Center's project. That include the item of support that it committed to at the time of the initial project proposal submittal.

6-4-1. Record of host institution support and its effects

・ In Appendix 6-1, describe the concrete measures being taken by the host institution.

From an organizational standpoint, IRCN is set up as a research center within the University of

Tokyo Institutes for Advanced Study (UTIAS). As such, the Center has been empowered to enact its own IRCN-specific internal rules on governance, personnel hiring and management over Center-wide research directions under the leadership of the Center Director, apart from other Faculties and Institutes of the University. The Director directly takes charge of the center's organizational management to maintain IRCN's strong positioning with its ambitious program of collaborative fusion research and aggressive recruitment of research experts from overseas.

Within this framework, the support extended to IRCN from UTokyo is extensive and wide-ranging. IRCN has been allowed occupancy of a large portion of Medical Building 1 to realize a nearly complete under-one-roof collection of its laboratories, partial financial support for the human fMRI rental expenses, part of research and administrative members' salaries, as well as part of its research funding. In addition, IRCN has been offered to join in Social Cooperation Programs of the University (SoftBank, Daikin), attaining a substantial amount of outside funding. Some of the IRCN faculty hired in part by WPI funds are offered dual teaching positions which contribute to the education program of the University as well as to enhance the recognition and presence of IRCN within the academic community of UTokyo. Finally, four junior PIs have been named UTokyo Excellent Young Scientists (Todai Takuetsu) and receive salary and startup funds.

6-4-2. Position of the Center within the host institution's mid-term plan

・ To Appendix 6-2, excerpt the places, in the host institution's "Mid-term objectives" and/or "Mid-term plan" that clearly show the positioning of the WPI center within its organization.

Prior to IRCN being awarded in October 2017, the "3rd phase mid-term objectives" and "mid-term plan" of the University of Tokyo published in 2016 could make no specific mention of the Center. However, "Vision 2020" of The University of Tokyo, announced in 2015, does refer to one of the planned actions of the University as, "… leading the world and unique areas of original research which should unwaveringly continue to be studied, promoting joint research and international collaboration that goes beyond the framework of the University of Tokyo, and creating new, interdisciplinary knowledge that is the first of its kind in the world."

This "Vision 2020" philosophy is generally inherited in The University of Tokyo's "3rd phase" mid-term research objectives of 2016: "…pro-actively engage itself in creation of new disciplines of science, thereby conducting the world-class academic endeavor to lead creation of new knowledge for the world". The accompanying medium-term plan has a statement: "…create research centers, which are capable of responding to social and academic problems in a pioneering, effective and practical manner, whereby facilitating fused and solution-oriented research activities." In this spirit and plan, the University of Tokyo has been extending its fullest support to IRCN.

6-5. Others

6-5-1. System for fostering young researcher (e.g. start-up funding)

Start-up funds are offered to incoming PIs for an initial three years, when hired from outside The University of Tokyo. These are negotiated on the basis of seniority and science content (eg. wet lab vs primarily computational work). To foster globalization, both new and old PIs are allowed to hire one foreign postdoc for their laboratory. These IRCN postdocs are provided with a small startup fund to be spent in consultation with the host PI.

6-5-2. Participation of female researchers

・ On the transition in the number of female researchers, enter the figures in Appendices 3-1 and 3-2.

A conscious effort has been made to hire outstanding female PIs at IRCN, which is housed in the UTokyo School of Medicine that has none. As of 2020, four out of 18 PIs are women keeping the fraction of female PIs at ~1/3. The fraction of female researchers (non-PI, postdocs) is 10%.

7. Future Prospects (within 2 pages)

7-1. Policy and plan for achieving the Center's research objectives in the future

The pursuit of HI will continue at IRCN driven by Team Science in each of the four intelligences.

Here, we have presented early examples from Core (Reinforcement, Prediction) and Diverse Intelligences (Psychosis Risk, Autism). Equally exciting progress is emerging from the Social Intelligence group, including the validation of inhibitory circuit function as a trigger for critical period timing across species (mouse, zebrafinch, human) and the powerful role of attention (neuromodulation) on plasticity. Such neurobiological solutions to flexible learning and the impact of early experience have evolved over millenia and can now be introduced into computational models and developmental robots. In turn, developmental changes in Reinforcement Learning and Prediction can start to be considered for the Core Intelligence group, as well as developmentally inspired interventions for cognitive disorders. Two areas of technology development are also showing promise, namely Multiscale Imaging and Critical Period Mapping tools.

Most of the growth in the second phase of IRCN can be expected in the outer ring of AI. Specifically, Team Science built around neuromorphic hardware and software architectures that more closely mimic brain processes are anticipated. These are also opportunities to build SCPs with industry, such as in areas of reservoir computing with Toyota Central R&D Labs or novel neuromorphic hardware designs with NTTRI and NTT. The fruits of the Moonshot Project for disease prediction are also expected to translate into applications or prophylactic treatments including wearable sensors that could interface with pharmaceutical or biofeedback companies. Such applications of IRCN science can contribute to the sustainability of the Center beyond the 10-year WPI period.

Policies for achieving these next steps will include the rigorous evaluation of individual Team Science by the Synergy Office. Eventually, the number of Teams will be reduced as a natural consequence of overlap and refinement. It is natural to expect 1-2 focused topics to dominate each of the four intelligence groupings as IRCN enters the post-WPI support phase.

In addition, IRCN strongly encourages promotion of the center's young researchers to become independent in other research institutes or universities worldwide. The alumni will continue to collaborate with IRCN researchers and are expected to contribute to team science to deepen the understanding of neurointelligence. As these researchers continue to circulate from IRCN, the center will also promote the healthy turnover of PIs at all career stages when mutually beneficial.

7-2. Center's plan to maintain its posture as a globally visible institute after WPI funding ends

To maintain global visibility, IRCN will prominently feature its science abroad in three ways:

1. Intensification of the DGA trainee exchange (especially outside of Japan) with existing partners; new partnerships to be formed with host institutes in Israel, Australia, South America
2. Hosting international symposia abroad (such as the annual Boston JSPS event below or other topical events that showcase IRCN science)
3. Roadshow of the Miraikan outreach exhibition at museums or public spaces abroad

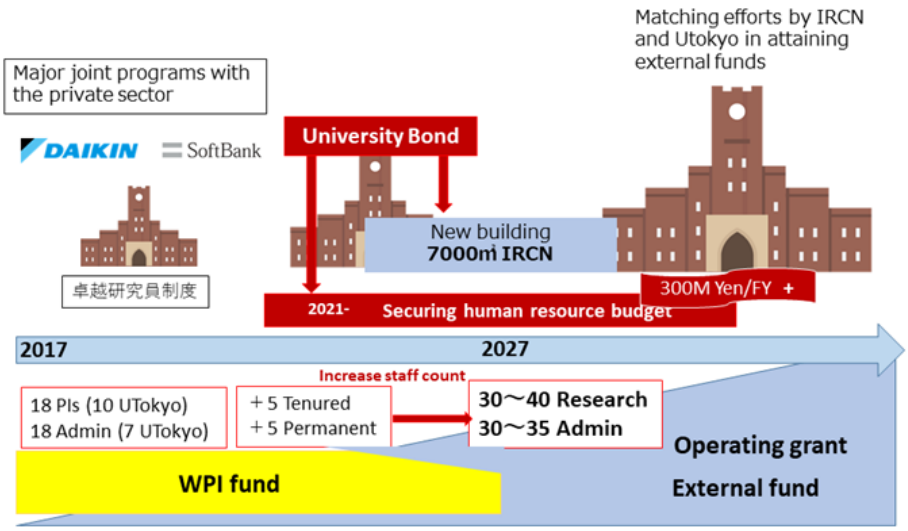
These efforts are designed to globalize Japanese students and attract foreign trainees to UTokyo, and to motivate foreign philanthropy or international group grants (eg. Wellcome Trust, HFSP).

8. Host Institution's Concrete Action Plan toward Making its center an autonomous research institute in the second half of the grant period (from the 6th year of the center's operation)

Describe the Host Institution's plan for realizing a research system including the allocation of resources (e.g. personnel, infrastructure) that will sustain the Center as a "top world-level research institute" after its WPI funding period ends. To enable this, describe the assets that the Host Institution will provide the Center (e.g. expected acquisition of external funding, allocation of personnel, provision of budgets). Describe actions that the Host Institution has taken toward achieving the Center's independence up to the point of this midterm evaluation.

The University of Tokyo has been developing several mechanisms for sustaining its long-term educational and research programs with funds that go beyond what has been traditionally available from governmental operating expenses and grants-in-aid for scientific research. Established in 2011, the "Social Cooperation Programs" (SCP) operate courses on critical research and educational topics of high public value, by utilizing funds received from the private sector. In 2020, IRCN started

receiving the benefit of this program with funding from Daikin Industries, Ltd. and initiated the "Beyond AI Joint Project" to form the "Institute for AI and Beyond" with SoftBank Corporation. The latter Beyond AI project shares a major overlap with the mandate of IRCN: namely, to create new academic fields by integrating fundamental technology and applied research that utilizes AI for various social and industrial issues. IRCN was awarded 1/3 of the major grants from this program, and it is hoped to become a powerful driving force for the long-term sustainability for IRCN.



In 2020, UTokyo also announced it will issue corporate finance-type university bonds, in order to finance part of its long-term operation. Together with these programs and IRCN's own effort to secure an increased amount of competitive research funds and/or donations, UTokyo will aggressively pave a way to transform IRCN into a permanent institution, increasing staff count and providing a new research building over the next ~10 years.

9. Others (within 1 page)

IRCN has served as a valuable gateway to introduce Japanese science abroad. Partnering with the JSPS Washington D.C. office, every November since the Center launched, Director Hensch has coordinated a trainee meeting in Boston. This event attracts talented graduate students and postdoctoral fellows from the Longwood Medical Area and local colleges, like MIT, Tufts, Harvard, and Boston Universities. In addition, Hensch has created the Japan Summer Science Undergraduate Research Program (JSSURP) at the Harvard Reischauer Institute to send younger student interns to Japan. This popular program has been cloned at MIT, Hiroshima Univ, OIST, Tokyo Tech, RIKEN (Wako, Yokohama, AIP) and Tsukuba IIIS. Reaching these budding scientists during a critical period in their lives helps to build social networks amongst their Japanese peers and opens a path for returning to the country as graduate students or postdoctoral fellows.

10. Center's Response to Results of FY 2020 Follow-up (including Site Visit Results)

* Describe the Center's response to results of FY 2020 follow-up. Note: If you have already provided this information, please indicate where in the report.

1) Because of the COVID-19 pandemic, it has become difficult for the Center Director to be physically present in Tokyo. It is therefore urgent to establish a system to exert his leadership in IRCN in a remote manner while the current situation lasts.

The COVID-19 pandemic has required a heroic effort from Director Hensch. First, his long-planned sabbatical stay at UTokyo was abruptly blocked by the Harvard University travel moratorium, which remains in place since March 2020. Second, low-density occupancy and emergency status were simultaneously implemented at the BCH satellite, Harvard University and UTokyo. Third, mouse colonies, patient recruitment, lab staff and resources were drastically reduced and priority placed on safety. These rules differed dramatically by location (country, university or hospital) and suffered a lack of guidance or misdirection from central authorities faced with creating them from scratch. Finally, the magnitude of U.S. cases (~600,000 deaths) coupled with mounting racial tensions were simply unimaginable in Japan. Despite such practical and psychological obstacles, the IRCN system of communication with Boston was already in place from the start. Thus, Director Hensch has remained in constant contact via nightly Zoom meetings (eg. from March 1, 2020 - March 1, 2021): EB meetings

(52), SC meetings (19), AD weekend meetings (47), job search-related (PI / AD candidates) (15), Synergy Office / Retreat-related (8), other (eg. VP/EVP, office staff, etc) (22), individual center members (46) = Total meetings (209) + total emails (>4800). The three DDs and acting AD/GM were needed conduits of information flow, which are expected to be improved with the addition of a full-time AD and SAD (below).

2) It is important to hire an appropriate person as the Administrative Director after Ms. Kubo stepped down at the end of May 2020.

After an intensive search spanning six months, two qualified AD candidates from industry and one from academia were identified. Prof. Nobukazu Toge from KEK was deemed most appropriate on the basis of his strong administrative experience, extensive research activities both in the US and Japan, completely fluent bilingual skills and patient personality. His career spent in high energy physics was considered an advantage for the spirit of fusion research and broad perspective as IRCN seeks its sustainable future. Fortunately, he accepted in late November and immediately began visiting with PIs as a Special Advisor to the Director (SAD) as of January 2021.

3) Establishment of 12 collaborative teams is a very positive development and should be encouraged. However, it will be critical to select the most promising avenue of research, one that can demonstrate a long-term impact on "neurointelligence". IRCN needs to think carefully about where it should focus its research in the coming five years and after the 10-year funding period ends.

The IRCN top-down view of HI composed of four intelligences (core + social + diverse + AI) is detailed in S1 above. The 12 collaborative teams fit neatly into the first three areas and will be evaluated by the Synergy Office semi-annually. In the coming five years, it is anticipated that the four key domains will each winnow down to a representative 1-2 Teams.

4) The center's effort to bridge the neuroscience and computation units should be strengthened. There needs to be more computation work done based on biological findings.

The arrival of DD Aihara as a permanent resident in the Medical Building 1 has catalyzed a bridge between the neuroscience and computation units. Apart from recruiting strategic PIs (Chao, Watanabe) into this space, a category for computational junior faculty (non-PI ARF) built around DD Aihara and PI Masashi Sugiyama to collaborate with companies (SCP) is expected to further drive a unique form of collaborative, interdisciplinary fusion.

5) IRCN's roadmap is very vague. It needs concrete targets and timelines for key decisions. There also need to be criteria for how these decisions will be made.

We understand; the roadmap is necessarily an evolving process as our research results emerge. As listed in the overview, we now see three deliverables: 1) disease prediction, 2) therapeutic plasticity reopening, and 3) enhancing cognition. The first two are already producing high-profile publications and attracting large external funding (Moonshot, Grants-in-Aid).

6) By next year, IRCN needs to give a number of concrete examples of progress being made toward its vision of neurointelligence. The center's progress report and presentations at the site visit should be intelligible in a way that clearly position the scientific activities of all PIs toward achieving the challenging goals of IRCN.

Concrete progress is documented in section 2-1 above and in the Research Results Appendix.

7) It would be valuable for IRCN to establish its own PhD program with "neurointelligence" in its name.

The motivation to build an *esprit de corps* through graduate training is deeply appreciated. We have begun to take first steps in this direction by participating as faculty, co-mentor and exam committee members in the newly awarded MEXT WISE FoPM training Program at UTokyo School of Science.

Appendix 1-1 List of Papers Underscoring Each Research Achievement

* List papers underscoring each research achievement [1] ~ [10] listed in the item 2-1 "Research results to date" of 2. "Advancing Research of the Highest Global Level" (up to 20 papers) and provide a description of the significance of each (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.
* Place an asterisk (*) in front of those results that could only have been achieved by a WPI center.

PRINCIPLES OF BRAIN DEVELOPMENT

*1. Neuronal Mechanisms of Schizophrenia

a. Iino Y, Sawada T, Yamaguchi K, Tajiri M, Ishii S, Kasai H, Yagishita S. Dopamine D2 receptors in discrimination learning and spine enlargement. Nature 2020. (DOI: 10.1038/s41586-020-2115-1)
The discovery of how striatal D2R signaling regulates reward learning and its link to psychosis-related behavior is one of the most important advances in psychiatric mechanism research of the last decade.

b. Nagahama K, Sakoori K, Watanabe T, Kishi Y, Kawaji K, Koebis M, Nakao K, Gotoh Y, Aiba A, Uesaka N, Kano M. Setd1a Insufficiency in Mice Attenuates Excitatory Synaptic Function and Recapitulates Schizophrenia-related Behavioral Abnormalities. Cell Reports 2020. (DOI: 10.1016/j.celrep.2020.108126)
These results explore the implication of epigenetic regulation in the pathophysiology of schizophrenia by linking novel principles of synaptic hypofunction in the developing prefrontal cortex to aberrant behavior.

*2. Modeling Autism Spectrum Disorder

c. Sacai H, Sakoori K, Konno K, Nagahama K, Honoka S, Watanabe T, Watanabe M, Uesaka N, Kano M. Autism spectrum disorder-like behavior caused by reduced excitatory synaptic transmission in pyramidal neurons of mouse prefrontal cortex. Nature Communications 2020. (DOI:10.1038/s41467-020-18861-3)
The findings suggest a common mechanism for social deficits in mice modeling genetic variants of autism spectrum disorder (and potentially in patients), and, that ampakine drugs may be candidate treatments.

d. Philippsen A, Nagai Y. Deficits in Prediction Ability Trigger Asymmetries in Behavior and Internal Representation. Front Psychiatry 11:564415, 2020. (DOI: 10.3389/fpsyt.2020.564415)
This computational study proposes a principle that network dysfunction in ASD occurs at both ends of the behavioral performance spectrum, mirroring symptomsm and providing an account for clinical variability.

*3. Auditory Neural Circuit Principles

e. Takesian AE, Bogart LJ, Lichtman JW, Hensch TK. Inhibitory circuit gating of auditory critical-period plasticity. Nat Neurosci. 21(2):218-227, 2018. (DOI: 10.1038/s41593-017-0064-2)
The findings pinpoint a novel microcircuit in the mouse auditory cortex for inhibitory gating of auditory critical period plasticity, a novel principle of neural development underlying the emergence of intelligence.

f. Tischbirek CH, Noda T, Tohmi M, Birkner A, Nelken I, Konnerth A. In Vivo Functional Mapping of a Cortical Column at Single-Neuron Resolution. Cell Rep. 27(5):1319-1326.e5, 2019. (DOI: 10.1016/j.celrep.2019.04.007)
This study used a novel 2-photon calcium imaging method at single cell resolution to conduct functional mapping of the cortical column. The results provide insights on the developmental wiring of sensory maps.

*4. Early Language/Song Development

g. Tsuji S, Jincho N, Mazuka R, Cristia AJ. Communicative cues in the absence of a human interaction partner enhance 12-month-old infants' word learning. Exp Child Psychol. 191:104740, 2020. (DOI:

10.1016/j.jecp.2019.104740)
As children increasingly learn from screens, the findings provide an empirical approach for understanding the role of social-communicative cues/environments in improving or degrading word acquisition outcomes.

h. Kudo T, Morohashi Y, Yazaki-Sugiyama Y. Early Auditory Experience Modifies Neuronal Firing Properties in the Zebra Finch Auditory Cortex. Front Neural Circuits 14:570174, 2020. (DOI: 10.3389/fncir.2020.570174)
The findings establish the developmental principle that physiological properties and memory encoding in NCM neurons reflect social auditory experience during the critical learning period for vocal communication.

