World Premier International Research Center Initiative (WPI)
FY 2019 WPI Project Progress Report

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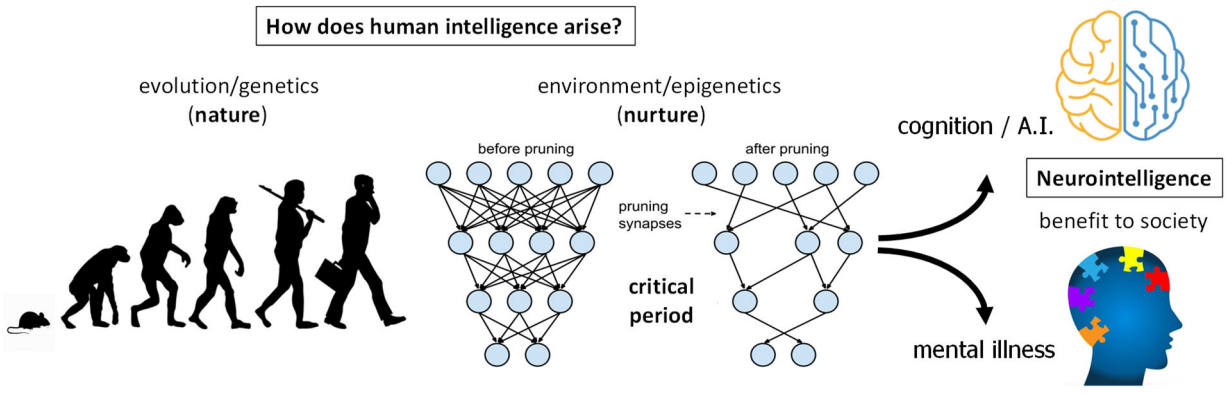
Common instructions:
* Unless otherwise specified, prepare this report based on the current (31 March 2020) situation of your WPI center.
* So as to execute this fiscal year's follow-up review on the "last" center project plan, prepare this report based on it.
* Use yen (¥) when writing monetary amounts in the report. If an exchange rate is used to calculate the yen amount, give the rate.

➢ Prepare this report within 10-20 pages (excluding the appendices, and including Summary of State of WPI Center Project Progress (within 2 pages)).

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

Intelligence is the ability to adapt to change – a feature of the brain's 'plasticity' that is typically enhanced early in life. At IRCN, we are tackling the challenge "how does human intelligence (H.I.) arise?" from a developmental perspective. Thus, H.I. is the product of both nature (brain evolution stretching across millenia) and nurture (the tailoring of circuits to suit the environment in one lifetime). Unlike any other time before, we are now poised to drive our own evolution through the fusion of neuroscience and computer science to create a novel "neuro" intelligence (N.I.). This promises advances toward deeper understanding of disorders of cognition, their prophylactic intervention and neuro-inspired artificial intelligence (A.I.). For example, inhibitory interneurons play a pivotal role on a millisecond scale (oscillatory activity), across the lifespan (timing critical periods of brain plasticity) and in the etiology of mental illnesses. Only now do we fully appreciate the rich diversity of inhibition – poetically termed "butterflies of the soul" by Cajal – which has hardly been considered in modern machine learning. In the words of Alan Turing: "*Instead of trying to produce a programme to simulate the adult mind, why not rather try to produce one which simulates the child's? If this were then subjected to an appropriate course of education one would obtain the adult brain.*" ("Computing Machinery and Intelligence", 1950).

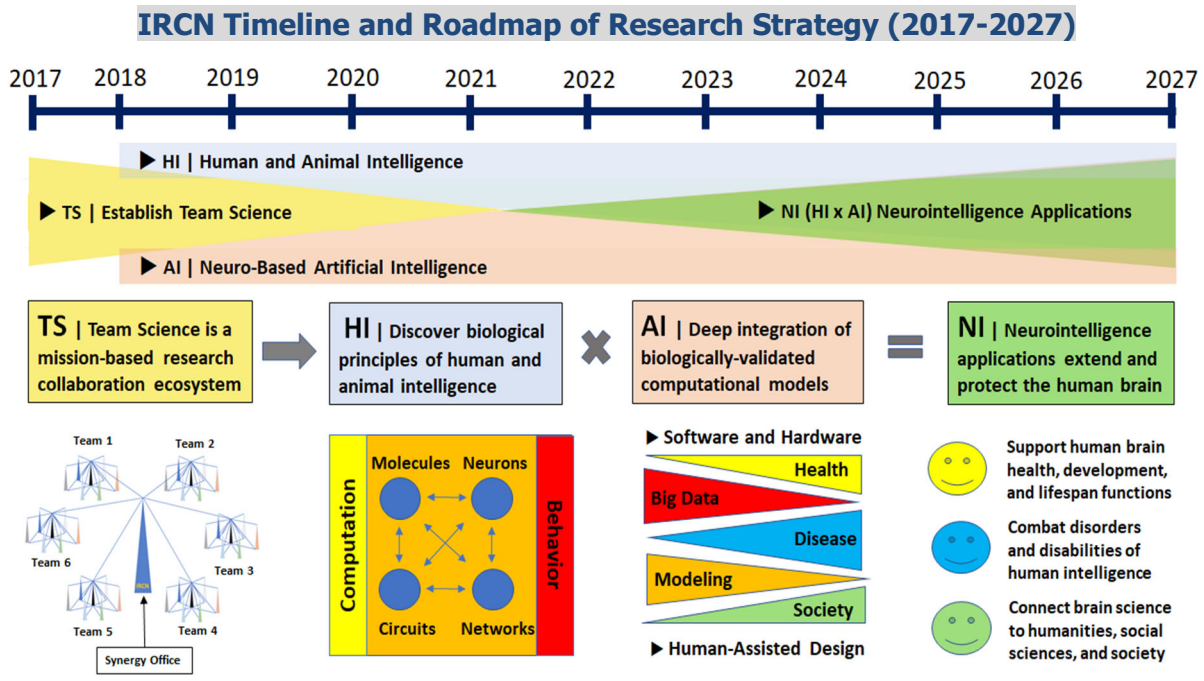


Infrastructure: The International Research Center for Neurointelligence (IRCN) launched October 2017 at the Hongo medical campus of UTokyo has taken a stepwise approach to establish a robust ecosystem for the integration across disciplines necessary to pursue our mission. To understand how H.I. arises, we must study humans and their brain development; to uncover basic mechanisms and underlying core concepts, we must study animals and disease etiology; to create next-generation A.I. based on these principles, we must re-engineer machine learning. Over the past 2.5 years, we successfully brought 'under-one-roof' neurobiologists, psychologists, clinicians and computational scientists from around the world. Specifically, in FY2019 the corps of PIs achieved greater balance in computation and human studies, by recruiting Drs Yukie Nagai, Zenas Chao, Mingbo Cai, Sho Tsuji, Takamitsu Watanabe, and relocating Prof Kazuyuki Aihara as a third Deputy Director from Komaba campus to Hongo. Over 35 Affiliated Faculty (AF) joined IRCN research fusion events and made use

of our five core facilities (cellular imaging, fMRI, ES mouse/virus, data science, science writing).

Globalization & Reform: With the support of UTokyo, IRCN successfully created an ecosystem in Japan to welcome the confluence of disciplines and strategic global partners. The latter include a growing international network now spanning Europe, North America, Asia and Japan to nurture the N.I. field through 'an appropriate course of education.' We are actively training the next generation fluent in both neuroscience and computer science. This includes multiple Workshops with global partners, our highly popular Neuro-inspired Computation Course in 2019, and courses in the new WISE graduate program (with Dept. Physics/Engineering). Moreover, IRCN has promoted ED Charles Yokoyama (former Cell Press editor) as a special discretionary Professor to teach English scientific writing skills across all of UTokyo. Finally, IRCN has dramatically expanded both the international and gender diversity at UTokyo School of Medicine.

Fusion: Together, PIs and AFs are now engaged in phase 1 'Team Science' to elucidate principles of neural circuit development and how it goes awry in psychiatric disorders using current A.I. tools. For example, in FY2019 IRCN research produced innovative probes (e.g. XCaMPs, *Cell*) and other tools that helped reveal how antidepressants rescue prefrontal circuit dysfunction (*Science*), and used deep neural networks to model altered arousal states in mouse models of autism that was successfully translated to rare human patient data (*PNAS*). In phase 2, we will seek new insights for truly neuro-inspired A.I. and innovative, next-generation approaches toward better understanding and improving the human condition.



What exactly is N.I.? We consider two views. First, N.I. lies at the intersection of H.I. and A.I. The common use of 'neurons' in both natural and artificial networks as a shared source of intelligent behavior motivates consortia and corporate efforts worldwide. Research at IRCN is uniquely aimed at the highly orchestrated stages of brain development, optimized through evolution, to reveal how emergent properties arise when neurons dynamically organize into connected ensembles and across individuals. Second, N.I. may be considered as a super-additive cooperation of H.I and A.I. contributing to the fruits of H.I. – the humanities and social sciences. By projecting a faithful replica of our inner selves, N.I. will allow mankind to strive for broader horizons currently beyond our reach – to adapt and make rational "human" decisions in the depths of the oceans or outer space. With increasing computational power and speed, some machines now outperform human experts, but not without shortcomings. Highly inefficient in their thirst for energy and input data, they lack the flexibility and generalizability that define H.I. Indeed, neuroscientists would argue that we are still far from understanding the living brain at sufficient detail, or even knowing what "sufficient" might mean. Our roadmap aims to fill this gap for the ultimate benefit to society.

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

1. Advancing Research of the Highest Global Level

* Among the research results achieved by the center, concretely describe those that are at the world's highest level. In Appendix 1, list the center's research papers published in 2019.
* Regarding the criteria used when evaluating the world level of center, note any updated results using your previous evaluation criteria and methods or any improvements you have made to those criteria and methods.