NOVEL COMPUTATIONAL PSYCHIATRY

***5. Machine Learning in Psychiatry**

i. Artoni P, Piffer A, Vinci V, LeBlanc J, Nelson CA, Hensch TK, Fagiolini M. Deep learning of spontaneous arousal fluctuations detects early cholinergic defects across neurodevelopmental mouse models and patients. Proc Natl Acad Sci USA 117(38):23298-23303, 2019. (DOI: 10.1073/pnas.1820847116)
The study applies neurodevelopmental principles, here, the utility of cross-species transfer learning and timing of cholinergic signaling in brain arousal, to engineer a novel bench-to-bedside AI-based application.

j. Yassin W, Nakatani H, Zhu Y, Kojima M, Owada K, Kuwabara H, Gonoi W, Aoki Y, Takao H, Natsubori T, Iwashiro N, Kasai K, Kano Y, Abe O, Yamasue H, Koike S. Machine learning classification using neuroimaging data in schizophrenia, autism, ultra-high risk and first episode psychosis. Translational Psychiatry 2020. (DOI: 10.1038/s41398-020-00965-5)
The results advance the selection of deep machine learning AI classifiers and their training parameters to effectively distinguish schizophrenia and ASD, and to predict psychosis, in psychiatric patient populations.

***6. Large-Scale Analyses of Psychiatric Disorders**

k. Koshiyama D, Fukunaga M, Okada N, Morita K, Nemoto K, Usui K, Yamamori H, Yasuda Y, Fujimoto M, Kudo N, Azechi H, Watanabe Y, Hashimoto N, Narita H, Kusumi I, Ohi K, Shimada T, Kataoka Y, Yamamoto M, Ozaki N, Okada G, Okamoto Y, Harada K, Matsuo K, Yamasue H, Abe O, Hashimoto R, Takahashi T, Hori T, Nakataki M, Onitsuka T, Holleran L, Jahanshad N, van Erp TGM, Turner J, Donohoe G, Thompson PM, Kasai K, Hashimoto R; COCORO. White matter microstructural alterations across four major psychiatric disorders: mega-analysis study in 2937 individuals. Molecular Psychiatry 2019. (DOI: 10.1038/s41380-019-0553-7)
The COCORO consortium compared DTI-based white matter microstructural differences in a large psychiatric cohort and found common and unique endophenotypes for disorders that will help clinicians.

l. Okada N, Yahata N, Koshiyama D, Morita K, Sawada K, Kanata S, Fujikawa S, Sugimoto N, Toriyama R, Masaoka M, Koike S, Araki T, Kano Y, Endo K, Yamasaki S, Ando S, Nishida A, Hiraiwa-Hasegawa M, Edden RAE, Barker PB, Sawa A, Kasai K. Neurometabolic and functional connectivity basis of prosocial behavior in early adolescence. Scientific Reports 2019. (DOI:10.1038/s41598-018-38355-z)
These findings pinpoint a novel brain circuit and neurochemical basis for the development of prosocial functioning, and reveal how critical the early adolescent period is for the emergence of social cognition.

***7. Dynamic Disease Prediction Algorithms**

m. Koizumi K, Oku M, Hayashi S, Inujima A, Shibahara N, Chen L, Igarashi Y, Tobe K, Saito S, Kadowaki M, Aihara K. Identifying pre-disease signals before metabolic syndrome in mice by dynamical network biomarkers. Scientific Reports 9:8767, 2019. (DOI: 10.1038/s41598-019-45119-w)
This computational study of a mouse disease model provides new insights into the measurement and mathematical theory of the pre-disease state that may have utility for the healthy and disordered brain.

n. Gabard-Durnam LJ, Wilkinson C, Kapur K, Tager-Flusberg H, Levin AR, Nelson CA. Longitudinal EEG power in the first postnatal year differentiates autism outcomes. Nat Commun. 10(1):4188, 2019. (DOI: 10.1038/s41467-019-12202-9)

The results introduce a powerful physiological tool and modeling approach for early ASD diagnosis and define the EEG dynamics and developmental timing useful for clarifying pathophysiological mechanisms.

NOVEL ARTIFICIAL INTELLIGENCE

*8. Deep Learning for Cellular Imaging

o. Nagao Y, Sakamoto M, Chinen T, Okada Y, Takao D. Robust Classification of Cell Cycle Phase and Biological Feature Extraction by Image-Based Deep Learning. Mol Biol Cell 2020. (DOI: 10.1091/mbc.E20-03-0187)
The results demonstrate that deep AI models are powerful classification tools for biological imaging, and for the interrogation of cell structure and dynamics with biological explainability and for drug development.

p. Lee S, Negishi M, Urakubo H, Kasai H, Ishii S. Mu-net: Multi-scale U-net for two-photon microscopy image denoising and restoration. Neural Networks 125:92, 2020. (DOI: 10.1016/j.neunet.2020.01.026)
The findings show that Mu-net, a novel CNN- and GAN-based AI architecture, was successful in removing noise from neuronal images and may become a standard for mapping of 3D brain structure and function.

*9. Reservoir Computing AI

q. Sakemi Y, Morino K, Leleu T, Aihara K. Model-size reduction for reservoir computing by concatenating internal states through time. Scientific Reports 2020. (DOI: 10.1038/s41598-020-78725-0)
In a collaborative study, IRCN and NEC researchers report improvements in reservoir computing efficiency after key changes to architecture and parameters that might facilitate an understanding of brain circuits.

r. Chen P, Liu R, Aihara K, Chen L. Autoreservoir Computing for Multi-Step Ahead Prediction Based on the Spatiotemporal Information Transformation. Nature Communications 2020. (DOI: 10.1038/s41467-020-18381-0)
Researchers used high-dimensional, short time-series data to generate the prediction of a target variable using a novel auto-reservoir computing framework that may have a wide range of real world applications.

*10. Novel AI Architectures

s. Yoshida T, Ohki K. Natural images are reliably represented by sparse and variable populations of neurons in visual cortex. Nature Communications 11(1):872, 2020. (DOI: 10.1038/s41467-020-14645-x)
The team employed cellular-scale imaging and computational modeling to show how the brain interprets sparse, stochastic activity for optimal image decoding with insights for novel AIs related to machine vision.

t. Fujita Y, Yagishita S, Kasai H, Ishii S. Computational Characteristics of the Striatal Dopamine System Described by Reinforcement Learning with Fast Generalization. Front. Comp. Neurosci. 14(66), 2020. (DOI: 10.3389/fncom.2020.00066)
This computational model based on the 2020 Nature paper from IRCN describes a novel AI related to reinforcement learning that employs the powerful learning architecture of the dopamine reward system.

Appendix 1-2 List of Papers of Representative of Interdisciplinary Research Activities

* List **up to 10 papers** underscoring each interdisciplinary research activity and give brief accounts (within 10 lines).
* For each, write the author name(s); year of publication; journal name, volume, page(s), and article title. Any listing order may be used as long as format is the same. If a paper has many authors, underline those affiliated with the Center.
* If a paper has many authors (say, more than 10), all of their names do not need to be listed.

A collaboration between the labs of Haruo Kasai, a neurobiologist, and Shin Ishii, a computer scientist, has yielded multiple high impact papers in the last few years, and promises even greater outcomes in the near future. The team's seminal work is Iino et al (2020) Nature describing novel principles of brain circuits for reward learning resulting in a novel computational AI framework based on reinforcement learning that is poised to advance the fields of neurobiology and computer science as a fused discipline.

1. Iino Y, Sawada T, Yamaguchi K, Tajiri M, Ishii S, Kasai H, Yagishita S. Dopamine D2 receptors in discrimination learning and spine enlargement. Nature 579:555-560, 2020. (DOI: 10.1038/s41586-020-2115-1). The authors investigate a poorly understood deep brain signaling system involving the dopamine D2 receptor (D2R), the major brain receptor for most antipsychotic medications. Reward omission in mice triggers a transient signal in D2R neurons, the dopamine dip, which facilitates discrimination learning. Using optogenetic technologies and pharmacology to control dips they show that aberrant discrimination learning causes reward misappropriation similar to that seen in psychosis.

2. Fujita Y, Yagishita S, Kasai H, Ishii S. Computational Characteristics of the Striatal Dopamine System Described by Reinforcement Learning with Fast Generalization. Front. Comp. Neurosci. 14(66), 2020. (DOI: 10.3389/fncom.2020.00066). A second study from the Kasai-Ishii collaboration explores the computational significance of the D2R signaling system. They developed a computational model based on D2R neurons as a novel form of reinforcement learning-type AI in a multilayered neural network configuration called extreme learning machine (ELM). In a virtual navigation task the model showed powerful discrimination learning and performance but when the D2R element was removed they observed psychosis-like behavior. The findings suggest that AI can be disordered like the human brain.

3. Lee S, Negishi M, Urakubo H, Kasai H, Ishii S. Mu-net: Multi-scale U-net for two-photon microscopy image denoising and restoration. Neural Networks 125:92, 2020. (DOI: 10.1016/j.neunet.2020.01.026) Their third study is potentially the most important work of the three, in developing an AI for the analysis of noisy 3D images from 2-photon microscopy. Image noise prevents the acquisition of clean, labelled images that deep networks require to learn and predict new data. The team built a novel AI architecture termed Mu-net with generative adversarial network (GAN) training that enabled the images to become more robust to noise. Such AI-driven deep analysis promises to decode the brain's neuronal networks.

Like the Kasai-Ishii laboratory collaboration outputs, other IRCN publications demonstrate the emergent fusion of biology and AI disciplines. While these studies were conducted mainly in one laboratory, they illustrate the change in fundamental perspective toward the integration of data analysis and modeling with traditionally descriptive biological data, with an eye toward novel AI that, for now, involves machine learning, but in IRCN will soon employ more innovative architectures and multi-lab team collaborations.

4. Nagao Y, Sakamoto M, Chinen T, Okada Y, Takao D. Robust Classification of Cell Cycle Phase and Biological Feature Extraction by Image-Based Deep Learning. Mol Biol Cell 2020. (DOI: 10.1091/mbc.E20-03-0187). The lab of Yasushi Okada with Daisuke Takao created a novel AI for image analysis. They used the classification of cell cycle phase as a model system to test their algorithm, examining whether changes in cell features such as the nucleus, Golgi apparatus, and cytoskeleton could be tracked by a convolutional neural network. The results demonstrated that their CNNs could extract cell features to classify cell cycle phase. AIs such as this effort are already becoming powerful classification tools for brain/biological imaging and IRCN will apply them to brain and cognitive studies.

5. Yoshida T, Ohki K. Natural images are reliably represented by sparse and variable populations of neurons in visual cortex. Nature Communications 11(1):872, 2020. (DOI: 10.1038/s41467-020-14645-x). Machine vision is one of the high profile fields in AI but can animal vision provide biological principles to guide AI development? The lab of Kenichi Ohki (Yoshida et al, 2020) sought to understand puzzling properties of biological vision observed in neurons of the visual cortex. Using cellular-scale imaging and

modeling of neuronal responses they found that sparse, stochastic activity can facilitate optimal image decoding, findings that may protect deep neural network AI performance against adversarial attack.

6. Koizumi K, Oku M, Hayashi S, Inujima A, Shibahara N, Chen L, Igarashi Y, Tobe K, Saito S, Kadowaki M, Aihara K. Identifying pre-disease signals before metabolic syndrome in mice by dynamical network biomarkers. Scientific Reports 9:8767, 2019. (DOI: 10.1038/s41598-019-45119-w). Novel methods to predict pre-disease states based on physiological measurements are of urgent medical and scientific interest. Kazuyuki Aihara, a computational mathematician, and his group have an ongoing project to fuse the modeling of pre-disease states with applied clinical fields and provide new insights into the measurement and mathematical theory of the pre-clinical state. Using a mathematical theory called dynamical network biomarkers (DNB), the researchers could predict metabolic syndrome phenotypes in an animal model. The interdisciplinary fusion of DNB is the basis of the PI's JST Moonshot Project.

Clinical psychiatry research is undergoing a revolution in methodology driven by the analysis and modeling of larger datasets coupled with a more precise mechanistic underpinning of disorders based on biology. AI tools are an emergent part of this field and IRCN is well positioned to coordinate progress with key clinical researchers in Japan and biological and neurocomputational researchers. The IRCN Boston Satellite is another key node for clinical translation and fusion as recent studies demonstrate.

7. Yassin W, Nakatani H, Zhu Y, Kojima M, Owada K, Kuwabara H, Gonoi W, Aoki Y, Takao H, Natsubori T, Iwashiro N, Kasai K, Kano Y, Abe O, Yamasue H, Koike S. Machine learning classification using neuroimaging data in schizophrenia, autism, ultra-high risk and first episode psychosis. Translational Psychiatry 2020. (DOI: 10.1038/s41398-020-00965-5). In a fusion of clinical and computer sciences, IRCN members analyzed structural brain imaging data from patients with schizophrenia or ASD, and subjects at risk for psychosis, with machine learning classifiers, and the outputs were correlated with behavioral prognoses. The classifiers accurately predicted disorder type and behavioral symptoms, providing insight on optimal machine learning classification for psychiatric disorder brain imaging data.

8. Artoni P, Piffer A, Vinci V, LeBlanc J, Nelson CA, Hensch TK, Fagiolini M. Deep learning of spontaneous arousal fluctuations detects early cholinergic defects across neurodevelopmental mouse models and patients. Proc Natl Acad Sci USA 117(38):23298-23303, 2019. (DOI: 10.1073/pnas.1820847116). The IRCN Boston Satellite developed a novel early biomarker for ASD based on spontaneous pupil fluctuations and heart rate, as key indicators of cholinergic modulation in brain circuits. A deep neural network trained on mouse pupillary data recognized abnormalities with 97% accuracy and a retrained algorithm was significantly accurate in identifying RTT patients from normative controls, revealing the power of neurodevelopmental principles to inspire the design of novel AI-based clinical applications.

Appendix 1-3
Major Awards, Invited Lectures, Plenary Addresses (etc.) (within 2 pages)

*Prepare the information below during the period from the start of the center through March 2021.

1. Major Awards

*List main internationally-acclaimed awards received/unofficially announced in order from the most recent.
*For each, write the recipient's name, the name of award, and the date issued.
In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
28.04.2021	Noboru Mizushima	Medal with Purple Ribbon
04.02.2021	Shigeo Okabe	Naito Memorial Award for the Advancement of Science
11.12.2020	Sho Tsuji	Jacobs Foundation Fellowship Class of 2021
14.11.2020	Ayuko Hoshino	The 2nd Brilliant Female Researchers Award (The Jun Ashida Award)
05.11.2020	Gouhei Tanaka, Hiroto Tamura	The 3rd ENNS Best Paper Award in 29th International Conference on Artificial Neural Networks
03.11.2010	Yukiko Gotoh	Medal with Purple Ribbon
01.11.2010	Noboru Mizushima	The Medical Award of the Japan Medical Association
15.10.2020	Takamitsu Watanabe	Healthy Longevity Global Grand Challenge Catalyst Award (United States National Academy of Medicine)
12.08.2020	Arthur Konnerth	Elected Chairman of the Brain Prize Academy
26.05.2020	Sho Tsuji	2020 Cohort of Young Scientists, World Economic Forum
23.03.2020	Yasushi Okada	Nakaakira Tsukahara Memorial Award
21.12.2019	Kazuyuki Aihara	MIMS Mimura Award
15.12.2019	Kazuo Emoto	TERUMO Foundation Award
01.11.2019	Yuri Etani, Yukie Nagai	JSAI Annual Conference Award of the 33rd Annual Conference of the Japanese Society for Artificial Intelligence
17.04.2019	Shoji Takeuchi	UNESCO Netexplo Award 2019
18.03.2019	Masashi Sugiyama	KDDI Foundation Awards, KDDI Foundation
20.02.2019	Shoji Takeuchi	Kyoto SMI Nakatsuji Award
01.11.2018	Masanobu Kano	Medical Award of The Japan Medical Association
29.04.2018	Haruo Kasai	Medal with Purple Ribbon
03.03.2018	Masashi Sugiyama	Fellow, The Institute of Electronics, Information and Communication Engineers (IEICE)
02.02.2018	Kenichi Ohki	Inoue Prize for Science

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

*List up to 20 main presentations in order from most recent.
*For each, write the lecturer/presenter's name, presentation title, conference name and date(s)

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
27.11.2020	Masashi Sugiyama	Robust Machine Learning for Reliable Deployment	World Intellectual Manufacturing Conference
25.10.2020	Yukie Nagai	Cognitive Development in Humans and Robots: New Insights into Intelligence (Plenary talk)	2020 IEEE/RSJ International Conference on Intelligent Robots and Systems
11.10.2020	Yukie Nagai	Cognitive Development Based on Predictive Coding	International Symposium on Artificial Intelligence and Brain Science
10.10.2020	Masashi Sugiyama	Recent Advances in Robust Machine Learning	International Symposium on Artificial Intelligence and Brain Science
20.09.2020	Kazuyuki Aihara	Complex Data Analysis and its Applications to Systems Biology	International Conference on Computational Systems Biology (ISB2020)
14.01.2020	Shoji Takeuchi	Emerging Technology for Biohybrid Robotics	Gordon Conference on Robotics
24.09.2019	Masanobu Kano	Neural Mechanisms of Synapse Remodeling in the Developing Brain	The 10th IBRO World Congress of Neuroscience
04.09.2019	Yasushi Okada	Dissecting Molecular Mechanisms by Optical Microscopy in Living Cells and in vitro	Cold Spring Harbor Conferences Asia, Cross-scale biological structure
02.09.2019	Yukie Nagai	AI that Simulates and Assists People with Autism Spectrum Disorder	Nature Conference on "AI & Robotics"
31.07.2019	Kenichi Ohki	Multiscale Calcium Imaging of Visual Cortex in Marmoset Monkeys	APCV2019: The 15th Asia-Pacific Conference on Vision
27.05.2019	Masashi Sugiyama	Recent Advances in Weakly-supervised and Robust Machine Learning	AI Experts Workshop & AI for Good Global Summit, Geneva, Switzerland
24.01.2019	Shoji Takeuchi	IdeasLab Biohybrid Robotics built from living tissue	Davos 2019, The World Economic Forum
09.12.2018	Yoko Yazaki-Sugiyama	Innate and Acquired Auditory Neuronal Pathways for Zebra Finch Song Learning	Special lecture at 5th annual meeting of the Society for Bioacoustics
18.10.2018	Arthur Konnerth	Dendritic Computation Underlying Orientation-tuning in Layer 4 Neurons of the Visual Cortex	2018 CSH-Asia meeting on New Advances in Optical Imaging of Cells and Organisms: Focus on the Brain, Suzhou, China

02.07.2018	Haruo Kasai	Synaptic Optogenetics for Memory Structures	World Congress of Pharmacological Sciences 2018
22.05.2018	Kenichi Ohki	Multiscale Functional Imaging of the Marmoset Visual Cortex	ISDN 2018: 22nd Biennial Meeting of the International Society for Developmental Neuroscience
10.05.2018	Yukiko Gotoh	Regulation of Embryonic and Adult Neural Stem Cell Fate	Cold Spring Harbor Asia, Stem Cell Crossroads
13.03.2018	Yasushi Okada	Live Cell Imaging Technologies for Single-cell Analysis: How Can Imaging Meet Genomics	Human Genome Meeting 2018
01.11.2017	Haruo Kasai	Dopamine Actions on Dendritic Spines and Conditioned Behaviors	The 48th NIPS International Symposium
17.10.2017	Kiyoto Kasai	Global Brain Projects: Goals and Inherent Ethical Questions Initially Identified. Japan Brain/MINDS	2017 Global Neuroethics Summit

Appendix 1.4 2020 List of Center's Research Results

Refereed Papers (PIs' co-authored publications)

- List only the Center's papers published in 2020. (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 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), 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 20), 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
         2. Review articles
         3. Proceedings
         4. Other English articles

      B. WPI-related papers
         1. Original articles
         2. Review articles
         3. Proceedings
         4. Other English articles

(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.)
   - These files do not need to be divided into 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.

A. WPI papers

(1) Original articles

1. Aoyama-Ishiwatari S, Okazaki T, Iemura SI, Natsume T, Okada Y, Gotoh Y. NUDT21 links mitochondrial IPS-1 to RLR-containing stress granules and activates host antiviral defense. J. Immunol. 206, 2020. (DOI: 10.4049/jimmunol.2000306)

2. Artoni P, Piffer A, Vinci V, LeBlanc J, Nelson CA, Hensch TK, Fagiolini M. Deep learning of spontaneous arousal fluctuations detects early cholinergic defects across neurodevelopmental mouse models and patients. Proc Natl Acad Sci USA 117(38):23298-23303, 2020. (DOI: 10.1073/pnas.1820847116)

3. Chen C, Li R, Shu L, He Z, Wang J, Zhang C, Ma H, Aihara K, Chen L. Predicting Future Dynamics from Short-term Time Series by Anticipated Learning Machine. National Science Review, nwaa025, 2020. (DOI: 10.1093/nsr/nwaa025)

4. Chen P, Liu R, Aihara K, Chen L. Autoreservoir Computing for Multistep Ahead Prediction based on the Spatiotemporal Information Transformation. Nature Communications, Vol.11, Article No.4568, pp.1-15, 2020. (DOI: 10.1038/s41467-020-18381-0)

5. Daikoku T, Yumoto M. Musical Expertise Facilitates Statistical Learning of Rhythm and the Perceptive Uncertainty: A cross-cultural Study. Neuropsychologia, 146:107553, 2020. (DOI: 10.1016/j.neuropsychologia.2020.107553)

6. Daikoku T. Statistical Properties in Jazz Improvisation Underline Individuality of Musical Representation. NeuroSci, 1(1):24-43, 2020. (DOI: 10.3390/neurosci1010004)

7. Dos Santos Kawata KH, Ueno Y, Hashimoto R, Yoshino S, Ohta K, Nishida A, Ando S, Nakatani H, Kasai K, Koike S. Development of Metacognition in Adolescence: The Congruency-Based Metacognition Scale. Front Psychol. 11:565231, eCollection 2020. (DOI: 10.3389/fpsyg.2020.565231)

8. Eto H, Kishi Y, Yakushiji-Kaminatsui N, Sugishita H, Utsunomiya S, Koseki H, Gotoh Y. The Polycomb group protein Ring1 regulates dorsoventral patterning of the mouse telencephalon. Nat. Comm. 11, 5709, 2020. (DOI: 10.1038/s41467-020-19556-5)

9. Fujioka M, Kirihara K, Koshiyama D, Tada M, Nagai T, Usui K, Morita S, Kawakami S, Morita K, Satomura Y, Koike S, Suga M, Araki T, Kasai K. Mismatch negativity predicts remission and neurocognitive function in individuals at ultra-high risk for psychosis. Front Psychiatry 11:770, 2020. (DOI: 10.3389/fpsyt.2020.00770)

10. Fujioka M, Kirihara K, Koshiyama D, Tada M, Nagai T, Usui K, Morita S, Kawakami S, Morita K, Satomura Y, Koike S, Suga M, Araki T, Kasai K. Mismatch Negativity Predicts Remission and Neurocognitive Function in Individuals at Ultra-High Risk for Psychosis. Front Psychiatry 11:770, eCollection 2020. (DOI: 10.3389/fpsyt.2020.00770)

11. Fujioka Y, Alam JM, Noshiro D, Mouri K, Ando T, Okada Y, May AI, Knorr RL, Suzuki K, Ohsumi Y, Noda NN. Phase separation organizes the site of autophagosome formation. Nature 578(7794), 301-305, 2020. (DOI: 10.1038/s41586-020-1977-6)

12. Fujita Y, Yagishita S, Kasai H, Ishii S. Computational Characteristics of the Striatal Dopamine System Described by Reinforcement Learning With Fast Generalization. Frontier in Computational Neuroscience, 2020. (DOI: 10.3389/fncom.2020.00066)

13. Fujita Y, Yagishita S, Kasai H, Ishii S. Computational characteristics of the striatal dopamine system described by reinforcement learning with fast generalization. Frontiers in Computational Neuroscience 2020. (DOI: 10.1101/2019.12.12.873950)

14. Funano S I, Tone D, Ukai H, Ueda HR, Tanaka Y. Rapid and easy-to-use ES cell manipulation device with a small groove near culturing wells. BMC Research Notes, 13(1), 2020. (DOI: 10.1186/s13104-020-05294-w)

15. Hasegawa R, Ebina T, Tanaka YR, Kobayashi K, Matsuzaki M. Structural dynamics and stability of corticocortical and thalamocortical axon terminals during motor learning. PLoS One 15, e0234930, 2020. (DOI: 10.1371/journal.pone.0234930)

16. Hasegawa S, Tanaka T, Saito T, Fukui K, Wakashima T, Susaki E A, Ueda HR, Nangaku M. The oral hypoxia-inducible factor prolyl hydroxylase inhibitor enarodustat counteracts alterations in renal energy metabolism in the early stages of diabetic kidney disease. Kidney International, 97(5), 934-950, 2020. (DOI: 10.1016/j.kint.2019.12.007)

17. Havron N, Bergmann C, Tsuji S. Preregistration in infant research - a primer. Infancy 25, 734–754, 2020. (DOI: 10.1111/infa.12353)

18. Hayashi N, Ando S, Jinde S, Fujikawa S, Okada N, Toriyama R, Masaoka M, Sugiyama H, Shirakawa T, Yagi T, Morita M, Morishima R, Kiyono T, Yamasaki S, Nishida A, Kasai K. Social withdrawal and testosterone levels in early adolescent boys. Psychoneuroendocrinology 116:104596, 2020. (DOI: 10.1016/j.psyneuen.2020.104596)

19. Hirata Y, Aihara K. Deep Learning for Nonlinear Time Series: Examples for Inferring Slow Driving Forces. International Journal of Bifurcation and Chaos, Vol.30, No.15, 2050226, pp.1-13, DEC 2020. (DOI: 10.1142/S0218127420502260)

20. Hoang H, Lang EJ, Hirata Y, Tokuda IT, Aihara K, Toyama K, Kawato M, Schweighofer N. Electrical Coupling Controls Dimensionality and Chaotic Firing of Inferior Olive Neurons. Plos Biology, Vol.16, No.7, e1008075, pp.1-26, 2020. (DOI: 10.1371/journal.pcbi.1008075)

21. Huang Z, Endo K, Yamasaki S, Fujikawa S, Ando S, Hiraiwa-Hasegawa M, Kasai K, Nishida A, Koike S: Bi-directional relationships between psychological symptoms and environmental factors in early adolescence. Front Psychiatry 11:574182, 2020. (DOI: 10.3389/fpsyt.2020.574182)

22. Iino Y, Sawada T, Yamaguchi K, Tajiri M, Ishii S, Kasai H, Yagishita S. Dopamine D2 receptors in discrimination learning and spine enlargement. Nature 579: 555-560, 2020. (DOI: 10.1038/s41586-020-2115-1)

23. Ikegame T, Bundo M, Okada N, Murata Y, Koike S, Sugawara H, Saito T, Ikeda M, Owada K, Fukunaga M, Yamashita F, Koshiyama D, Natsubori T, Iwashiro N, Asai T, Yoshikawa A, Nishimura F, Kawamura Y, Ishigooka J, Kakiuchi C, Sasaki T, Abe O, Hashimoto R, Iwata N, Yamasue H, Kato T, Kasai K, Iwamoto K. Promoter activity-based case-control association study on SLC6A4 highlighting hypermethylation and altered amygdala volume in male patients with schizophrenia. Schizophr Bull 46(6):1577-86, 2020. (DOI: 10.1093/schbul/sbaa075)

24. Imafuku M, Fukushima H, Nakamura Y, Myowa M, Koike S. Interoception is associated with the impact of eye contact on spontaneous

facial mimicry. Sci Rep 10(1):e19866, 2020. (DOI: 10.1038/s41598-020-76393-8)

25. Imaizumi Y, Furutachi S, Watanabe T, Miya H, Kawaguchi D, Gotoh Y. Role of the imprinted allele of the Cdkn1c gene in mouse neocortical development. Sci. Rep. 10, 1884, 2020. (DOI: 10.1038/s41598-020-58629-9)

26. Ishii S, Lee Sehyung, Urakubo H, Kume H, Kasai H. Generative and discriminative model-based approaches to microscopic image restoration and segmentation. Microscopy 69, 79-91, 2020. (DOI: 10.1093/jmicro/dfaa007)

27. Itahashi T, Okada N, Ando S, Yamasaki S, Koshiyama D, Morita K, Yahata N, Koike S, Nishida A, Kasai K, Hashimoto RI. Functional connectomes linking child-parent relationships with psychological problems in adolescence. Neuroimage 219:117013, 2020. (DOI: 10.1016/j.neuroimage.2020.117013)

28. Itoh Y, Uenohara S, Adachi M, Morie T, Aihara K. Reconstructing Bifurcation Diagrams Only from Time-series Data Generated by Electronic Circuits in Discrete-time Dynamical Systems. Chaos, Vol.30, No.1, 013128, pp.1-11, 2020. (DOI: 10.1063/1.5119187)

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(4) Other English articles

None

Appendix 2　FY 2020 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).

e.g., a) usually stays at the center,

e.g., send/accept young

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

<Results at the end of FY2020> **Principal Investigators Total: 18**

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 Takao Kurt Hensch*	54	Director, Project Professor, International Research Center for Neurointelligence, The University of Tokyo Institutes for Advanced Study	Ph.D. Neurophysiology	80	October 2017	Communicates often by 20 emails or more per day, and multiple weekly video conferences. Cannot enter Japan in 2020-2021 due to the coronavirus pandemic, but stays at the Boston Children's Hospital IRCN Satellite, and promotes IRCN's interests at universities, research institutions, and academic societies around the world	manages and directs center operations
Masanobu Kano*	63	Deputy Director, International Research Center for Neurointelligence, The University of Tokyo Institutes for Advanced Study Professor, Department of Neurophysiology, Division of Functional Biology, Graduate School of Medicine, The University of Tokyo	M.D. & Ph.D. Neurophysiology	80	October 2017	Stays at the center and participates in the center's activities as Deputy Director and an Executive Board member	

	<Results at the end of FY2020>					Principal Investigators Total: 18
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
Kazuo Emoto*	52	Deputy Director, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study Professor, Department of Biological Sciences, Graduate School of Science, the University of Tokyo	Ph.D. Neural Network	80	October 2017	Stays at the Graduate School of Science next to the center building, and participates in the center's activities as Deputy Director and an Executive Board member	
Kazuyuki Aihara*	66	Deputy Director, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study University Professor, the University of Tokyo	Ph.D. Biological Information Systems	80	October 2017	Stays at the Center and participates in the center's activities as Deputy Director and an Executive Board member	
Haruo Kasai*	64	Professor, Center for Disease Biology and Integrative Medicine, Graduate School of Medicine, the University of Tokyo	MD & PhD Neurophysiology	80	October 2017	Stays at the center and participates in the center's activities as a Steering Comittee member	

<Results at the end of FY2020> **Principal Investigators Total: 18**

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
Kiyoto Kasai*	50	Professor, Department of Neuropsychiatry, Graduate School of Medicine, The University of Tokyo	MD & PhD Neuroimaging and Early Intervention for Schizophrenia	80	October 2017	Stays at the center and participates in the center's activities as a Steering Comittee member	
Kenichi Ohki*	49	Professor, Department of Integrative Physiology, Division of Functional Biology, Graduate School of Medicine, the University of Tokyo	M.D. & Ph.D. Neuroscience	80	October 2017	Stays at the center and participates in the center's activities as a Steering Comittee member	
Arthur Konnerth*	67	Director, Institute of Neuroscience, Technical University of Munich	M.D. & Ph.D. Neurophysiology	50	October 2017	Joined 1st IRCN RETREAT and regularly communicates by email.	

<Results at the end of FY2020> **Principal Investigators Total: 18**

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
Yukiko Gotoh*	56	Professor, Department of Pharmaceutical Sciences, Graduate School of Pharmaceutical Sciences, the University of Tokyo	Ph.D. Neural Stem Cells	80	October 2017	Stays at the Graduate School of Pharmaceutical Sciences and participates in the center's activities	
Yasushi Okada*	52	Professor, Department of Physics, Graduate School of Science, the University of Tokyo	M.D. & Ph.D. Bioimaging	32	October 2017	Stays at the Graduate School of Science and participates in the center's activities	
Shoji Takeuchi*	48	Professor, Department of Mechanical and Biofunctional Systems, Institute of Industrial Science, the University of Tokyo	Ph.D. Biohybrid Systems	80	October 2017	Stays at the Institute of Industrial Science and participates in the center's activities	

<Results at the end of FY2020> **Principal Investigators Total: 18**

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
Masashi Sugiyama*	46	Professor, Department of Complexity Science and Engineering, Graduate School of Frontier Sciences, the University of Tokyo	Ph.D. Statistical Machine Learning	16	October 2017	Stays at the Graduate School of Frontier Sciences and participates in the center's activities	
Takamitsu Watanabe	39	Associate Professor,International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	MD & PhD Cognitive Neuroscience	100	April 2020	Stays at the center and participates in the center's activities	
Yoko Yazaki-Sugiyama	49	Project Associate Professor,International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Biological Science	80	April 2018	Stays at the center and participates in the center's activities	

	<Results at the end of FY2020>					Principal Investigators Total: 18	
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
Yukie Nagai	46	Project Professor,International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Engineering	100	April 2019	Stays at the center and participates in the center's activities	
Sho Tsuji	36	Assistant Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Psycholinguistics	100	April 2019	Stays at the center and participates in the center's activities	
Zenas C. Chao	45	Associate Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Biomedical Engineering	100	September 2019	Stays at the center and participates in the center's activities	

<Results at the end of FY2020> **Principal Investigators Total: 18**

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
Mingbo Cai	35	Assistant Professor,International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Neuroscience	100	December 2019	Stays at the center and participates in the center's activities	

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

Principal investigators unable to participate in project in FY 2020

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age): Takamitsu Watanabe (39 yo)

Affiliation and position: Associate Professor, Principal Investigator, UTokyo Excellent Young Researcher in the WPI-IRCN in UTokyo.

Academic degree and speciality: Academic degree: MD, PhD (Physiology). Specialties: cognitive neuroscience, psychiatry, human brain imaging

Effort: 100 %

Research and education history: After graduation from The University of Tokyo (M.D., 2007) and two-year clinical work in The University of Tokyo Hospital (2007-2009), the PI completed a Ph.D. program in the Department of Physiology at The University of Tokyo School of Medicine (Prof. Yasushi Miyashita; 2009-2013) with support from the JSPS Fellowship program (DC1). He then moved to the UK and started post-doctoral research in the group of Prof. Geraint Rees in the Institute of Cognitive Neuroscience (ICN) in University College London (UCL) under the support of the JSPS Research Abroad Fellowship Program (2013-2015). In 2015, he was awarded the Marie Skłodowska-Curie Individual Fellowship (European Commission) and continued research in the UCL ICN as a Marie-Curie Research Fellow (2015-2018). In 2018, he moved back to Japan as a Deputy Team Leader at the Center for Brain Science in RIKEN and in 2020 launched his own laboratory in the UTokyo IRCN as an Associate Professor supported by the UTokyo Excellent Young Researcher Program.

Achievements and highlights of past research activities: The PI has been attempting to understand how many brain regions interact with each other to realize — or fail to realize in brain disorders — complex, dynamic and unstable human cognitive activity. To this end, he adopted various approaches ranging from theoretical analysis and numerical simulation to psychophysical experiments and brain imaging using functional MRI and clinical trials employing autistic individuals. These activities resulted in 43 original research papers—26 first/last-author studies— in prestigious academic journals, including *Nature Communications*, *Brain*, *PNAS, JAMA Psychiatry*, *Molecular Psychiatry* and *eLife*.

Investigation of oxytocin's effects on autism. One of the significant research achievements of the PI is the discovery of macroscopic neurobiological mechanisms underlying oxytocin's effects on the core symptoms of autism. Until 2014, the therapeutic effects of the neuropeptide on autism were not known. In a case-control study (*PLOS One*, 2012) and a randomized, double-blind, placebo-controlled, clinical trial (*JAMA Psychiatry*, 2014; *Brain,* 2015), the PI identified beneficial effects of oxytocin behaviourally, neurobiologically and clinically. Moreover, he found that this effect is attributable to the elevation of a neurochemical substance in the medial prefrontal cortex (*Molecular Psychiatry,* 2015). Furthermore, along with other studies revealing new neuroanatomical underpinnings of autism (*Scientific Reports,* 2015, 2016), the PI developed a novel deep-learning algorithm and identified genetic variations that can accurately

predict the individual efficacy of oxytocin before actual administration (*Soc. Cog. Affect. Neurosci.,* 2016). Some of these studies are recognized as the first empirical evidence for th beneficial effects of oxytocin on autism, and currently larger randomized clinical trials are proceeding in the US, Australia and Japan.

Brain-dynamics-based novel insights into human cognition. Another significant scientific contribution of the PI is the identification of global and local brain dynamics behind fluctuating but consistent human mental activity, such as uncertain perceptual experience and hesitation before decision making. In conventional analyses used in human neuroimaging studies, it was difficult to characterize spatially and temporally high-dimensional neural data underlying such unstable cognitive activities in a biologically understandable manner. The PI addressed this problem by introducing a new data-driven analysis, the energy landscape analysis, to human neuroimaging research.