How does human intelligence arise? At IRCN, we tackle this challenging question in three domains:
①Establish bottom-up principles of neural circuit **development**
②Innovate **computation** (A.I.) based on these principles
③Unravel mechanisms of **human clinical** neurodevelopmental disorders
Supporting these missions is a fourth domain of **technology** development. We summarize below our progress in these four dimensions at the world's highest level.

In FY2019, IRCN PIs published 90 original papers altogether (56 WPI papers and 34 WPI-related papers: See Appendix 1) in high-impact, globally-renowned scientific journals, including *Nature, Science, Cell, Cell Reports, eLife, PLoS Biology, Nature Communications, Journal of Neuroscience, Molecular Psychiatry,* and *Proceedings of the National Academy of Sciences USA*. These journal articles were often the result of international collaborations and received global press releases and coverage that drew worldwide attention. In parallel, PIs in computer science and engineering fields focused on rapidly reporting their breakthroughs at international conferences of the highest scientific quality and rigor. Team Science was launched, and IRCN sharpened its focus on collaborative, interdisciplinary research.

[Development Unit]

Neural Network Formation in Brain Development (Kano, Emoto Lab)

The human brain achieves intelligence in part by pruning excessive synapses and neurites from the neural network during early postnatal development. Conversely, autism spectrum disorder (ASD) patients often have major defects in the elimination process resulting in too many or too few synapses. To understand the origins of intelligence, the Kano and Emoto labs are investigating the molecular, cellular and neural circuit mechanisms of synapse pruning/elimination in the cerebellum, a model system involving the postnatal refinement of climbing fiber to Purkinje cell synapses. The Kano lab found that a key intracellular signaling enzyme, phospholipase C β3, is required for climbing fiber synapse elimination in Purkinje cells after postnatal day 15 (P15) of cerebellar development (in submission). Current findings implicate the further involvement in synaptic pruning of a cohort of key molecules, including transcription factors, cell adhesion proteins, and ASD-related factors. Neurite regeneration is an opposing process to pruning. The Emoto lab performed a genome-wide screen for genes involved in neurite degeneration and regeneration in Drosophila and discovered a microRNA called miR87 that serves as a critical molecular switch to reactivate dendrite regeneration (in press, PLOS Genetics). They also found that different E3 Ubiquitin ligases contribute to synapse elimination and dendrite pruning in neurons (unpublished). In collaboration with the Computational Unit and the Kano lab, the Emoto lab modeled the elimination of extra synaptic connections in a theoretical brain network during development to regulate computational efficiency and energy conservation, suggesting potential network mechanisms (63).

4-Dimensional Mapping of Critical Periods (Yazaki-Sugiyama, Hensch, Kopell, Okada Lab)

The Hensch lab made seminal observations on the mechanisms of early postnatal critical period timing. Notably, his lab has accumulated evidence that a pivotal inhibitory (PV) cell type controls the opening and closure of such early windows of circuit rewiring (Reh et al (2020) *PNAS*, in press). Now, they and other IRCN labs are pursuing a detailed understanding of critical period plasticity in time and space in the developing brain, with insights expected to outline the roots of human intelligence. First, his lab has found that oscillatory activity in the γ-frequency (30-80 Hz) range is a signature of the open critical period state due to a rapid plasticity of input onto PV-cells (submitted). Genetically induced γ-oscillations extend the critical period into adulthood by destabilizing the perineuronal nets (PNN), which enwrap PV-cells (submitted). Both findings are faithfully captured in

new computational models of emergent excitatory/inhibitory (E/I) circuit balance constructed in collaboration with two Affiliated Faculty, Nancy Kopell and Michelle McCarthy, which can now be applied to neuro- developmental disorders.

Second, the Yazaki-Sugiyama lab uses bird song learning as a model of vocal communication to understand how brain circuits and social behavior are shaped by the sensory environment during the critical period for song production. For example, they previously showed how auditory memories acquired at different time points are expressed in the brain when zebra finches learn two songs sequentially during development. Parallel work in mice and birds now examines how critical period timing, the opening and closing of the brain's developmental windows, is affected by sedative drugs. Thus, the critical period timing of zebra finch song learning can be accelerated by exposure to pre-critical period diazepam, a GABA-A receptor agonist, resulting in impaired song acquisition (submitted). Likewise, repeated anesthesia early in life acts on GABA receptors to accelerate critical period development in mice (in preparation). Taken together, these results strongly urge caution for the pediatric use of selected anesthetics in human infants to avoid altering trajectories of cognitive functions such as language (see Human/Clinical unit described later). Finally, the Yazaki-Sugiyama, Hensch and Okada labs are mapping the emergence of PNNs across mouse brain regions and anatomical connections that are active between the higher auditory cortex, where early auditory memories are stored, and higher vocal centers, where sensory-motor information is integrated, during developmental song learning, using tissue clearing methods on whole brains (see Technology unit described later).