In a series of studies (*Nature Communications,* 2013, 2014, 2017*; NeuroImage,* 2014*; Front Neuroinfo.,* 2014*; Phil Trans A,* 2017; *Human Brain Mapp*, 2018; *Communications Biol*, 2020), the PI demonstrated that this energy landscape analysis can automatically identify latent brain states even in spatiotemporally high dimensional data and depict whole-brain neural dynamics as local minima and transitions between such brain states. In particular, applying this analysis to resting-state functional MRI data, he found that the core symptoms of high-functioning autistic adults and their unique cognitive skills can be explained by their atypically stable intrinsic brain dynamics (*Nature Communications*, 2017). This work also revealed that the intelligence of healthy typically-developing adults is attributable to the flexibility of their brain dynamics. Other studies of the PI identified brain state dynamics underlying age-related cognitive changes (*Human Brain Mapp*, 2018) and a theoretical properties of an IQ-brain-dynamics association (*Communications Biol*, 2020).

In recent work (*eLife*, 2019), the PI applied another novel analysis to brain dynamics and found that atypical intrinsic neural timescales in focal brain regions can explain autistic symptoms and its atypical neural development during adolescence. This study is regarded as a breakthrough that could lead to novel diagnosis and treatment regimes for neuropsychiatric disorders (Gollo, *eLife*, 2019).

Achievements

(1) International influence

a) Recipient of international awards

- US National Academy of Medicine Healthy Longevity Global Grand Challenge Catalyst Award (2020).
- The Interstellar Initiative (New York Academy of Sciences, US; AMED in Japan; 2019)
- Marie Skłodowska-Curie Individual Fellowship (2015)

b) Member of a scholarly academy in a major country

Society for Neuroscience (US), Japan Neuroscience Society, The Physiology Society of Japan.

c) Guest speaker or chair of related international conference and/or director or honorary chairman of a

major international academic society in the subject field

- A special speaker at The Meeting of the Japanese Association of Communication Disorders (2020).
- A guest speaker at The Winter Workshop on the Mechanism of Brain and Mind, Japan (2020).
- A special speaker at the Annual Conference of The Japanese Society for Psychiatry and Neurology (2019).
- A chair for a symposium in the annual meeting of Japan Neuroscience Society (Neuro2020).

d) Editor of an international academic journal

Associate Editor for Frontiers in Neuroscience.

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

Swiss National Science Foundation, European Commission, Auckland Medical Research Foundation (New Zealand).

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

- US NAM HLGC Catalyst Award (2020)
- Interstellar Initiative (NYAS, AMED) (2019)
- JSPS Grant-in-aid for Scientific Research (B) (2019-2023)
- JSPS Grant-in-aid for Research Activity Start-up (2018-2019)
- Marie Skłodowska-Curie Individual Fellowship (2015-2017)

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

1. Neurochemical evidence for differential effects of acute and repeated oxytocin administration. 2021. *Molecular Psychiatry.* Citations: 21.
2. Atypical intrinsic neural timescale in autism. 2019. *eLife*. Citations: 31.
3. Brain network dynamics in high-functioning individuals with autism. 2017. *Nature Communications*. Citations: 54.
4. Clinical and neural effects of six-week administration of oxytocin on core symptoms of autism. 2015. *Brain*. Citations: 156.
5. Oxytocin's neurochemical effects in the medial prefrontal cortex underlie recovery of task-specific brain activity in autism: a randomized controlled trial. 2015. *Molecular Psychiatry*. Citations: 91.
6. Energy landscape and dynamics of brain activity during human bistable perception. 2014. *Nature Communications.* Citations: 71.
7. Oxytocin improves behavioural and neural deficits in inferring others' social emotions in autism. 2014. *Brain*. Citations: 147.
8. Two distinct neural mechanisms underlying indirect reciprocity. 2014. *Proc Natl Acad Sci USA.* Citations: 71.
9. Mitigation of Sociocommunicational Deficits of Autism Through Oxytocin-Induced Recovery of Medial Prefrontal Activity: A Randomized Trial. 2014. *JAMA Psychiatry*. Citations: 146.
10. A pairwise maximum entropy model accurately describes resting-state human brain networks. 2013. 4: 1370. *Nature Communications*. Citations: 111.
11. Functional connectivity between anatomically unconnected areas is shaped by collective network-level effects in the Macaque cortex. 2012. 22:1586–1592. *Cerebral Cortex*. Citations: 175

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

- The PI administered the translation of "Rhythms of the Brain" by György Buzsáki, which was published by Misuzu-shobo (Tokyo, Japan) in 2019.

Appendix 3-1 FY 2020 Records of Center Activities

1. Researchers and other center staffs, satellites, partner institutions

1-1. Number of researchers and other center staffs

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

a) Principal Investigators

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

(number of persons)

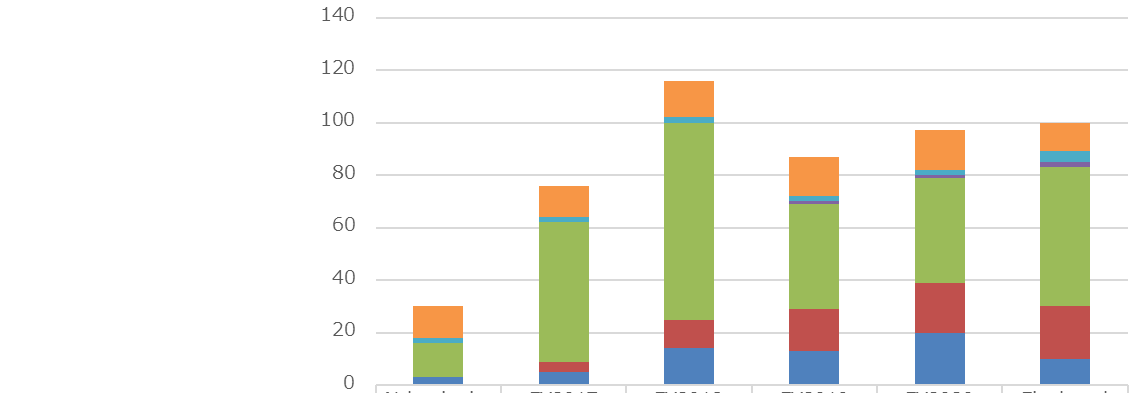
	At the start of the project	At the end of FY 2020	Final goal (March 31, 2027)
Researchers from within the host institution	12	15	11
Researchers invited from abroad	2	2	4
Researchers invited from other Japanese institutions	0	1	2
Total principal investigators	14	18	17

b) Total members

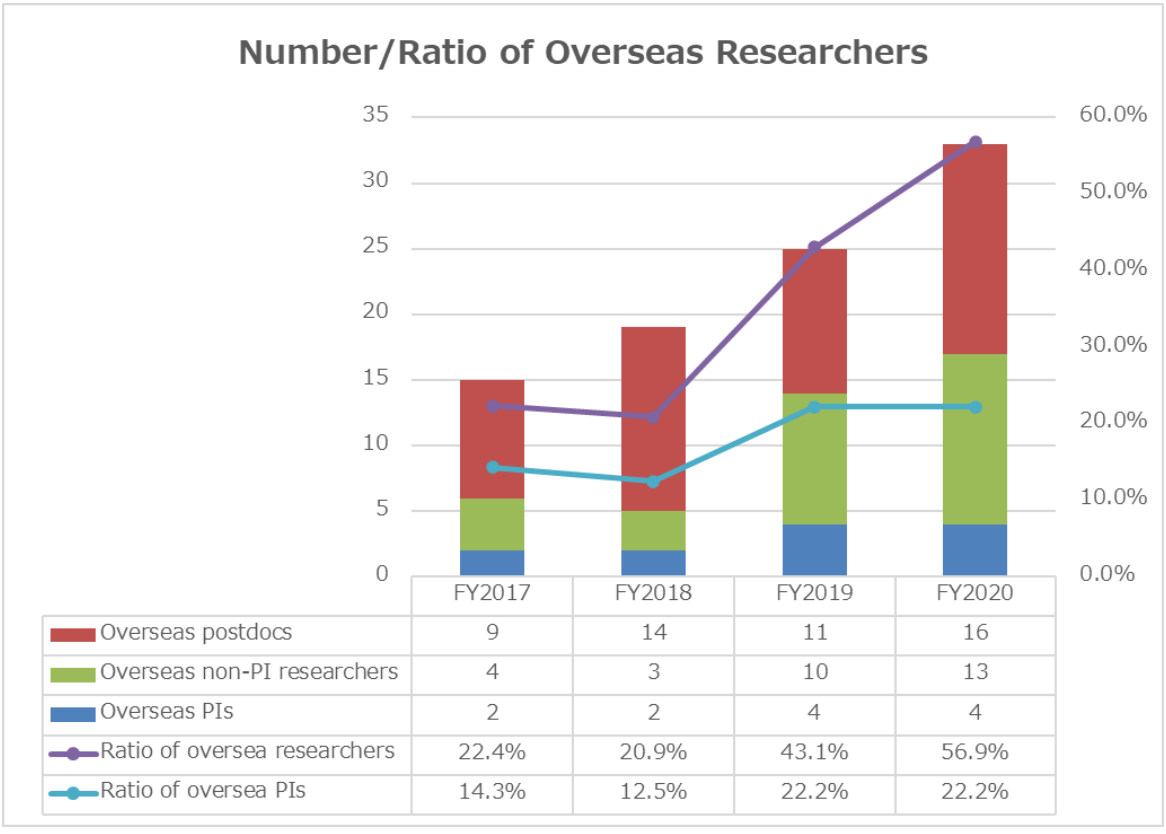
	At the beginning of project		At the end of FY 2020		Final goal (March 31, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	27		75		70	
Overseas researchers	3	11	33	44	24	34
Female researchers	4	15	13	17	12	17
Principal Investigators	14		18		17	
Overseas PIs	2	14	4	22	4	24
Female PIs	1	7	4	22	2	12
Other researchers	13		40		40	
Overseas researchers	1	8	13	33	10	25
Female researchers	3	23	4	10	5	13
Postdocs	0		17		13	
Overseas postdocs	0		16	94	10	77
Female postdocs	0		5	29	5	38
Research support staffs	0		19		20	
Administrative staffs	3		20		10	
Total number of people who form the "core" of the research center	30		114		100	

Appendix 3-2　Annual Transition in the Number of Center Personnel

*Make a graph of the annual transition in the number of center personnel since the start of project.

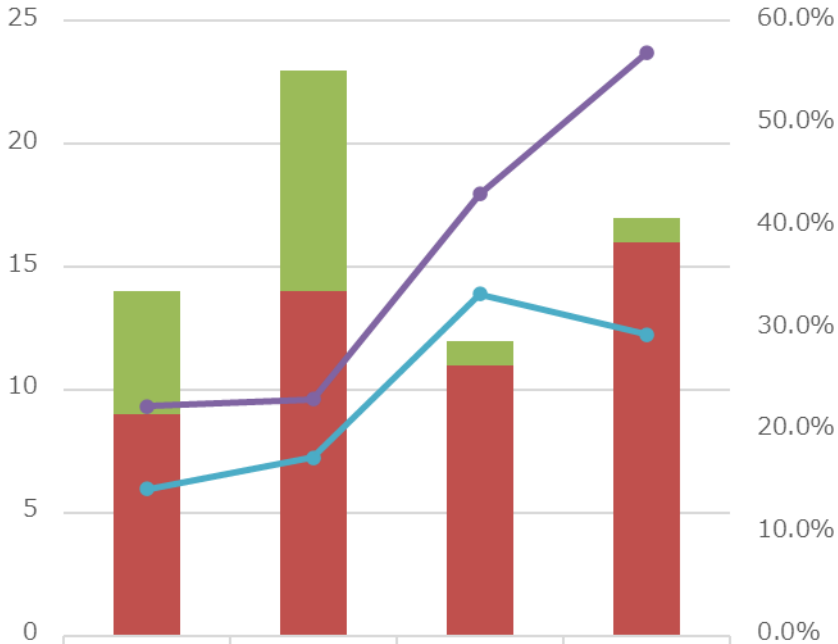


	At beginning	FY2017	FY2018	FY2019	FY2020	Final goal
PI : Researchers from within host institution	12	12	14	15	15	11
PI : Researchers invited from abroad	2	2	2	2	2	4
PI : Researchers invited from other Japanese institutions	0	0	0	1	1	2
Other researchers (incl. postdocs)	13	53	75	40	40	53
Research support staffs	0	4	11	16	19	20
Administrative staffs	3	5	14	13	20	10



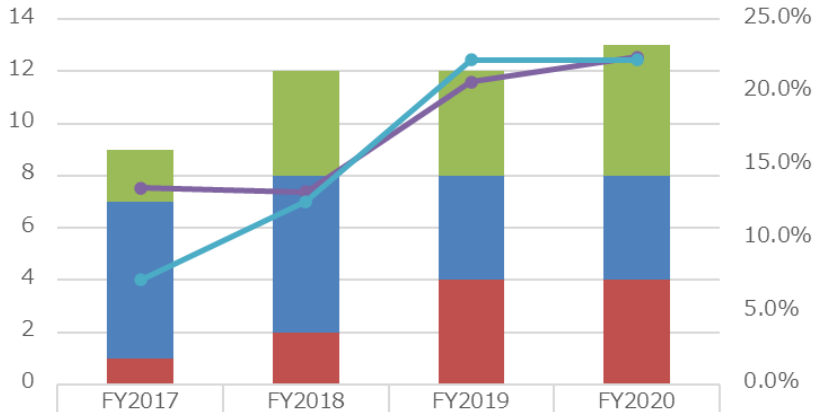
	FY2017	FY2018	FY2019	FY2020
Overseas postdocs	9	14	11	16
Overseas non-PI researchers	4	3	10	13
Overseas PIs	2	2	4	4
Ratio of oversea researchers	22.4%	20.9%	43.1%	56.9%
Ratio of oversea PIs	14.3%	12.5%	22.2%	22.2%

Number/Ratio of Overseas Postdoc



	FY2017	FY2018	FY2019	FY2020
Japanese postdocs	5	9	1	1
Overseas postdocs	9	14	11	16
Ratio of oversea researchers	22.4%	23.1%	43.1%	56.9%
Ratio of female postdocs	14.3%	17.4%	33.3%	29.4%

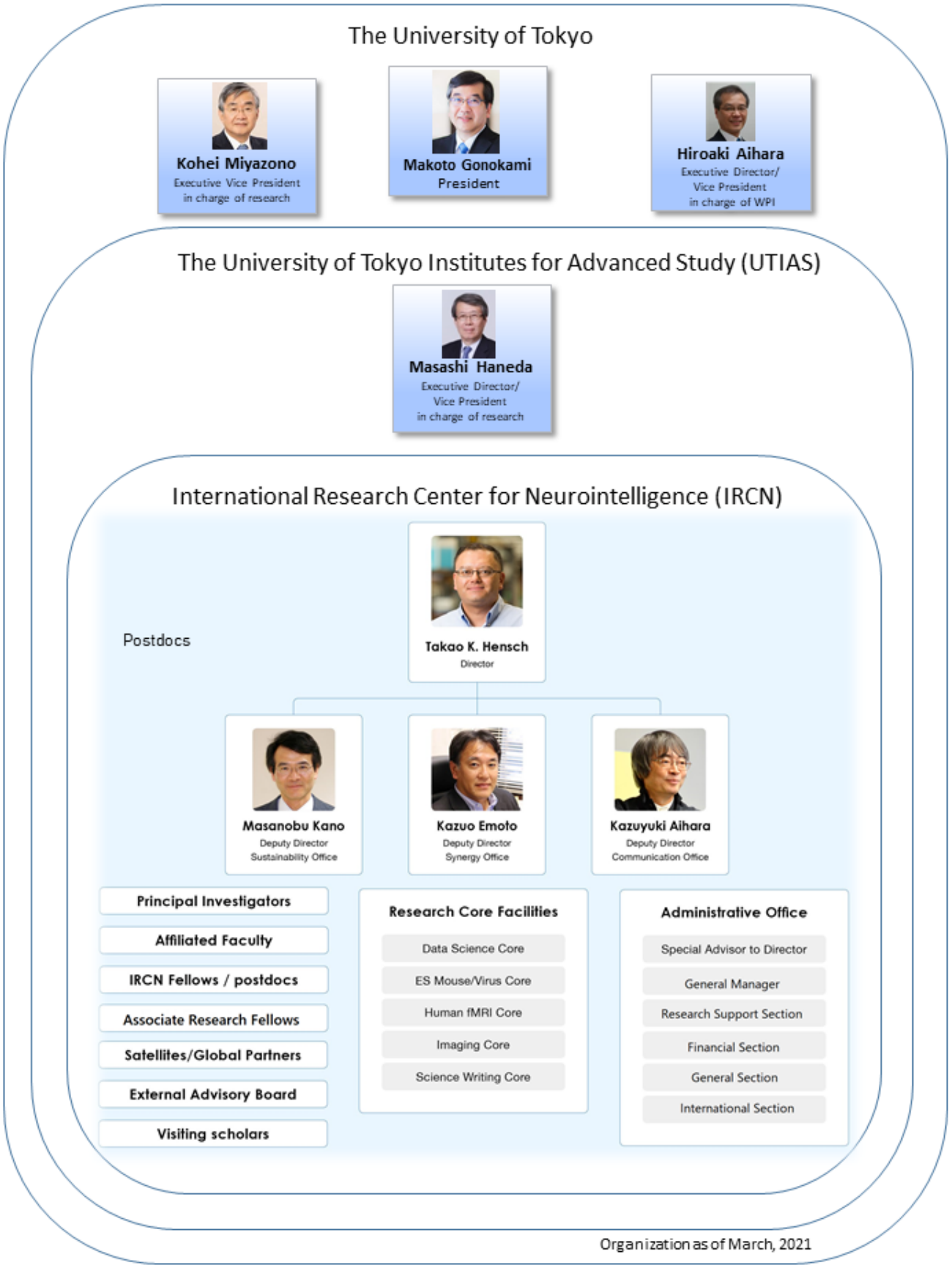
Number/Ratio of Female Researchers



	FY2017	FY2018	FY2019	FY2020
Female postdocs	2	4	4	5
Female non-PI researchers	6	6	4	4
Female PIs	1	2	4	4
Ratio of female researchers	13.4%	13.2%	20.7%	22.4%
Ratio of female PIs	7.1%	12.5%	22.2%	22.2%