Neural Information Processing in Neocortical Circuits (Ohki, Kano, Gotoh Lab)

One of the hallmarks of mammalian intelligence is the sheer power of information processing by the cerebral cortex. The Ohki lab studied how sparsely active neurons in the primary visual cortex (V1) reliably represent complex natural images and how information is optimally decoded from these representations. They recorded visual responses to natural images from several hundred V1 neurons and computationally reconstructed the images from neural activity in awake mice. A single natural image was linearly decodable from a surprisingly small number of highly responsive neurons, and the remaining neurons even degraded decoding accuracy. Furthermore, these neurons reliably represented the image across multiple trials despite trial-to-trial response variability. Evidently, diverse, partially overlapping receptive fields ensure sparse and reliable representation. Collecting only the activity of highly responsive neurons is an optimal decoding strategy for the downstream neurons and may inspire the design of novel AI architectures (Yoshida and Ohki (2020), *Nature Communications*). Brain information processing requires the maintenance of a fine balance between excitation and inhibition in the cortex. The Gotoh and Kano labs explored the underlying mechanisms of E/I balance in developmental disease models. They generated a mouse model of ASD that showed transient brain overgrowth at early postnatal stages. Analyses of the electrophysiological features of pyramidal neurons in layer 2/3 located in the prefrontal cortex (PFC) indicated an altered E/I balance (unpublished). Furthermore, the Gotoh lab found ASD-related phenotypes in mice induced by maternal immune activation was ameliorated by suppression of microglial activation (unpublished). In another mouse disease model, loss of the schizophrenia-related gene Setd1a reduced the E/I balance of synaptic inputs to layer 2/3 pyramidal neurons in the medial PFC and caused behavioral abnormalities mirroring symptoms of schizophrenia patients (in submission). Thus, neocortical networks regulate information flow by fine tuning and rebalancing neural activity in local circuits.

Development of Reinforcement Learning and Memory (H. Kasai, Ishii Lab)

Reinforcement learning governs brain responses to reward and punishment contingencies in the environment. Haruo Kasai's lab studied discrimination learning in the mouse, developing new behavioral tasks and photometric measurements of dopamine activity using a new optical dopamine sensor, GRAB-DA in a subcortical brain area called the nucleus accumbens. They studied the properties of dopamine neuron firing in reward conditioning, and detected a characteristic pattern called the dopamine dip occurring in neurons that express dopamine D2 receptors (D2Rs). The D2R-dependent discrimination learning is used to refine generalized reward conditioning mediated by dopamine D1 receptors found in neighboring neurons. Strikingly, discrimination learning was impaired in psychosis model mice, and rescued by an antipsychotic drug. In collaboration with the lab of computational IRCN Affiliated Faculty Member Shin Ishii, they found that over-generalization of conditioning by impairment of discrimination learning may contribute to the development of psychosis in disorders such as schizophrenia (Iino et al. (2020), *Nature*). These findings open a door

to a new framework for the development of psychosis in neural circuits. In ongoing computational studies, novel reinforcement learning algorithms for AI are under formulation by the Ishii lab.

[Technology Unit]

***In vivo* Optical and Acoustical Imaging Methods** (H. Kasai, Konnerth, Ishii, Ohki, Hensch Lab)

The Haruo Kasai lab developed an innovative set of optical probes (AS/BS probes) to study memory functions of the cerebral cortex *in vivo*. AS/BS can label enlarged synapses, and erase them afterwards with blue laser irradiation (Hayashi-Takagi et al. (2015) *Nature*). In 2019, the probes were used to study mouse models of depression in collaboration with the Liston Lab at Cornell University. In these models, spines were eliminated in the prefrontal cortex (PFC), and the anti-depressant ketamine induced spine generation and mitigated depressive symptoms. Moreover, when generated spines were removed by blue laser irradiation to the AS-probe, depressive symptoms and cortical activities were reversed. Thus, AS-probe technology demonstrated that ketamine-induced spine generation in the PFC caused the long-term anti-depressant effects of ketamine (14). The lab also developed a method to induce spine enlargement or shrinkage by *in vivo* two-photon uncaging. Although spine shrinkage could be induced with similar efficiency as that *in vitro*, enlargement occurred only in 20% of small spines, suggesting the presence of preparatory states for spine enlargement *in vivo* in the neocortex (15). Another technological breakthrough in optical sensing was reported by Affiliated Faculty Haruhiko Bito whose lab developed calcium sensors called XCaMPs for fast imaging of neural activity (4).

The Konnerth group is developing an *in vivo* imaging method specifically for the cerebellar cortex using a novel two-photon oblique scanning microscope. The key technological breakthrough was separating the emission and excitation light paths and placing an optical lens-containing pathway in front of the microscope. The lab can now combine targeted cell-attached or whole-cell recordings with oblique scanning in the same cell in order to study the electrophysiological properties related to local dendritic Ca^{2+} signaling in Purkinje neurons expressing calcium probes which are expressed by single-cell electroporation of DNA constructs and subsequent monitoring of dendritic Ca^{2+} signals (unpublished). The Ohki lab is constructing what is expected to be the world's largest two-photon microscope to capture the activity of around 50,000 neurons in a 5.0 mm field of view at single-cell resolution (unpublished).

One of the newest brain recording methods is fast functional ultrasound (fUS), which uses sound instead of light waves. By establishing whole-brain fUS imaging in awake mice during visual stimulation, the Hensch lab found that arousal states shape visual-evoked functional connectivity and neural gain at the mesoscopic level. In a mouse model of Rett Syndrome (RTT) lacking the *MeCP2* gene, the long-range disconnection typical of autism spectrum disorder (ASD) and low neural gain could be rescued by restoring *MeCP2* within ACh circuits. Further, this aberrant developmental trajectory of cortical gain was confirmed in RTT patients (submitted). After a trial of fUS in the Boston Children's Hospital Satellite, IRCN recently installed the first fast fUS machine in Asia to conduct brain mapping studies of cognition in healthy mice and disease models. The fUS technology will enable multi-scale imaging at the mesoscopic level.

Super-Resolution Optical Tools for Cellular Imaging (Okada, Gotoh Lab)

For super-resolution live imaging of neurons, the Okada lab has developed a new fluorescent probe to visualize the inner membrane structure, or cristae, of mitochondria in living cells in collaboration with chemists in the WPI-ITbM at Nagoya University. They achieved a resolution around 50 nm or twice the resolution previously achieved with conventional probes. The probe can visualize the dynamic changes in the cristae structure regulated by the cell's metabolic status (16). This work was featured in the "PNAS Highlights" and reported in the media and newspapers.

In collaboration with the Noda lab at the Institute of Microbial Chemistry, the Okada lab measured the dynamics of a GFP-labeled Atg13 protein in the pre autophagosomal structure (PAS) in yeast. For this purpose, they improved a single molecule measurement technique called fluorescence correlation spectroscopy, and succeeded to measure protein dynamics for the first time in sub-micrometer sized structures in living cells. The results demonstrated that PAS is a liquid-like condensate of Atg proteins (Fujioka et al. (2020), *Nature*).

Chromatin, the cell nuclear genetic material, is essential for brain development and function, and is the substrate for epigenetics, which can regulate many aspects of behavior. The lab also developed

a novel fluorescent protein probe that specifically binds to the open chromatin regions of genomic DNA, and colocalizes with conventional epigenetic markers for open chromatin regions. The same probe can also be used ATAC-seq and ChIP-seq, and deep sequencing results confirm that the probe binds to open chromatin regions detected by ATAC-seq. The Okada lab is currently trying to employ this tool to visualize epigenetic changes in the developing brain (patent pending). The Gotoh lab is collaborating with Affiliated Faculty Yoshito Hirata to study chromatin topology and dynamics in brain development using computational methods to analyze data at the single cell level (unpublished).

Green fluorescent RNAs are essential tools for the study of mRNAs but existing versions such as Spinach and Broccoli were too dim to visualize mRNAs in living cells. The Okada lab has developed a more than 300 times brighter variant of Broccoli and this probe can visualize Arc RNA transport in dendrites (patent application). Super-resolution microscopy and novel fluorescent proteins under development will unlock insights at cellular level and pave the way for understanding intelligence at the cellular and *in vivo* levels.

Tissue Clearing and Light Microscopy Methods (Okada, Hensch, Yazaki-Sugiyama Lab)

Global imaging of the brain at the single cell resolution will reveal new insights into circuit and network functions. The Okada group developed a novel rapid light-sheet fluorescent microscope (LSFM) with a spatially-uniform thin light-sheet illumination, which provides a three-dimensionally isotropic resolution to cover a wide area of visualization in a few minutes. Cellular structures in mammalian brains can be imaged without any mechanical slicing/cutting. Isotropic voxel data will enable the analysis of neuronal architecture based on three-dimensional morphology regardless of the illumination and imaging axis. This advantage will be a significant technical asset for comparing whole-brain networks between individuals and for tracing a time series in brain development research. Using this system, the Yazaki-Sugiyama group is studying the neuronal anatomical connections between higher auditory cortex, where early auditory memories are formed, and the apex of the song system, where sensory-motor information is integrated during the developmental song learning period but not in adult birds. Combining tissue clearing methods and optical sectioning on whole brain samples, the Yazaki-Sugiyama lab will build the first 3D map of zebra finch brain (unpublished).

Engineered Biosensors for Brain Neuromodulation (Takeuchi, Yazaki-Sugiyama lab)

The Takeuchi lab applies bio-engineering technologies to neuroscience. In a current collaboration with the Yazaki-Sugiyama lab they are developing a biohybrid approach for the detection of neurotransmitters in vivo. The approach involves fusing cell-based sensors onto a microstructure fabricated on the tip of an optical fiber. As a proof of concept, they used a norepinephrine sensor ($GRAB_{NE}$) expressed on HEK293T cell membranes. The cells were mixed with a collagen matrix and its response to norepinephrine solution was observed in an optical fiber using a fluorescence microscope. The results of diffusion constant measurement indicated that the sensor would have a time response of ~5 s for a sensor size of 100 mm, a time response short enough to monitor the concentration of norepinephrine in the zebra finch brain during the learning of songs (unpublished). Further miniaturization of the sensor, or extraction of the sensor proteins from cells would realize faster responses and higher stability in the future. The continued development of this biohybrid probe will enable a key technology for visualizing the dynamics of neuromodulation in the living animal brain. This interdisciplinary collaboration earned a 2018 IRCN Science Salon Director's Collaboration Award.