Appendix 3-3 Diagram of Management System

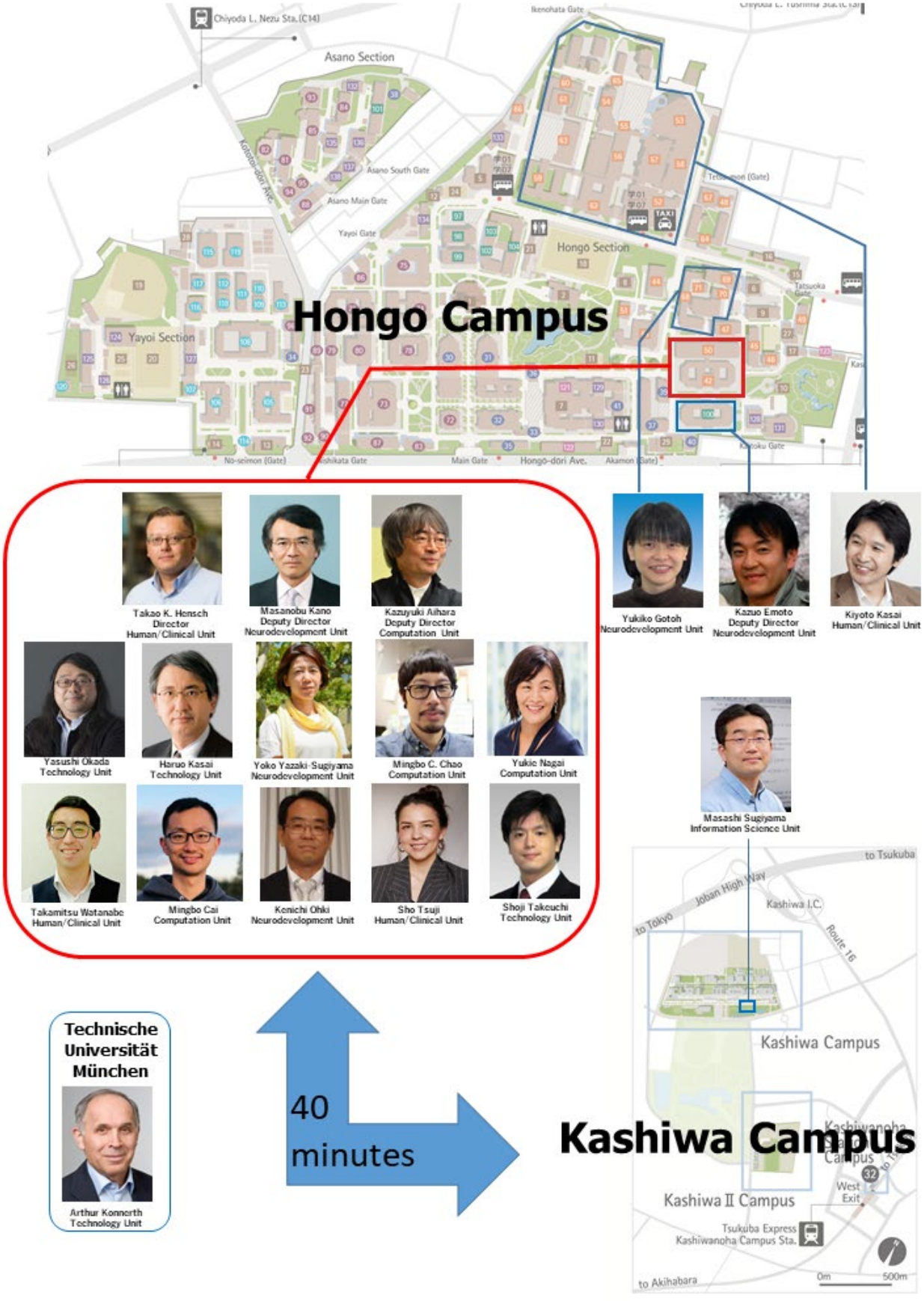
- Diagram the center's management system and its position within the host institution in an easily understood manner.
- If any changes have been made in the management system from that in the latest "center project" last year, describe them. Especially describe any important changes made in such as the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



- Ms. Maki Kubo, Administrative Director, resigned on May 31, 2020, and Mr. Akira Sakurai, General Manager, assumed the acting role of Administrative Director. On January 13, 2021, Dr. Nobukazu Toge joined as Special Advisor to Director and became AD in April 1, 2021.

Appendix 3-4 Campus Map

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



Appendix 3-5　Project Expenditures in FY2020

1) Overall project funding

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

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center director and administrative director	24	24
	Principal investigators (no. of persons):15	178	30
	Other researchers (no. of persons):24	151	137
	Research support staffs (no. of persons):18	64	64
	Administrative staffs (no. of persons):18	111	50
	Subtotal	528	305
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):0		
	Cost of dispatching scientists (no. of persons):0		
	Research startup cost (no. of persons):26	48	48
	Cost of satellite organizations (no. of satellite organizations):1	80	80
	Cost of international symposiums (no. of symposiums):0		
	Rental fees for facilities	66	
	Cost of consumables	18	17
	Cost of utilities	5	
	Other costs	127	66
	Subtotal	344	211
Travel	Domestic travel costs	0	0
	Overseas travel costs	0	0
	Travel and accommodations cost for invited scientists (no. of domestic scientists):0 (no. of overseas scientists):0		
	Travel cost for scientists on transfer (no. of domestic scientists):2 (no. of overseas scientists):5	 1 2	 1 2
	Subtotal	3	3
Equipment	Depreciation of buildings	7	
	Depreciation of equipment	117	
	Subtotal	124	0
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	26	
	KAKENHI	879	
	Commissioned research projects, etc.	1,412	
	Joint research projects	163	
	Ohers (donations, etc.)	170	
	Subtotal	2,650	0
Total		3,649	519

Costs (Million yens)

WPI grant in FY 2020

Costs of establishing and maintaining facilities	8
Establishing new facilities (Number of facilities: , OO m²)	0
Repairing facilities (Number of facilities: , OO m²)	0
Others	8
Costs of equipment procured	72
DGX-StationA100 1set	12
eego mylab recording & review licence	3
Others	57

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

2) Costs of satellites

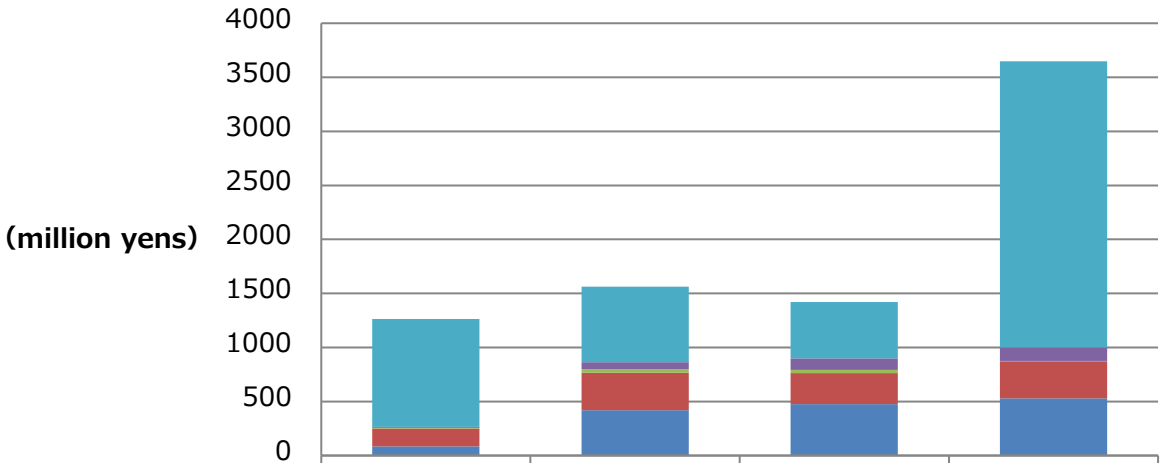
(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):OO		
	Other researchers (no. of persons):OO		
	Research support staffs (no. of persons):OO		
	Administrative staffs (no. of persons):OO		
	Subtotal	0	38
Project activities	Subtotal		42
Travel	Subtotal		
Equipment	Subtotal		
Research projects	Subtotal		
Total		0	80

Appendix 3-6　Annual Transition in the Amounts of Project Funding

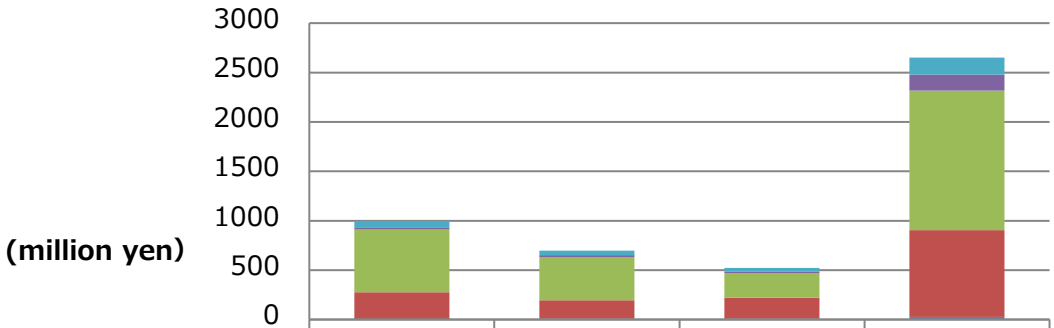
*Make a graph of the transition in the number of overall project funding.

Transition of Project Expenditures



	FY2017	FY2018	FY2019	FY2020
Research Projects	1000	698	523	2650
Equipment	7	65	107	124
Travel	8	34	28	3
Project Activities	164	345	287	344
Personnel	85	420	476	528

Transition of Research Project Expenditures



	FY2017	FY2018	FY2019	FY2020
Ohers (donations, etc.)	72	47	38	170
Joint research projects	16	18	15	163
Commissioned research projects, etc.	636	438	250	1412
KAKENHI	276	189	213	879
Project supported by other government subsidies, etc. *1		6	7	26

*1 Definition is as shown in Appendix 3-5 (Project Expenditures)

Appendix 4-1 FY 2020 Status of Collaboration with Overseas Satellites

- If satellite and partner institutions have been established, fill in required items of the form below.

1. Satellites and partner institutions

- List the satellite and partner institutions in the table below (including the domestic satellite institutes).
- Indicate newly added and deleted institutions in the "Notes" column.

<Satellite institutions>

Institution name	Principal Investigator(s), if any	Notes
Boston Children's Hospital	Takao Hensch	

< Partner institutions>

Institution name	Principal Investigator(s), if any	Notes
The Max Planck Florida Institute for Neuroscience		
Agency For Science, Technology And Research (A*STAR)		
Istituto Italiano di Tecnologia (IIT)		
RIKEN Center for Advanced Intelligence Project (AIP), RIKEN Center for Biosystems Dynamics Research (BDR)	Masashi Sugiyama Yasushi Okada	
National Centre Competence in Research (NCCR) Synapsy		
The Edwin O. Reischauer Institute of Japanese Studies at Harvard University	Takao Hensch	
Asian Consortium on MRI studies on Psychosis	Kiyoto Kasai	
Okinawa Institute of Science and Technology Graduate University	Yoko Yazaki-Sugiyama	
The University of British Columbia		
The Hong Kong University of Science and Technology		
Collège de France		
CIFAR, The Canadian Institute for Advanced Research	Takao Hensch	
Institute of Neuroscience (ION), Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences		
Stockholm University		newly added institution
KTH Royal Institute of Technology		newly added institution
Karolinska Institutet		newly added institution
Tsinghua University		newly added institution

Bielefeld University		newly added institution
École normale supérieure		newly added institution

- If overseas satellite institutions have been established, fill in required items on the form below. If overseas satellite institutions have not been established, it is not necessary to complete the form.

2. Coauthored Papers

- List the refereed papers published in FY 2020 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 1-4. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1-4 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2021 and not described in Appendix 1-4.

Overseas Satellite 1 Boston Children's Hospital (Total: 4 papers)

1) Artoni P, Piffer A, Vinci V, LeBlanc J, *Nelson CA*, *Hensch TK*, *Fagiolini M*. (2020) Deep learning of spontaneous arousal fluctuations detects early cholinergic defects across neurodevelopmental mouse models and patients. Proc Natl Acad Sci USA. 117 (38) 23298-23303.

2) Reh RK, Dias BG, *Nelson CA* 3rd, Kaufer D, *Werker JF*, Kolb B, *Levine JD*, *Hensch TK*. (2020) Critical period regulation across multiple timescales. Proc Natl Acad Sci U S A. 117(38):23242-23251 (cover article).

3) Yamagata T, Raveau M, Kobayashi K, Miyamoto H, Tatsukawa T, Ogiwara I, Itohara S, *Hensch TK*, Yamakawa K. (2020) CRISPR/dCas9-based Scn1a gene activation in inhibitory neurons ameliorates epileptic and behavioral phenotypes of Dravet syndrome model mice. Neurobiol Dis. 141:104954.

4) Kalish BT, Barkat TR, Diel EE, Zhang EJ, Greenberg ME, *Hensch TK*. (2020) Single-nucleus RNA sequencing of mouse auditory cortex reveals critical period triggers and brakes. Proc Natl Acad Sci U S A. 117(21):11744-11752.

Partner Institution 1 University of British Columbia / CIFAR (Total: 2 papers)

1) Maurer D, Ghloum JK, Gibson LC, Watson MR, Chen LM, Akins K, Enns JT, *Hensch TK*, *Werker JF*. (2020) Reduced perceptual narrowing in synesthesia. Proc Natl Acad Sci U S A. 117(18):10089-10096.

2) Reh RK, *Hensch TK, Werker JF*. (2021) Distributional learning of speech sound categories is gated by sensitive periods. Cognition. 19:104653.

3. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2020. 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: Boston Children's Hospital

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2020	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
FY2020	0	0	0	0	0

	0	0	0	0	0

Overseas Partner 1: 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
FY2020	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
FY2020	0	0	0	0	0
	0	0	0	0	0

Appendix 4-2 FY 2020 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: 0

	Name	Age	Affiliation		Academic degree, specialty	Record of research activities (Awards record, etc.)	Time, duration	Summary of activities during stay at center (e.g., participation as principal investigator; short-term stay for joint research; participation in symposium)
			Position title, department, organization	Country				
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								

Appendix4-3 Postdoctoral Positions through Open International Solicitations

* In the column of number of applications and number of selection, put the total number (upper), the number and percentage of overseas researchers in the < > brackets (lower).

Fiscal year	number of applications	number of selection
FY 2017	0	0
	< , %>	< , %>
FY 2018	7	1
	< 7, 100%>	< 1, 100%>
FY 2019	23	2
	<20 , 87%>	< 2, 100%>
FY 2020	23	2
	<20 , 87%>	< 1, 50%>

Appendix 4-4 Status of Employment of Postdoctoral Researchers

Enter the information below during the period from the start of the center through the end of FY 2020.

- For each person, fill in the spaces to the right. More spaces may be added.
- Leave "Position as of April 2021" blank if unknown.
- Enter the host institution name and the center name in the footer.

Japanese Postdocs

Employment period	Position before employed at WPI center		Next position after WPI center		Position as of April 2021*	
	Position title, organization	Country where the organization is located	Position title, organization	Country where the organization is located	Position title, organization	Country where the organization is located
2018.10.1-2021.3.31	The University of Tokyo・Project Researcher	Japan	The University of Tokyo・Project Research Associate	Japan	The University of Tokyo・Project Research Associate	Japan

Overseas Postdocs

Employment period	Position before employed at WPI center		Next position after WPI center		Position as of April 2021*		Nationality
	Position title, organization	Country where the organization is located	Position title, organization	Country where the organization is located	Position title, organization	Country where the organization is located	
2018.5.1-2018.10.31	UniverSity of Tokyo・Project Academic Support Staff	Japan	–		–		France
2018.12.1-2020.3.15	University of Illinois・Postdoctoral Research Associate	USA	HT Hervey and Associates Ecologist	USA	HT Hervey and Associates Ecologist	USA	USA
2019.4.1-2020.3.31	UniverSity of Tokyo・Research student	Japan	Karolinska Institute Postdoctoral Fellow	Sweden	Karolinska Institute Postdoctoral Fellow	Sweden	Brazil
2020.9.1-2020.12.31	University of Bristol・Graduate student	UK	Roundtower Arbitrage Ltd Quantitative Researcher	Ireland	Roundtower Arbitrage Ltd Quantitative Researcher	Ireland	Ireland
2019.9.1-2021.1.31	Peking University・Graduate student	China	Southeast University Assistant Professor	China	Southeast University Assistant Professor	China	China
2018.5.1-2021.1.31	Technische Universitat Munchen・Postdoc	Germany	Hanyang University Researcher	Korea	Hanyang University Researcher	Korea	Korea
2019.4.1-2021.3.31	National Institute of Information and	Japan	Neurocat GmbH・Research Scientist	Germany	Neurocat GmbH・Research Scientist	Germany	Germany

Appendix4-5 List of the Cooperative Research Agreements with Overseas Institutions

*Prepare the information below during the period from the beginning of the Center through March 2021.

1. Name of an Agreement: IRCN Collaboration agreement between The University of Tokyo and Boston Children's Hospital
   Dates of an Agreement: October 10, 2017
   Counterpart of an Agreement: Boston Children's Hospital
   Summary of an Agreement: Joint Project shall be conducted jointly by BCH and IRCN. BCH agrees to permit utilization of the space, equipment, and facilities allocated by BCH to Dr. Takao Hensch for his laboratory and BCH personnel designated for the performance of the Joint Project. IRCN provides necessary funding to BCH to proceed with the Joint Project at BCH.

2. Name of an Agreement: Japan Summer Science Undergraduate Research Program Memorandum of Understanding
   Dates of an Agreement: June 4, 2018
   Counterpart of an Agreement: Edwin O. Reischauer Institute of Japanese Studies (RIJS), Harvard University
   Summary of an Agreement: Kavli IPMU and IRCN accept RIJS students as research interns.

3. Name of an Agreement: Memorandum of Understanding on Academic and Clinical Research Collaboration Between IRCN and Translational Neuroscience Program, Singapore Institute for Clinical Sciences or the Agency for Science, Technology & Research, Singapore
   Dates of an Agreement: June 13, 2018
   Counterpart of an Agreement: Translational Neuroscience Program, Singapore Institute for Clinical Sciences or the Agency for Science, Technology & Research, Singapore (ASTAR* Singapore)
   Summary of an Agreement: Promote international academic collaboration through
   (1) Exchange of faculty, researchers, and administrative staff.
   (2) Exchange of students.
   (3) Conducting collaborative research.
   (4) Holding joint lectures and symposia.
   (5) Exchange of academic information and materials.

4. Name of an Agreement: Memorandum of Understanding on Academic and Clinical Research Collaboration Between IRCN and NCCR "SYNAPSY"-the synaptic bases of mental diseases" University of Geneva-Faculty of Medicine, Switzerland
   Dates of an Agreement: June 14, 2018
   Counterpart of an Agreement: NCCR "SYNAPSY"-the synaptic bases of mental diseases" University of Geneva-Faculty of Medicine, Switzerland
   Summary of an Agreement: Promote international academic collaboration through
   (1) Exchange of faculty, researchers, and administrative staff.
   (2) Exchange of students.
   (3) Conducting collaborative research.
   (4) Holding joint lectures and symposia.
   (5) Exchange of academic information and materials.