[Human/Clinical Unit]

Critical Periods of Human Infancy and Childhood (Hensch, Fagiolini, Nelson, Nagai lab)

Pioneering animal work from the Hensch lab identified GABA circuit maturation as a key trigger of critical period onset and this line of research continues (Reh et al (2020) *PNAS*, in press). Whether the same principles hold true in human brain development is undetermined. A cornerstone of IRCN's mission is the translation of basic neurodevelopmental principles from animals to humans, and the Boston Children's Hospital satellite with Affiliated Faculty Charles Berde, Laura Cornelissen, and Charles Nelson designed and implemented an ambitious clinical study of the cognitive impact of early exposure to anesthetic drugs during the first few months of life. This clinical study was paralleled by animal research in mice and zebra finch described earlier in the development unit. In

a separate study, event-related and spontaneous potentials from infants 'at-risk' for autism, by virtue of having an older brother with ASD, were recorded. The researchers observed that a developmental shift in signal-to-noise ratio is a potent biomarker of E/I imbalance and human cortical critical period timing, accurately predicting which infants would go on to be diagnosed with ASD (in preparation). Together, these studies estimate the optimal timing of therapeutic interventions and call for caution when using GABA-active anesthetics in pediatric medicine, revealing a role for critical periods in human health based on neurobiology.

In a translational study spanning species and measures with Affiliated Faculty Michela Fagiolini and Charles Nelson, the Boston Children's Hospital satellite showed that a deep learning neural network trained on mouse spontaneous pupillometry data can be refined by transfer learning to be predictive for ASD patients, even when different proxies of arousal fluctuations are used. This A.I.-based analysis offers a quantitative, non-invasive, and highly translational biomarker for the early detection of ASD and potentially other developmental and psychiatric disorders where arousal state variability is symptomatic (45). Related work in Yazaki-Sugiyama lab on neuromodulatory signaling in zebra finch auditory areas appears to explain how neural activity is tuned to behavioral context such as attention and reward (unpublished).

The Nagai lab investigated the occurrence of atypical auditory perception in ASD and what environmental stimuli may contribute to such atypicality (in submission). They developed a novel computational approach to retrieve and analyze the subjective experience of auditory perception. The experiments revealed several common perceptual patterns among diverse participants with ASD including the amplification of sounds in quiet environments, and phantom perception (e.g., echo and noise) induced by intensive and unsteady audiovisual stimuli from the environment. The findings connect neural/behavioral data to subjective difficulties in ASD patients. The social context influences learning outcomes in human infants, with potentially relevant shifts for critical periods. Tsuji lab investigates the mechanisms by which social context enhances attention and alters learning outcomes (Tsuji et al. (2020) *J Experimental Child Psychology*).

Critical Periods of Human Adolescence and Adulthood (K. Kasai, Koike, Nagai Lab)

Critical periods of adolescence are poorly understood compared to their earlier counterparts but they have a clear relationship with mental health. Psychiatric disorders such as schizophrenia or bipolar disorder begin to emerge from late adolescence and represent disabilities of human intelligence. The Kiyoto Kasai lab in the Department of Psychiatry at the University of Tokyo Hospital is a leader in adolescent psychiatry. They launched a large-scale population-based cohort study of adolescents called the Tokyo TEEN Cohort (37), the first of its kind in the world. The questionnaire and interview are complemented by biological and brain imaging subsampling, to understand brain developmental trajectories associated with adolescent development and its related psychiatric disorders (43).

The Kasai lab is also a key member in multi-center MRI studies in Japan and worldwide whose mission is to reveal the pathophysiology associated with an increased risk for developing psychosis. Within IRCN, in addition to K. Kasai, AFs Koike and Okanoya, and fMRI core manager Okada have played leading roles in the harmonization of multiple scanners in an All-Japan human MRI project (in submission), and they have developed a computational algorithm for brain MRI scans across multiple sites (39). In a recent study, a mega-analysis diffusion tensor imaging study of 2,937 individuals showed white matter microstructural alterations across four major psychiatric disorders (Koshiyama et al. (2020) *Molecular Psychiatry*). The K. Kasai and Koike labs also coordinate the Asian Consortium of MRI studies on Psychosis (ACMP) project, in which 13 sites in 4 countries and regions in Asia have participated in its development (in submission).

The Kiyoto Kasai lab has developed translatable neurophysiological markers including mismatch negativity (MMN; 61) and the auditory steady state response (ASSR; 60) to track the pathophysiology of emergent psychiatric disorders such as schizophrenia. Using these biomarkers, they have shown that schizophrenia is associated with deficits in auditory prediction and not reduced adaptation after repeated sensory information (Koshiyama et al. (2020) *Schizophrenia Bulletin*).

Social and collective intelligence starts to develop in infancy with carer-child bonding and the process continues through to adulthood. The Nagai lab investigated the mechanisms of social bonding during human-human and human-robot interactions. Humans are known to synchronize their behaviors with those of a partner when they establish a social bond but whether a humanoid robot can also induce such synchronization with a human, and what behavioral and physiological factors are crucial for synchronization were unknown. The findings revealed that biological

characteristics of the robot's bodily movements such as speed of hand movements and eye blinks (unpublished) and the physiological sensitivity of human participants affected synchronization. Cultural differences in speed adaptation to human-robot interaction tasks also played a role in social bonding (56). These results reveal how human social abilities contribute to intelligence and how to design robots in support of humans.

[Computation Unit]

Cutting-Edge Tools for Neural and fMRI Data Analysis (Ishii, Morita, Cai, Aihara, K. Kasai, Koike, Morishima Lab)

Human fMRI studies are a cornerstone of IRCN's intelligence research with the acquisition of the 3T Siemens Prisma scanning facility in the main experimental research building. Several projects aim to overcome existing biases in functional MRI (fMRI) data analysis to provide major improvements in resolution. In functional connectivity analyses of fMRI data across multiple research sites, the Kasai lab studied biological sampling bias (differences between participant groups) and engineering measurement bias (differences in the properties of MRI scanners). These biases are greater or equal to the meaningful difference due to psychiatric disorders. They developed a novel harmonization method that removed measurement bias on a traveling-subject dataset. The results are important for future IRCN research using multisite, multidisorder resting-state fMRI data (39). In another project, the Cai lab found that statistical bias in traditional fMRI representational similarity analysis (RSA) may generate artifacts that mask real neural structures, and developed a Bayesian approach that reduces this bias (Cai et al. (2019) *PLoS Computational Biology*).

The increasing size and complexity of datasets in neuroscience require new analysis tools to derive insights. IRCN produces data from animal and human imaging, electrophysiology, and behavioral studies. In the area of mouse in vivo two-photon imaging at cellular resolution, a major bottleneck is how to clean up noisy unlabeled data. The Ishii group developed a new algorithm based on deep convolutional neural networks (CNNs) to improve the image quality obtained by two photon and light-sheet microscopy. Their model is a stacked architecture consists of multiple U-nets in which individual U-nets remove noise at different scales for performance improvements based on a coarse-to-fine strategy. The constituent CNNs can therefore handle 3-dimensional (3D) convolution operations for efficient denoising and reconstruction of imaged volumes. This form of advanced architecture enables the model to facilitate end-to-end learning without pre/post processing. Based on two-photon data from the H. Kasai lab, the new algorithm demonstrated a substantial performance improvement over competing methods (Lee et al. (2020) *Neural Networks*). The method will facilitate the powerful analysis of many forms of imaging data by the center's labs.

The Morita lab developed tools for the study of decision-making in corticostriatal circuits. In the area of neuronal structure analysis, they studied two major types of corticostriatal neurons, the intratelencephalic and pyramidal-tract neurons, using the Janelia MouseLight database (Morita et al. (2019) *Frontiers in Neural Circuits*). The method will allow biologically realistic computation of decision-making behavior and neural activity that incorporates different neuronal types.

The Aihara lab has been developing mathematical methods to analyze spatio-temporal brain dynamics with data produced by the IRCN's labs. Extending their randomly distributed embedding (Ma et al. (2018), *PNAS*), a new algorithm was proposed for better prediction by dynamically combining multiple forecasts using multivariate time series data (54).

The lab of K. Kasai collaborated with IRCN Affiliated Faculty Koike and Morishima to develop a new method for the analysis of electroencephalography (EEG) data by combination of two existing methods, 1) microstates, or short time periods of stable scalp potential fields, and 2) an energy-landscape analysis, which captures large-scale brain dynamics. The method applied to human data revealed detailed functional interactions in brain networks that could not be identified by the standard functional connectivity analysis using dynamic causal modelling (DCM) (in submission). The Koike and K. Kasai labs have also discovered differences in functional connectivity networks in the midbrain dopaminergic system in psychiatric disorders (Nakamura et al. (2020) *Schizophrenia Bulletin*). For the innovative integration of computational neuroscience, neuroimaging, and psychiatry, these labs earned a 2019 IRCN Science Salon Director's Collaboration Award.

Brain Models of Neural Dynamics, Prediction and Learning (Aihara, Ishii, Cai, Chao, Kanamaru Lab)

Computational modeling is necessary to understand neural circuit principles and serves as an

essential bridge between the data analysis from biological and human studies and the development of neuro-inspired and human-centered A.I. algorithms and applications. Brain-based computational modeling is a remarkably broad field with many competing paradigms. However, in IRCN three major classes of models emerged in FY2019 as promising avenues for collaboration with experimentalists with the aim of building toward a neuro-inspired A.I., namely 1) neural dynamics such as state-dependent attentional effects, spontaneous activity, and network oscillations, 2) predictive coding in hierarchical cortical networks, and 3) reinforcement learning in basal ganglia circuits.