5. Name of an Agreement: Memorandum of Understanding between IRCN and RIKEN AIP
   Dates of an Agreement: June 20, 2018
   Counterpart of an Agreement: RIKEN Advanced Intelligence Project
   Summary of an Agreement: Promote international academic collaboration through
   a) Exchange of research and academic materials, and publications.
   b) Exchange of faculty and research scholars including students.
   c) Holding meetings for education and research including seminars and symposia.
   d) Establishment of joint research projects.

6. Name of an Agreement: Memorandum of Understanding between IRCN and Fondazione Institute Italiano di Tecnologia, Italy
   Dates of an Agreement: June 22, 2018
   Counterpart of an Agreement: Fondazione Institute Italiano di Tecnologia, Italy
   Summary of an Agreement: To implement scientific collaboration in areas of mutual interest, mainly but not exclusively in the field of computational neuroscience through
   (1) Exchange of faculty, researchers, and students.
   (2) Conducting collaborative research projects.
   (3) Holding joint lectures and symposia.
   (4) Exchange of research information and materials.

7. Name of an Agreement: Memorandum of Understanding on Scientific Collaboration Between IRCN and the Chair of Morphogenetic Processes of the Collège de France
   Dates of an Agreement: January 16, 2019
   Counterpart of an Agreement: The Chair of Morphogenetic Processes of the Collège de France
   Summary of an Agreement: The collaboration will include
   1. Development of scientific collaboration in any research field of mutual interest.
   2. Researchers' mobility program, in a spirit of reciprocity and mutual benefit, through short and long-term invitations, visiting professorships, and mobility of PhD students and postdoctoral researchers.
   3. Joint organization of conferences, seminars, symposia, workshops, and other scientific Events.
   4. Exchange of information and good practices with the aim to promote the IRCN in France and the research activity of the Chair of Morphogenetic Processes in Japan.
   5. Any other mutually beneficial activity.

8. Name of an Agreement: Memorandum of Understanding between IRCN and RIKEN Center for Biosystems Dynamics Research
   Dates of an Agreement: May 31, 2019
   Counterpart of an Agreement: RIKEN Center for Biosystems Dynamics Research
   Summary of an Agreement: Implement exchanges and other activities in areas of collaboration of mutual interest through
   (1) Exchange of faculty, researchers, and administrative/technical staff.
   (2) Exchange of students.
   (3) Conducting collaborative research.
   (4) Holding joint lectures and symposia.
   (5) Exchange of academic information and materials.

9. Name of an Agreement: Memorandum of Understanding on Mutual Collaboration Between IRCN and CIFAR
   Dates of an Agreement: October 18, 2019
   Counterpart of an Agreement: CIFAR
   Summary of an Agreement: Promote research and other collaborative activities through
   (1) Holding joint workshops and meetings.
   (2) Sharing of academic information and materials.
   (3) Facilitating collaborative research.
   (4) Facilitating visits of faculty, researchers, and administrative staff.

10. Name of an Agreement: Memorandum of Understanding on Research Collaboration Between IRCN and The Hong Kong University of Science and Technology
    Dates of an Agreement: December 13, 2019
    Counterpart of an Agreement: The Hong Kong University of Science and Technology
    Summary of an Agreement: Promote international academic collaboration through
    (1) Exchange of faculty, researchers, and administrative staff.
    (2) Exchange of students.
    (3) Conducting collaborative research.
    (4) Holding joint lectures and symposia.
    (5) Exchange of academic information and materials.

11. Name of an Agreement: Memorandum of Understanding between IRCN and CEBSIT/ION
    Dates of an Agreement: December 20,2019
    Counterpart of an Agreement: CEBSIT/ION
    Summary of an Agreement: Explore opportunities to establish cooperation in the research activities through a program of exchange and collaboration in areas of interest to both institutions, including but not exclusive to neuroscience, brain-machine interfaces, understanding of the structural and functional mesoscopic connectome of the human and animal brain, brain diseases and disorders. Both institutions carry out
    - Visits between institutions by academic staff (faculty), technical and administrative staff.
    - Research collaboration.
    - Joint publications.
    - Joint organization of conferences, seminars or other academic events.
    - Joint delivery of short courses and programs.

12. Name of an Agreement: Agreement concerning Strategic Partnership between the University of Tokyo and Karolinska Institutet・Kungliga Tekniska Högskolan・Stockholm Universitet
    Dates of an Agreement: September 25, 2017 (IRCN joined from FY2020)
    Counterpart of an Agreement: Karolinska Institutet・Kungliga Tekniska Högskolan・Stockholm Universitet
    Summary of an Agreement: implement exchanges, activities and to develop program that will include, though not be limited to
    (a) Exchange of doctorate, Master's, and undergraduate students
    (b) Exchange of academic and administrative staff and researchers
    (c) Organization of Lectures, conferences, and symposia as well as other activities which may be mono-disciplinary or interdisciplinary in nature
    (d) Cooperate in faculty and staff development
    (e) Exchange of materials, publications, and academic information
    (f) Joint research programs and joint publications
    (g) Other cooperative activities as appropriate

13. Name of an Agreement: Memorandum of Understanding on Strategic Partnership
    Dates of an Agreement: July 23, 2018 (IRCN joined form FY2020)
    Counterpart of an Agreement: Tsinghua University
    Summary of an Agreement: The Strategic Partnership will facilitate collaborative advanced research, enhance the mobility of faculty, administrative staff, and students, and provide cross cultural experience for students at various levels.

14. Name of an Agreement: Memorandum of Understanding on Research Collaboration Between IRCN and Faculty of Technology, Bielefeld University
    Dates of an Agreement: February 10, 2020
    Counterpart of an Agreement: Faculty of Technology, Bielefeld University
    Summary of an Agreement: Implement exchanges and other activities in areas of collaboration of mutual interest through
    (1) Exchange of faculty, researchers, and administrative staff.
    (2) Exchange of students.
    (3) Conducting collaborative research.
    (4) Holding joint lectures and symposia.
    (5) Exchange of academic information and materials.

15. Name of an Agreement: Accord D'Echanges Academiques L'Universite de Tokyo et L'Ecole Normale Superieure
    Dates of an Agreement: March 3, 1993 (IRCN joined from FY2020)
    Counterpart of an Agreement: École Normale Supérieure
    Summary of an Agreement: Promote international academic collaboration through
    (1) Exchange of students.
    (2) Exchange of faculty and researchers.
    (3) Exchange of academic information and materials.

Appendix4-6 Holding International Research Meetings

* Indicate up to two of most representative international research conferences or symposiums each financial year and give the number of participants using the table below.

FY2017-FY2018: 20 meetings

Date	Meeting title and Place held	Number of participants
July 24	"Frontiers of Neurointelligence" - Satellite Symposium for The 41st Annual Meeting of the Japan Neuroscience Society Tetsumon Memorial Hall, Hongo campus, UTokyo	From domestic institutions: 202 From overseas institutions: 11
March 21-23	Neuro-inspired Computation Course Sanjo Kaikan and IRCN Seminar Room, Hongo campus, UTokyo	From domestic institutions: 76 From overseas institutions: 39

FY2019: 18 meetings

Date	Meeting title and Place held	Number of participants
September 18	CDKL5 Workshop Ito International Research Center, Hongo campus, UTokyo	From domestic institutions: 78 From overseas institutions: 25
January 26	IRCN-Stockholm Trio Workshop "Neuronal Circuits and Intelligence" Sanjo Kaikan and IRCN Seminar Room, Hongo campus, UTokyo	From domestic institutions: 72 From overseas institutions: 11

FY2020: 8 meetings

Date	Meeting title and Place held	Number of participants
October 10-12	International Symposium on Artificial Intelligence and Brain Science Online	From domestic institutions: 859 From overseas institutions: 948
December	IRCN Deep Learning Online Workshop Online	From domestic institutions: 87 From overseas institutions: 0 (41 UTokyo International researchers/students participated)

Appendix 5 List of Achievements of Center's Outreach Activities between FY 2017 – 2020

* Using the table below, show the achievements of the Center's outreach activities from FY2017 through FY2020 (number of activities, times held).
*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 below, 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

Activities	FY2017 (number of activities, times held)	FY2018	FY2019	FY2020
PR brochure, pamphlet	1	2	1	NA
Lectures, seminars for the general public	1	6	8	3
Teaching, experiments, training for elementary, secondary and high school students	NA	1	10	2
Science cafe	NA	NA	NA	NA
Open house	NA	1	1	NA
Participating, exhibiting in events	2	3	3	3
Press releases	5	11	12	25
Publications of the popular science books	—	NA	12	10
Others	—	*1	*2	*3

*1: Neuro-inspired Computation Course
*2: Open Lab Experiment at Miraikan (first for a WPI Institute)
Workshops on ASD VR Simulator (for patient groups, educators, and Juvenile Medical Reformatory)
*3: Open Lab experiment at Miraikan
Miraikan permanent exhibition, Advancing "neurointelligence" - Brain Observers and Creators

Appendix 5 List of Media Coverage of Projects Carried out between FY 2017 – 2020

* Select main items of press releases, media coverage, and reports for FY 2017-2020 (especially by overseas media)

1) Japan

No.	Date	Type of the media (e.g., newspaper, magazine, television)	Description
1	25-Aug-2017	television	TV program "Shiten Ronten" on NHK with commentary on AI and brain
2	12-Nov-2017	newspaper	Nikkei Shimbun "Kasai et al. conducted a multi-center MRI study on ultra-high risk individuals for developing schizophrenia, and found that increased cortical gyrification may be a promising biomarker for prediction of psychosis
3	19-Dec-2017	news website	Science Newsline Technology "University of Tokyo International Research Center for Neurointelligence holds first annual symposium"
4	9-Jan-2018	press release	Press release at IIS entitled "To jump or not to jump: Impact of renewables and trading on power grid frequency fluctuations" (Announcement on the publication of the article "Non-Gaussian power grid frequency fluctuations characterized by Lévy-stable laws and superstatistics" in Nature Energy
5	9-Jan-2018	newspaper	Nagasaki Shimbun "Non-Gaussian power grid frequency fluctuations characterized by Lévy-stable laws and superstatistics" in Nature Energy
6	9-Jan-2018	newspaper	Ise Shimbun "Non-Gaussian power grid frequency fluctuations characterized by Lévy-stable laws and superstatistics" in Nature Energy
7	12-Jan-2018	newspaper	Nikkan Kogyo Shimbun "Non-Gaussian power grid frequency fluctuations characterized by Lévy-stable laws and superstatistics" in Nature Energy
8	16-Jan-2018	newspaper	Nikkei Business Daily "Non-Gaussian power grid frequency fluctuations characterized by Lévy-stable laws and superstatistics" in Nature Energy
9	9-Mar-2018	newspaper	Kagaku shimbun "Construction of a Single-cell Resolution Whole-brain Atlas"
10	12-Mar-2018	newspaper	Nikkei shimbun "Observation of fluorescent-labeled cells in the well-cleared mouse brain"
11	22-May-2018	newspaper	Yomiuri Shinbun: The launch of Center for Adolescents and Young Adults, UTokyo Hospital **[K. Kasai]**
12	31-May-2018	news agency	Kyodo News: 培養筋肉で動く指ロボット開発　構造工夫で長持ち **[Takeuchi]**
13	31-May-2018	newspaper	Yamanashi Nichi Nichi Shimbun: 培養筋肉で指ロボット(Top news) **[Takeuchi]**
14	31-May-2018	newspaper	The Asahi Shimbun: 筋肉の伸縮で動くロボット **[Takeuchi]**
15	31-May-2018	newspaper	Nikkei Sangyo Shimbun: 生体素材使う指型ロボ　東大、長時間動作可能に **[Takeuchi]**
16	31-May-2018	newspaper	Nikkan Kogyo Shimbun: 東大、筋肉と機械融合　バイオハイブリッドロボ　義手などに応用 **[Takeuchi]**
17	31-May-2018	newspaper	The Sankei Shimbun: 筋肉ロボ　人の腕と同じ動き **[Takeuchi]**
18	31-May-2018	television	TV Asahi: 世界初　筋肉と機械で構成したロボット　東大が開発 **[Takeuchi]**
19	31-May-2018	television	Nippon Television Network: 動物の筋肉と機械組み合わせた指型ロボット **[Takeuchi]**
20	1-Jun-2018	Web	Gigazine: 培養した筋肉を搭載したハイブリッドロボットが開発される **[Takeuchi]** https://gigazine.net/news/20180601-robotic-finger-use-muscles/
21	6-Jun-2018	newspaper	Mainichi Shimbun: ラット細胞で指型ロボット　義手や義足開発に道 **[Takeuchi]**
22	11-Jun-2018	Web	Gizmode: より人間らしく。東京大学による、機械と筋肉を融合したバイオハイブリッドロボットの研究 **[Takeuchi]** https://www.gizmodo.jp/2018/06/tokyouni-biohybrid.html
23	25-Jun-2018	newspaper	Nippon Keizai Shinbun: Strengthening the support for adolescents and young adults with schizophrenia **[K. Kasai]**
24	27-Aug-2018	Web	Yahoo News: Toward integrative care for children with intractable diseases **[K. Kasai]**
25	29-Aug-2018	newspaper	Asahi digital:「夢見ないマウス」遺伝子操作で作製　レム睡眠ほぼゼロ **[Ueda]**
26	29-Aug-2018	newspaper	Mainichi shinbun:「レム睡眠」二つの必須遺伝子を特定 **[Ueda]**

27	29-Aug-2018	Newspaper	Nikkan Kogyo Shinbun: レム睡眠の遺伝子、東大が発見　薬剤開発応用に期待 **[Ueda]**
28	29-Aug-2018	Newspaper	Nikkei Shinbun: 理研、レム睡眠に必須の遺伝子発見　眠りの仕組み解明へ **[Ueda]**
29	11-Sep-2018	Web	HERO-X: 医療に大きな変革をもたらす培養筋肉の研究は、もうここまで来た！ **[Takeuchi]** http://hero-x.jp/article/4992/
30	13-Sep-2018	magagine	第96回　夢見る睡眠をなくしたマウスの誕生から考える **[Ueda]**
31	1-Mar-2019	press release	Symposium and Fashion Show on Considering Symbiosis and the Future of HI and AI through Fashion **[Aihara & Sugiyama]**
32	7-Mar-2019	press release	Teaching AI to Improve Visual Recognition **[Ohki]** (Ukita et al., Characterisation of nonlinear receptive fields of visual neurons by convolutional neural network. Scientific Reports, 2019)
33	8-Mar-2019	Web	Research-er.jp **[Ohki]**
34	18-Mar-2019	Web	Univ Journal Online **[Ohki]**
35	17-Mar-2019	Dempa Newspaper	KDDI Foundation Award **[Sugiyama]**
36	28-Mar-2019	newspaper	NIKKEI SANGYO SHIMBUN: Dresses Designed by AI and Human. The University of Tokyo and RIKEN unveiled 20 Dresses **[Aihara & Sugiyama]**
37	4-Apr-2019	Medical Technology News (website)	**【Ohki】** "Development the Method of Visualization of Neurons by Convolutional Neural Network" "脳細胞の活動を深層ニューラルネットワークに写し取る手法を開発"
38	8-Apr-2019	Asahi Shinbun (website)	**【Takeuchi】** Article on a sensor for human sweat developed by Takeuchi lab "科学の扉　未来創る異分野タッグ　研究現場に「使う側の目線」、実用化へつなぐ"
39	9-Apr-2019	Radio Nikkei (radio)	**【KKasai】** Radio Program about Research on Adolescent Children "思春期の子どもを対象とする主体価値発展学の研究を通して（小児科診療 UP-to-UPDATE番組内）"
40	16-Apr-2019	Harvard Business Review (website)	**【Aihara】** Researcher Interview: Kazuyuki Aihara about "Fashion Show with Collaboration of AI and HI" "100に1つプロのデザイナーが驚くものができればAIをファッションに使う意味はある"
41	4-May-2019	Yomiuri Shinbun (newspaper)	**【Aihara】** "AI takes over a designer?"
42	27-May-2019	Asahi Shinbun (website)	**【Aihara】** "AI takes over HI? - Fashion and AI" "人間はもう超えた！　ファッション向けAIの進化 モードの世界は「創造」も「分析」も、すでに人工知能の得意分野だ"
43	29-May-2019	Nihone Keizai Shinbun (newspaper)	**【IRCN】** "Pioneer of Research Globalization - IRCN, The University of Tokyo" "東大ニューロインテリジェンス国際研究機構 脳科学の謎、世界と挑む"
44	3-Jun-2019	Tokyo Shinbun (newspaper)	**【Nagai】** "Pseudo Experience of ASD with VR Simulator" "VRでリアルに 発達障害の感覚を疑似体験"
45	3-Jun-2019	Chunichi Shinbun (newspaper)	**【Nagai】** "Pseudo Expeirnce of ASD with VR Simulator- For Better Work Environment for Mental Disorders" "発達障害の感覚、VRで疑似体験 職場環境づくりに生かす"
46	11-Jul-2019	CNET Japan (website)	**【Sugiyama】** "Selected by Google AI for Japan" "グーグル、日本のAI人材育成を支援するプログラム「Google AI for Japan」発表"
47	14-Jul-2019	Nikkei Kogyo Shinbun (newspaper)	**【Sugiyama】** "Selected by Google AI for Japan" "グーグル、日本でAI人材育成プロジェクト　東大研究者ら6人に5万ドル"
48	25-Jul-2019	Nikkei Shinbun (website)	**【Okada】** "Nagoya Univ, UTokyo & RIKEN - Development of a Photostable Fluorescent Marker for Super-Resolution Live Imaging of the Dynamic Structure of Mitochondrial Cristae" "名大・理研、細胞が生きたままでミトコンドリアの内膜構造を鮮明―ミトコンドリア蛍光標識剤を開発"
49	7-Aug-2019	Todai Shinbun (newspaper)	**【IRCN】** "To Experience Cutting-Edge Technology for the Next Generation" "IRCN 次世代を支える新技術を体感"
50	16-Aug-2019	Nikkei Sangyo Shinbun (newspaper)	**【Okada】** "Super-Resolution Live Imaging of the Dynamic Stucture of the Mitochondrial Cristae" "ミトコンドリア内部生きたまま観察"

51	18-Aug-2019	Yakuji Nippo (newspaper)	**【Okada】** "Live-Imaging of Cell Structure" "生きたまま細胞の構造観察"
52	20-Aug-2019	PR times (website)	**【Sugiyama】** AI-talented Researcher Interview Series - Masashi Sugiyama "「AIタレントインタビュー」シリーズ「日本におけるAI人材育成について」-Appier チーフAIサイエンティスト ミン・スンと理化学研究所 兼 東京大学 杉山教授が対談"
53	4-Sep-2019	Nihon Keizai Shinbun (newspaper)	**【Aihara】** "Do you want to know your life expectancy?" "未病・未健をデータ解析で知る"
54	21-Sep-2019	Sankei Shinbun and others (newspaper)	**【KKasai】** The launch of "Hikikomori" Committee, Tokyo Metropolitan Government (nominated Kiyoto Kasai as the Committee Chair) "『ひきこもり支援協議会』発足"
55	23-Sep-2019	AERA (magazine)	**【Aihara】** Article about AI and Fashion "AIソールは靴ずれ知らず"
56	5-Oct-2019	NHK news (television)	**【KKasai】** The launch of "Hikikomori" Committee, Tokyo Metropolitan Government (nominated Kiyoto Kasai as the Committee Chair) "『ひきこもり支援協議会』発足"
57	10-Oct-2019	Japanese Journal of Molecular Psychiatry (journal)	**【Hensch】** "Prominent researchers series Vol. 28 featuring Takao K. Hensch" "注目の研究者 Vol. 28　Takao K. Hensch"
58	14-Nov-2019	Exhibition at Miraikan (exhibition)	**【Sugiyama】** "Digitally Natural - Naturally Digital" 3F Miraikan - Supervision Cooperation "計算機と自然、計算機の自然"
59	19-Nov-2019	Nikkei Sangyo Shinbun (newspaper)	**【Aihara】** "Pre-disease signals: Detected by genes" "未病・未健をデータ解析で知る　投薬続投の判断にも"
60	29-Nov-2019	Yomiuri Shinbun （website)	**【KKasai】** "White matter microstructural alterations across four major psychiatric disorders" mega-analysis study in 2937 individuals. Mol Psychiatry, 2019 "4大精神疾患の大脳白質構造の大規模解析を実施、共通の異常を発見"
61	2-Dec-2019	QLifePro Medical NEWS, CB News and others (website)	**【KKasai】** "White matter microstructural alterations across four major psychiatric disorders" mega-analysis study in 2937 individuals. Mol Psychiatry, 2019 "4大精神疾患の大脳白質構造の大規模解析を実施、共通の異常を発見"
62	4-Dec-2019	IT Media News (website)	**【Sugiyama】**「日本は存在感が薄い」東大AI研究者が危機感　国際会議でも「日本人同士で閉じこもっている」
63	6-Dec-2019	Kagaku Shinbun (newspaper)	**【KKasai】** "White matter microstructural alterations across four major psychiatric disorders" "「統合失調症と双極性障害」大脳白質に共通の異常"
64	14-Dec-2019	Chunichi Shinbun (newspaper)	**【Nagai】** "To Experience ASD with ASD VR Simulator" "発達障害を体感し支援 見づらい聞きづらい… VRで"
65	27-Dec-2019	Internet news by LITALICO Inc. (website)	**【Nagai】** News: ASD Simulator Workshop at Medical Juvenile Training School LITALICO発達ナビ, "医療少年院の職員と少年がASDのある人の知覚世界をVR体験–知的障害や発達障害がある少年たちの支援での配慮を考えるワークショップを開催"
66	27-Jan-2020	Nihon Kyoiku Shinbun (newspaper)	**【Nagai】** "Pseudo Experience of ASD with VR Simulator - for Teachers of Special Class for Handicapped Children " "VRで発達障害特有の視覚を疑似体験　特別支援教育コーディネーターに研修"
67	30-Jan-2020	Internet news by LITALICO Inc. (website)	**【Nagai】** Researcher Interview: Yukie Nagai by LITALICO Inc. about ASD Simulator LITALICO研究所 研究者インタビュー vol.3, "ロボット工学の研究者が、発達障害の理解に取り組む理由｜研究者インタビューVol.3・長井志江"
68	13-Feb-2020	Nihon Keizai Shinbun (website)	**【Ohki】** "Univ. Tokyo developed a method to reconstruct what mice see" "マウスが見ている世界を再現する手法を開発"
69	19-Feb-2020	QLifePro Medical NEWS (website)	**【KKasai】**"Reduced Auditory Mismatch Negativity Reflects Impaired Deviance Detection in Schizophrenia" Schizophr Bull, 2020 "統合失調症における脳予測性の障害メカニズムの一端を明らかに"

70	13-Mar-2020	Nikkei Keizai Shinbun (newspaper)	**【Aihara】** "Coronavirus Spread: No Signs of Dying Down" "コロナウイルス感染拡大 - 終息せず"
71	22-Mar-2020	Jiji Tsushin (website)	**【Hkasai】** "Discrimination of Learning in the Brain - Delusions in Schizophrenia" "脳で訂正機能が低下か 統合失調症の妄想―東大"
72	27-Mar-2020	Kagaku Shinbun (newspaper)	**【Hkasai】** "Elucidation of the Mechanism of Antipsychotics and Delusions" "抗精神病薬や妄想症状の機構解明 東大 新たなシナプス仮設導く 統合失調症の早期治療に貢献期待"
73	6-Apr-2020	newspaper	統合失調薬の効用 仕組みを実験で発見 Discovering the Benefits and Mechanisms of Schizophrenia Drugs through Experiments
74	16-Apr-2020	newspaper	Newspaper article entitled "<Restrictions on outings until 2022> US University, Early termination of the state of emergence could lead to resurgence of COVID-19" written by NIHON KEIZAI SHIMBUN
75	18-Apr-2020	Online news	Jiji Press：First identification of primate pheromones in ring-tailed lemurs
76	23-Apr-2020	Press Release	[Okada] Robust Classification of Cell Cycle Phase and Biological Feature Extraction by Image-Based Deep Learning
77	27-Apr-2020	Press release	Press release for Susaki et al. Nat Comm, 2020
78	21-May-2020	Web Magazine	(MONOist) Established observation technology for all organs and whole body scale by 3D histology
79	15-Jul-2020	Press Release	[Daikoku] Musical Expertise Facilitates Statistical Learning Of Rhythm And The Perceptive Uncertainty: A Cross-Cultural Study
80	13-Aug-2020	Press Release	[Watanabe] Humanities and Social Sciences Communications
81	18-Aug-2020	Press Release	[Koike] Machine learning classification using neuroimaging data in schizophrenia, autism, ultra-high risk and first episode psychosis
82	24-Aug-2020	newspaper	朝日新聞「人」https://www.asahi.com/articles/DA3S14595867.html
83	24-Aug-2020	Tokyo Institute of Technology News (Press Releases)	Tiny Protein Packages Released from Cells May Serve as Biomarkers for Early Blood-Based Cancer Diagnosis
84	26-Aug-2020	TV	NHK E, 又吉直樹のヘウレーカ「それでもお肉は食べられる!?」
85	27-Aug-2020	interview	WPIフォーラム "ロボットが教えてくれる「偏見のない世界」の作り方（上・下）" (https://wpi-forum.jsps.go.jp/research/vol6-1/)
86	27-Aug-2020	interview	講談社ブルーバックス "ロボットが教えてくれる「偏見のない世界」の作り方" (https://gendai.ismedia.jp/articles/-/74998)
87	3-Sep-2020	Knowledge & Opinion imidas(Web)	An interview with Associate Professor Hoshino
88	4-Sep-2020	UTokyo Press Release	Autophagosome formation involves dynamic and continuous morphological changes.
89	7-Sep-2020	Nihon Keizai Shimbun(Newspaper)	An article about cancer diagnostic biomarkers
90	11-Sep-2020	press release	[Aihara] Press release at IRCN entitled "Auto-reservoir computing: Construction of a new AI prediction theory" (Announcement on the publication of the article "Autoreservoir computing for multistep ahead prediction based on the spatiotemporal information transformation" in Nature Communications)
91	16-Sep-2020	press release	[Kano] Setd1a Insufficiency in Mice Attenuates Excitatory Synaptic Function and Recapitulates Schizophrenia-Related Behavioral Abnormalities
92	17-Sep-2020	Integrated analysis and regulation of cellular diversity Innovative Areas（Web）	Research Results: Extracellular Vesicle and Particle Biomarkers Define Multiple Human Cancers,Morita Award for Encouragement of Scientific Research
93	18-Sep-2020	new	NIKKEI Business Daily
94	22-Sep-2020	press release	[Emoto] Drosophila miR-87 promotes dendrite regeneration by targeting the transcriptional repressor Tramtrack69
95	25-Sep-2020	newspaper	(The Science News) Autophagosome formation involves dynamic and continuous morphological changes.
96	12-Oct-2020	press release	[Kano] Autism spectrum disorder-like behavior caused by reduced excitatory synaptic transmission in pyramidal neurons of mouse prefrontal cortex
97	14-Oct-2020	JST (Press Releases)	Winners of the 2nd Brilliant Women Researcher Award (Jun Ashida Award) have been selected.

98	15-Oct-2020	newspaper	Nikkan Sangyo Shimbun, Innovation 牛の細胞から「培養肉」
99	19-Oct-2020	magazine	AERA, 培養ステーキ肉　食べ頃近づく
100	25-Oct-2020	web	ニュースイッチ, 日清食品と東大が培養肉の商品化へ、技術開発とルール形成に着手
101	2-Nov-2020	Tokyo Institute of Technology News (Press Releases)	Associate Professor Ayuko Hoshino wins the 2nd Shining Female Researcher Award (President's Award, Japan Science and Technology Agency)
102	3-Nov-2020	press release	[Emoto] A pair of ascending neurons in the subesophageal zone mediates aversive sensory inputs-evoked backward locomotion in Drosophila larvae.
103	3-Nov-2020	tv	NHK 視点・論点　https://www.nhk.or.jp/kaisetsu-blog/400/438700.html
104	6-Nov-2020	magazine	料理王国, 実用化はすぐそこまで来ている!?　実験室から生まれる培養ステーキ肉の現在地
105	9-Nov-2020	tv	日テレThe Social　https://www.news24.jp/articles/2020/11/09/07758009.html
106	11-Nov-2020	press release	The Polycomb group protein Ring1 regulates dorsoventral patterning of the mouse telencephalon
107	15-Nov-2020	JST Activity Report(Web)	Announcement of Winners and Awards Ceremony for the 2nd Brilliant Female Researchers Award (The Jun Ashida Award)
108	28-Nov-2020	web	ニュースイッチ, 日清×東大も培養肉で参入！「フードテック」の進化が止まらない
109	9-Dec-2020	UTokyo Press Release	The mechanism to inflate the lung or swim bladder is related to autophagy.
110	9-Dec-2020	press release	[Emoto] Adeno-associated virus-mediated single cell labeling of mitral cells in the mouse olfactory bulb: Insights into the developmental dynamics of dendrite remodeling.
111	9-Dec-2020	online newspaper	(NIKKEI) The mechanism to inflate the lung or swim bladder is related to autophagy.
112	10-Dec-2020	press release	Press release at IRCN entitled "Digital-Analog conversion scheme capable of reproducing biophysiologically plausible synaptic responses" (Announcement on the publication of the article "Time-domain digital-to-analog converter for spiking neural network hardware" in Circuits, Systems, and Signal Processing)
113	11-Dec-2020	press release	Press release at IRCN entitled "Extended SEIR model and parameter estimation method for outbreak prediction of COVID-19 epidemic" (Announcement on the publication of the article "Inferring key epidemiological parameters and transmission dynamics of COVID-19 based on a modified SEIR model" in Mathematical Modelling of Natural
114	11-Dec-2020	press release	Press release at IRCN entitled "Success in size reduction of reservoir computing model for edge AI" (Announcement on the publication of the article "Model-Size Reduction for Reservoir Computing by Concatenating Internal States Through Time" in Scientific Reports)
115	15-Dec-2020	newspaper	NIKKEI: New technology to visualize single neurons in vivo (introduction for Front Cell Neurosci paper)
116	17-Dec-2020	television	NHK BS Premium 'Humanience'
117	18-Dec-2020	newspaper	(The Science News) The mechanism to inflate the lung or swim bladder is related to autophagy.
118	28-Dec-2020	online newspaper	(NIKKAN KOGYO)The mechanism to inflate the lung or swim bladder is related to autophagy.
119	8-Jan-2021	newspaper	Newspaper article entitled "Consideration of viral transmission from asymptomatic individuals, Extension of conventional mathematical model, highly accurate preprediction of COVID-19 epidemic outbreak" written by KAGAKU
120	14-Jan-2021	Press Release	[Takeuchi] Highly sensitive VOC detectors using insect olfactory receptors reconstituted into lipid bilayers
121	14-Jan-2021	web	Nikkei, 東大とKISTEC、蚊の嗅覚受容体を用いたセンサにより0.5ppbレベルの匂いの検出に成功
122	14-Jan-2021	web	Nikkei BP Beyond Health Report, 「蚊の嗅覚」で呼気中の肝臓がんバイオマーカーを検出、東大　がんや糖尿病の「呼気診断」への応用目指す
123	14-Jan-2021	web	Jiji.com, 蚊の嗅覚、がん診断に利用　小型高精度のセンサー開発ー東大など
124	14-Jan-2021	web	Sankei Shimbun, 蚊の嗅覚で微量のにおい検出成功　東京大　がんの予兆感知に期待
125	14-Jan-2021	web	Kabushiki Shimbun, 蚊の嗅覚用いたがん診断技術ー関連企業に住友化
126	15-Jan-2021	web	EE Times Japan, 0.5ppbレベルの匂いを検出：蚊の嗅覚受容体を用いた匂いセンサーを高精度化

127	18-Jan-2021	web	Mynavi, News, 東大など、蚊の嗅覚受容体を組み込んだ高感度匂いセンサの開発に成功
128	18-Jan-2021	web	NHK News Web, "蚊のタンパク質”人工的に作り高感度の匂いセンサー開発”
129	18-Jan-2021	newspaper	Nikkan Kogyo Shimbun, 肝がん目印　低濃度でも検出　東大，小型においセンサー
130	21-Jan-2021	web	Asahi Shimbun Digital, 蚊の嗅覚の仕組みで肝臓がんを感知　　東大などのチーム、呼気に含まれるにおい物質検出
131	21-Jan-2021	newspaper	Asahi Shimbun, 蚊の嗅覚の仕組みで肝臓がんを感知　　東大などのチーム　呼気に含まれるにおい物質検出
132	21-Jan-2021	UTokyo Press Release	Fluidophagy, a new mechanism for autophagic degradation of phase-separated droplets
133	23-Jan-2021	newspaper	Asahi Syogakusei Shimbun, 蚊のしくみで肝臓がん感知　においを感じる感覚を再現
134	26-Jan-2021	radio	J-WAVE, KONICA MINOLTA GLOBAL SCALE
135	29-Jan-2021	web	Yomiuri Shimbun Online, フードテックで地球を救うために
136	29-Jan-2021	magazine	Yomiuri Quarterly, フードテックで地球を救うために
137	8-Feb-2021	press release	Press release at IRCN entitled "Success in development of optimization method for controlling large group of traffic signals using quantum computing"
138	9-Feb-2021	web	MONOist, 微量の匂い分子を検出する、蚊の嗅覚受容体を利用した匂いセンサーを開発
139	10-Feb-2021	newspaper	Newspaper article entitled "UTokyo and Toyota Central R&D Labs, Development of optimization technique for controlling large-scale group of traffic signals using quantum computer" written by NIHON KEIZAI SHIMBUN
140	11-Feb-2021	newspaper	Newspaper article entitled "Toyota Central R&D Labs, Controlling traffic signals by quantum computer, 10% improvement of traffic flow" written by NIKKAN KOGYO SHIMBUN
141	13-Feb-2021	website	Website article entitled "Methodology for coordination control of traffic signals in large city - collaborative development by Toyota Central R&D Labs and UTokyo" written by RESPONSE (https://this.kiji.is/733226962948177920?c=62479058578587648)
142	14-Feb-2021	newspaper	(Kochi Shinbun) Visualization by light in cells in living organisms, bio-imaging
143	18-Feb-2021	newspaper	(Tokyo Shinbun) Visualization by light in cells in living organisms, bio-imaging
144	19-Feb-2021	newspaper	(Kumamoto Nichinichi shinbun) Visualization by light in cells in living organisms, bio-imaging
145	20-Feb-2021	newspaper	(Hokkaido shinbun) Visualization by light in cells in living organisms, bio-imaging
146	20-Feb-2021	newspaper	(Kobe shinbun) Visualization by light in cells in living organisms, bio-imaging
147	20-Feb-2021	newspaper	(Kawakita shinpo) Visualization by light in cells in living organisms, bio-imaging
148	21-Feb-2021	newspaper	Newspaper article entitled "New Method for COVID-19 Prediction" written by MAINICHI SHIMBUN (Morning edition, page 14)
149	21-Feb-2021	webnews (robotstart)	より賢い人工知能とは何か、AIの根本や社会へのインパクトを問う 東大×ソフトバンク「Beyond AI 研究推進機構 発足記念シンポジウム」
150	22-Feb-2021	newspaper	Newspaper article entitled "10% improvement of traffic flows, Experiments with quantum computers" written by NIHON KEIZAI SHIMBUN (Morning edition, page 11)
151	22-Feb-2021	newspaper	Shimbun Akahata, 蚊の臭覚システム利用　ガン検知
152	24-Feb-2021	newspaper	Newspaper article entitled "Lowering the number of infected individuals, Now is the time to survey close-contact persons, Model analysis" written by NIHON KEIZAI SHIMBUN
153	3-Mar-2021	television	NHK 'Asaichi'
154	10-Mar-2021	press release	Press release at IRCN entitled "Development of a new method for easily predicting flood only from observation data without physical models" (Announcement on the publication of the article "Practical data-driven flood forecasting based on dynamical systems theory" in Water Resources Research)
155	10-Mar-2021	TV	TV Tokyo News, 目指すは“本物” 東大生研×日清食品の培養ステーキ肉【理系通信】
156	13-Mar-2021	magazine	東京大学広報誌 淡青 "ロボットを創ることで人を知る"
157	23-Mar-2021	press release	[Aihara] A quantitative model used to compare within-host SARS-CoV-2, MERS-CoV and SARS-CoV dynamics provides insights into the pathogenesis and treatment of SARS-CoV-2
158	29-Mar-2021	press release	Entropy

2) Overseas

No.	Date	Type of the media (e.g., newspaper, magazine, television)	Description
1	19-Dec-2017	news website	Eurekalert! "University of Tokyo International Research Center for Neurointelligence holds first annual symposium"
2	15-Mar-2018	news website	ALZFORUM "Compact Mouse Brain Atlas: A New Tool for Studying Neurodegeneration?"
3	22-Mar-2018	journal	Nature "In addition to the Kavli Institute for the Physics and Mathematics of the Universe, the International Research Center for Neurointelligence was selected in 2017 as our second WPI centre"
4	22-May-2018	Web	Techrunch: Reseachers recreate a brain, piece by piece **[Takeuchi]** https://techcrunch.com/2018/05/22/researchers-recreate-a-brain-piece-by-piece/
5	22-May-2018	Web	Scince Daily: Building a brain, cell by cell: Researchers make a mini neuron network (of two) **[Takeuchi]** https://www.sciencedaily.com/releases/2018/05/180522114607.htm
6	23-May-2018	Web	Phys.org: Reseachers make a two-neuron network **[Takeuchi]** https://phys.org/news/2018-05-two-neuron-network.html
7	30-May-2018	magagine	National Geographic：New hybrid robot uses living muscles to move **[Takeuchi]** https://news.nationalgeographic.com/2018/05/robotic-living-muscle-tissue-science/
8	31-May-2018	magagine	Futurism: The Cyborgs are here: Researchers put living cells in a robotic finger **[Takeuchi]**
9	31-May-2018	magagine	Forbes: Scientists uncover ways to integrate living muscle into machines to create a 'Biohybrid' Robot **[Takeuchi]** https://www.forbes.com/sites/leebelltech/2018/05/31/scientists-uncover-way-to-integrate-living-muscle-into-machines-to-create-a-biohybrid-robot/#5560fb1d659c
10	1-Jun-2018	magagine	L'express: Ce mini robot a de vrais muscles **[Takeuchi]** https://www.lexpress.fr/actualite/sciences/ce-mini-robot-a-de-vrais-muscles_2013135.html
11	1-Jun-2018	television	Xinhua News Agency: 日本研究人員発明"生物合成机器人 **[Takeuchi]** http://www.xinhuanet.com/2018-06/01/c_1122925312.htm
12	4-Jun-2018	Web	Digital Trends: Japanese researchers have made robots with living muscle tissue **[Takeuchi]**
13	4-Jun-2018	press release	Early-Life Seizures Disrupt Critical Period Plasticity **[Hensch]** Cell Reports 23, May 29, 2018
14	11-Jun-2018	television	BBC World News: Robotic fingers flex their human muscles **[Takeuchi]** https://www.bbc.com/news/av/technology-44371062/robotic-fingers-flex-their-human-muscles
15	7-Sep-2018	press release	Transparent EEG Array Allows Visual Access to Brain **[Hensch]** Science Advances 05 Sep 2018: Vol. 4, no. 9, eaat0626 DOI: 10.1126/sciadv.aat0626
16	18-Sep-2018	press release	Sleep Duration is Determined by Leak Potassium Channels **[Ueda]** (Yoshida et a., Leak potassium channels regulate sleep duration. Proc. Natl. Acad. Sci. USA 115: E9459-E9468. 2018)
17	19-Sep-2018	Web	China Central Television: 聚焦夏季达沃斯论坛 生物混合机器人话题引发热烈 **[Takeuchi]** https://www.youtube.com/watch?v=OPN0Rkc_cXM (2:13~)
18	9-Oct-2018	press release	Dividing Time and Space to Predict the Future **[Aihara]** (Announcement on the publication of the article "Randomly distributed embedding making short-term high-dimensional data predictable" in Proceedings of the National Academy of Sciences of the United
19	18-Dec-2018	press release	Growing a brain: Two-step control mechanism identified in mouse stem cells **[Gotoh]** (Tsuboi et al., Ubiquitination-Independent Repression of PRC1 Targets during Neuronal Fate Restriction in the Developing Mouse Neocortex. Developmental Cell 47, 758-772.e5)
20	31-Jan-2019	press release	Prosocial Behavior and the Teenage Brain **[K. Kasai]** (Okada et al., Neurometabolic and functional connectivity basis of prosocial behavior in early adolescence. Scientific Reports, 2019)
21	31-Jan-2019	press release	New Analog Neural Network to Solve Combinatorial Optimization Problems Effectively **[Aihara]** (Announcement on the publication of the article "Destabilization of local minima in analog spin systems by correction of amplitude heterogeneity" in Physical Review Letters)
22	14-Feb-2019	newspaper	News on the publication of the article "Destabilization of local minima in analog spin systems by correction of amplitude heterogeneity" in Physical Review Letters written by NIKKEI SANGYO SHIMBUN (Morning edition, page 5) **[Aihara]**
23	18-Feb-2019	press release	How the antidepressant ketamine rapidly awakens the brain, and why its effects vary more in women **[Hensch]** (Picard et al., NMDA 2A receptors in parvalbumin cells mediate sex-specific rapid ketamine response on cortical activity. Molecular Psychiatry. 2019)
24	18-Jul-2019	Financial Times (website)	**【Sugiyama】** "Japan falling behind in artificial intelligence, warns SoftBank founder" (Sugiyama's comment included)

25	4-Aug-2019	Interesting Engineering (website)	**【Hensch】** "AI Algorithm Might Detect Autism Early Using Pupil Dialation, Heart Rate"
26	8-Oct-2019	robohub (website)	**【Nagai】** "30 women in robotics you need to know about – 2019"
27	10-Oct-2019	nexus experiments (website)	**【Nagai】** "SARE UND YUKIE NAGAI"
28	27-Dec-2019	Japan Times (newspaper)	**【Nagai】** "VR builds bridge between staff and young detainees with developmental disorders in Japan"
29	20-Mar-2020	Le Monde, in collaboration with CNRS Images (website)	**【Tsuji】** Short documentary on my experiments at ENS babylab https://www.lemonde.fr/sciences/video/2020/03/20/comment-les-bebes-apprennent-a-parler_6033811_1650684.html?fbclid=IwAR0ifjf44047hxEeYzf52qE1uZDUjPDgXUbjOiWycb01Rz6jcSAHOdz--B4
30	16/04/2020	Online news	Nature Research: Lemurs' love language is fragrance
31	16/04/2020	Online news, Video news	CNN: Lemurs' love language is fragrance
32	17/04/2020	Online news	Reuters：Stink flirting' is a thing - just ask a ring-tailed lemur
33	28/07/2020	UTM Biology News (website)	Prof. Joel Levine is awarded 1 of 6 CIFAR & Manulife grants
34	29/07/2020	U of T news (website)	Researchers from U of T, Harvard study collective human behaviour amid COVID-19
35	12/08/2020	news	CNN medical minute, Digital Eye Strain - broadcast on local news outlets around the US
36	13/08/2020	Weill Cornell Medicine Newsroom(Press Releases)	Tiny Protein Packages Released from Cells May Serve as Biomarkers for Early Blood-Based Cancer Diagnosis
37	09/09/2020	magazine	Technology Review, FOKUS BIO-TECH "Es lebe der Roboter"
38	26/10/2020	UTM Biology News (website)	Gut feeling: New research reveals how honeybees identify outsiders
39	27/10/2020	U of T news (website)	Gut feeling: U of T Mississauga research reveals how honeybees identify outsiders
40	01/11/2020	web	Nikkei Asia, Is lab-grown steak coming to a grill near you?
41	13/01/2021	web	EurekAlert!, How does your computer smell? Researchers create a highly sensitive biohybrid olfactory sensor
42	13/01/2021	web	Tech Xplore, Researchers create a highly sensitive biohybrid olfactory sensor
43	14/01/2021	web	TECHNOLOGY NETWORKS, The Smell of Progress: Researchers Create Biohybrid Scent Sensor
44	15/01/2021	web	The Japan Times, Japanese team develops cancer detector using mosquito's sense of smell
45	15/01/2021	web	nano werk, How to give computers a sense of smell
46	15/01/2021	web	CHEMIE.DE, Wie kann Ihr Computer riechen? Forscher schaffen einen hochempfindlichen biohybriden Geruchssensor
47	15/01/2021	web	CHEM Europe.com, How does your computer smell? Researchers create a highly sensitive biohybrid olfactory sensor
48	15/01/2021	web	Chemistry Views, Highly Sensitive, Biobased Detectors for Volatile Organic Compounds
49	16/01/2021	web	gidahatti, Japonlardan çığır açan buluş: Sivrisineklerden kanser dedektörü geliştirildi!
50	19/01/2021	web	7News, Video Mosquitos can be an early warning system for cancer, report finds
51	21/01/2021	web	La Vanguardia, Los mosquitos son capaces de oler los primeros signos de cancer humano
52	24/01/2021	web	Giving Computers a Keen Sense of Smell-Researchers Create a Biohybrid Olfactory Sensor
53	12/02/2021	website	Website article entitled "Will quantum computers control traffic?" written by RealClearWire (https://www.news-daily.com/news/will-quantum-computers-control-traffic/article_0ade9c9d-d78b-5308-8511-2403e95325fc.html)
54	02/03/2021	web	New Scientist, Lab-grown meat now mimics muscle fibres like those found in steak
55	02/03/2021	web	SciTechDaily, Meeting the Meat Needs of the Future: Innovative Biofabrication of Beef Muscle Tissue in the Lab
56	24/03/2021	online magazine	【Frontiers Science News】Study shows stronger brain activity after writing on paper....

57	24/03/2021	website press release	【PR】Study shows stronger brain activity after writing on paper than on tablet or smartphone, UTokyo
58	26/03/2021	website press release	【PR】Measurable changes in brain activity during first few months of studying a new language, UTokyo
59	26/03/2021	online magazine	【Frontiers Science News】Learning a new language gives your brain a temporary activity boost
60	31/03/2021	website press release	【PR】Multilingual people have an advantage over those fluent in only two languages, UTokyo

Appendix6-1 Host Institution's Commitment (Fund, Personnel)

1. Contributions from host institution

(1) Fund, Personnel

* Regarding "Fund" entry, describe with reference to the items in the Progress Report (Jisseki-hokoku-sho) based on Article 12 of the Grant Guidelines (Kofu-yoko).

* Don't include competitive funding obtained by researchers (used as research project funding)

(FY 2017-2020)

<Fund> **(million yen)**

Fiscal Year	2017	2018	2019	2020
Personnel	61	211	223	222
Faculty members	46	150	155	162
Full-time	46	150	155	162
Concurrent				
Postdocs				
RA etc.				
Research support staffs				
Administrative staffs	15	61	68	60
Full-time	15	61	68	60
Concurrent				
Project activities		49	20	131
Travel	0	16	3	0
Equipment			34	46
Research projects	999	698	526	2650
Total	1060	974	806	3049

<Personnel> **(person)**

Fiscal Year	2017	2018	2019	2020
Personnel	15	23	26	22
Faculty members	12	16	17	13
Full-time	12	16	17	13
Concurrent				
Postdocs				
RA etc.				
Research support staffs				
Administrative staffs	3	7	9	9
Full-time	3	7	9	9
Concurrent				

Appendix6-1 Host Institution's Commitment

1. Contributions from host institution

(2) Provision of land and/or building(s), lab space, etc.

The University of Tokyo has provided IRCN with spaces within a part of the Faculty of Medicine Building 1 (1,727m^2), where the University Administrative Council has established a policy of prioritized use by IRCN whenever a vacancy becomes available. IRCN is also provided with part of Faculty of Medicine Experimental Research Bldg (302m^2). This has allowed IRCN to establish the "under one roof" concept of its PI labs and administrative offices. As of March, 2021, the total area available for exclusive use by IRCN is 2,029m^2, and will grow to approximately 2,800m^2 in FY2021.

2. System under which the center's director is able to make substantive personnel and budget allocation decisions

Executive Board (EB)
Key issues pertaining to decisions to be made by the Center Director are discussed at a weekly Executive Board meeting (EB). EB meetings are attended by the Director, Administrative Director and three Deputy Directors, where each of the three directors leads the Sustainability Office, the Synergy Office and the Community Office, respectively. Outcomes from EB discussions are shared, as found appropriate, with members of the Steering Committee, Principal Investigators (PIs), administrative staff and general members within IRCN. Starting in April 2021, the EB meeting will be joined by the Special Advisor to Director, expanding the expertise and knowledge on managerial matters within IRCN.

Steering Committee (SC)
The final decisions on budget, personnel and scientific policy matters are made at Steering Committee (SC) meetings, which are held twice a month and chaired by the Center's Director. SC meetings are attended by members of EB, plus four senior members of IRCN, which allow sound and balanced judgement over a wide range of scientific and technical matters to arise in IRCN. Discussions at SC meetings are in English to allow rapid and effective communication of decisions with non-Japanese members of IRCN.

Principal Investigator Meeting (PI meeting)
IRCN holds a monthly meeting with all Principal Investigators (PI meeting), chaired by the Center Director. Discussions which are made in English and serve as a direct communication channel between the Director and leaders of scientific research at IRCN in both top-down and bottom-up pathways.

Sustainability Office, Synergy Office and Community Office
Three offices, each led by a Deputy Director, serve to strengthen the link between the EB, SC, PIs and all the members of IRCN for the effective management of operations for scientific research at IRCN.
The Sustainability Office is for securing funds, infrastructure and personnel, which includes fundraising, renovation of the building/rooms for the 'under-one-roof' environment, strategic recruiting with an emphasis on diversity, IRCN budget, evaluation and other tasks as a member of the WPI organization.
The Synergy Office is for promoting research fusion and synergy. Suggested by the IRCN Program Committee, it holds workshops, seminars, and salons to foster team science. The office grants a 'Director's Prize' for exemplary team science and science salons.
The Community Office is in charge of education and outreach activities. It handles matters related to teaching of students/researchers, outreach activities, and various learning opportunities within IRCN. It also establishes support mechanisms for foreign researchers.

3. Support for the center director in coordinating with other departments at host institution when recruiting researchers, while giving reasonable regard to the educational and research activities of those departments

While the Center Director personally remains on a constant lookout for new members to join IRCN,

whether as research associates, post-docs, technical staff, affiliated faculties or associated research fellows, all PIs are continually encouraged in parallel to look for strong candidates as new members. Proposals for new recruitment are handled by a filtering process of EB and SC, together with regularly held IRCN Salons attended by the Center Director, where candidates are invited to give a seminar and to participate in subsequent discussions therein. This ensures IRCN to maintain the highest quality of new members' academic capabilities and their contributions to interdisciplinary fusion research.

4. Revamping host institution's internal systems to allow introducing of new management methods

(e.g., English-language environment, merit-based pay, cross appointment, top-down decision making unfettered by conventional modes of operation)

IRCN within The University of Tokyo has been established as a research center under The University of Tokyo Institutes for Advanced Study (UTIAS). In this set-up the Center Director is allowed to put in place the IRCN-specific special internal rules on salaries, management structure and governance over center-wide research directions, with approval by UTIAS, being apart from other faculties and institutes of The University of Tokyo. In this way, the Center Director may directly take change in its organizational management, and may maintain IRCN's strong positioning within The University of Tokyo, with its ambitious programs for fusion research and aggressive recruitment of international researchers, despite its relatively small size in terms of budget and personnel.

5. Utilities and other infrastructure support provided by host institution

(*In addition to those listed in the item 1. "Contributions from host institution")

In 2020 the main headquarters office of The University of Tokyo took charge of leasing the spaces in the Faculty of Medicine Building 1. This allows shortening of the negotiation process for IRCN to acquire new laboratory and office spaces, while maintaining the assistance extended by the Faculty of Medicine on general utilities matters. Long-range plans to meet a growing need for lab space and research infrastructure continues to be an important topic of discussion between IRCN and the headquarters office of the University.

6. Support for other types of assistance

In addition to the aforementioned items, support for other types of assistance from The University of Tokyo are listed as follows:

Budget support for materials, operation and personnel

Part of the rental fees for the fMRI apparatus is supported by The University of Tokyo and by the Faculty of Medicine, respectively.
Part of the salaries for a University Professor (one of the Deputy Directors) is supported in part by The University of Tokyo.
A main part of the salary for the Executive Director is supported directly by The University of Tokyo.
Salaries and University start-up funds for three of the principal investigators who had been awarded "The University of Tokyo Excellent Young Researcher" are supported directly by The University of Tokyo.
Salaries of administrative members at IRCN, who had been hired by the headquarters of The University of Tokyo, are supported directly by the University.
The University of Tokyo extended its support to IRCN in the total amount of approximately 100MYen in FY2018 through FY2019 for employment of URAs.
The University in 2020 has approved a budget of 3MYen for a public event for IRCN to be hosted by the University's New York office in US. The event is scheduled to be held in 2021.
A University budget in the amount of 15MYen was appropriated for supporting a part of the Team Science research program.

Programs which helps enhance the presence of IRCN within the University

Members of IRCN, who are participating in the FoPM (Forefront Physics and Mathematics Program to Drive Transformation, https://www.s.u-tokyo.ac.jp/en/FoPM/) at the University Tokyo are gaining teaching opportunities in formal courses at the School of Science, which are otherwise unavailable for

academic members with Project positions.
IRCN is one of the affiliated centers in the Next Generation Artificial Intelligence Research Center (https://www.ai.u-tokyo.ac.jp/en/) .
Some PIs, Core Managers and researchers of IRCN have been offered dual teaching positions by Graduate Schools of the University of Tokyo, such as Information Science and Technologies, and School of Engineering, to direct education programs of graduate students.
These opportunities have increased the recognition and presence of IRCN within the academic community of the University.

Other support
An internship program to train visiting students from Harvard University in 2019 was supported (annual budget allocation of 7MYen for four years) by an International Exchange Program for Young Scientists as hosted by the School of Medicine.
In the Strategic Partnership Project of the University of Tokyo, IRCN received support of 1.17MYen for its collaborative research with Tsinghua University in China and 1.18MYen with the Group of Stockholm in Sweden from the University through the Faculty of Engineering.

Appendix6-2 The Host Institution's Mid-term Plan

* Excerpt the places in the host institution's "Mid-term objectives" and/or "Mid-term plan" that clearly show the positioning of the WPI center within its organization.

Regarding IRCN as a WPI center within the University of Tokyo, the "Mid-term Objectives" and "Mid-term Plan" of The University of Tokyo has no specific mention of the center's name. However, "Vision 2020" of The University of Tokyo (https://www.u-tokyo.ac.jp/content/400039193.pdf), announced in 2015, states one of the planned actions of the University as, "… leading the world in unique areas of original research which should unwaveringly continue to be studied, promoting joint research and international collaboration that goes beyond the framework of The University of Tokyo, and creating new, interdisciplinary knowledge that is the first of its kind in the world."
The declaration in "Vision 2020" is inherited in The University of Tokyo's "3rd phase" mid-term research objectives of 2016 (https://www.u-tokyo.ac.jp/content/400158043.pdf) which includes a general statement: "pursue excellence and diversity in all branches of research, and, on this basis, pro-actively engage itself in creation of new disciplines of science, thereby performing the world-class academic endeavor to lead production of new knowledge for the world". The accompanying medium-term plan has a statement: "create research centers, which are capable of responding to social and academic problems in a pioneering, effective and practical manner, whereby facilitating fused and solution-oriented research activities."
It is under this spirit and plan that The University of Tokyo has been extending its fullest support to IRCN.