In neural network dynamics, state-dependent changes such as attention are critical for regulating information processing. The Aihara and Kanamaru labs modeled attention as a transitive attractor neural network. Acetylcholine modified the attractor landscape permitting top down attention to improve the responses of bottom up sensory inputs (52). Current work also suggests that transitive attractor networks can model disease. The Aihara lab in collaboration with the K. Kasai lab analyzed human EEG data from schizophrenic patients, and proposed that the brain networks of patients with schizophrenia may be trapped in an attractor state and are less flexible compared to the normal brain (unpublished).

Neural dynamics also involves brain oscillations driven either by intrinsic pacemaker mechanisms within individual neurons or network interactions between neurons. In ongoing work, the Aihara lab is collaborating with the Ohki lab in the Development Unit to create a neural network to model the complex large-scale oscillatory dynamics of spontaneous neuronal activity recorded from the mouse cortex with calcium imaging (unpublished). The collaboration was a winner of the 2018 IRCN Science Salon Director's Collaboration Award. In a study with implications for the development of neuro-inspired AI, the Ohki lab reported that sparse coding in the visual cortex in mice involves diverse and overlapping receptive fields for the reliable representation of natural images (Yoshida and Ohki (2020) *Nature Communications*).

Predictive coding is a leading brain theory based on bidirectional communication in hierarchical networks for prediction and prediction error signals where subjects aim to minimize errors for more accurate forecasting of the environment. Thus, the brain serves as a biological prediction machine that balances internal expectations against external sensory information. The Aihara lab created a neural network with reservoir computing to investigate how predictive coding can explain internal visual perception and its contextual dependency (104). The theoretical framework has also been tested by the Chao lab in human EEG experiments, where the brain's prediction ability is challenged by unexpected auditory sequences with different levels of temporal irregularity (unpublished). Prediction coding can also extend to disease. The Nagai lab implemented a predictive coding model in a recurrent neural network suggesting how insufficient reliance on priors in sensory predictions may result in incomplete performance by chimpanzees compared to human children (71).

In experimental animals and humans, reinforcement learning (RL) is a common framework for decision-making in complex environments containing rewards and punishments. Recently, RL is also emerging as a valid alternate model to conventional machine learning for AI. The biological instantiation of RL involves the neuromodulator dopamine in the basal ganglia while theoretical models propose that cortico-basal ganglia circuits use dopamine to perform temporal difference learning for reward prediction. An ongoing collaboration between the labs of Haruo Kasai and Affiliated Faculty Shin Ishii recently revealed how reward can be generalized and discriminated during learning in mice by different types of dopamine receptors (Iino et al. (2020) *Nature*). The collaboration between the labs merited a 2018 IRCN Science Salon Director's Collaboration Award.

Artificial Intelligence Based on Deep Neural Networks and Beyond (Sugiyama, Nakayama, Aihara Lab)

Research on artificial intelligence, primarily on deep neural networks (DNN), has made great progress in the last decade, achieving performance close to human levels in various tasks. Nevertheless, DNNs are far from achieving human general intelligence. IRCN will develop novel neuro-inspired AI based on brain development principles from several complementary approaches.

The first approach is termed human-assisted machine learning. In this new research paradigm, human-centered factors are incorporated into the current machine learning framework. In a recent study, the Sugiyama lab developed the first method that can simultaneously learn a DNN classifier and a noise model (how humans often mistake one class of data for another) making machine learning more robust against human error (75). Another research project addressed the safety of machine learning systems, where mistakes in applications such as medical diagnosis or autonomous

driving can be costly or even life-threatening. They trained the machine learning system to decide when to give up making a decision and request the assistance of human experts. The work provides a foundation for ML classification with rejection, and the first theoretically justifiable rejection criterion for multiclass problems (74). Finally, a third study developed a human-oriented machine learning method for labeling data. Instead of asking humans for absolute labels in training data, the method employs triplet comparison data in the form of "A is closer to B than C" (Cui et al. (2020) *Neural Computation*). Future work will further develop human-centered machine learning methods in broader contexts and incorporate more elements of neuroscience into compute models.

A second approach to A.I. focuses on developing DNNs with novel architectures to achieve faster speed, accuracy, or learning efficiency. In machine translation, DNNs are slow because their autoregressive computation is difficult to parallelize at inference time. To solve this issue, the Sugiyama lab proposed a model with continuous latent variables and deterministic inference procedures that is 8.6x faster compared to baseline models (Shu et al. (2020) Proceedings of the AAAI Conference on Artificial Intelligence). Another study used a novel convolutional neural network (CNN) architecture incorporating Squeeze-and-Excitation (SE) blocks into a U-Net for more effective biomedical image segmentation and cross-dataset generalization from MRI images (Rundo et al. (2019) *Neurocomputing*). Current research by the Nakayama lab aims to extend the CNN architecture by introducing spatially shuffled convolution to improve classification performance (unpublished). Finally, to address the issue of limited amounts of training data, Han et al. developed a method using conditional progressive growing generative adversarial networks (CPGANs) employing additional data trained on a DNN for computer-assisted diagnosis. The method boosted sensitivity in diagnosis by 10% with clinically acceptable additional false positives (Han et al. (2019) *Proceedings of the ACM International Conference on Information and Knowledge Management*).

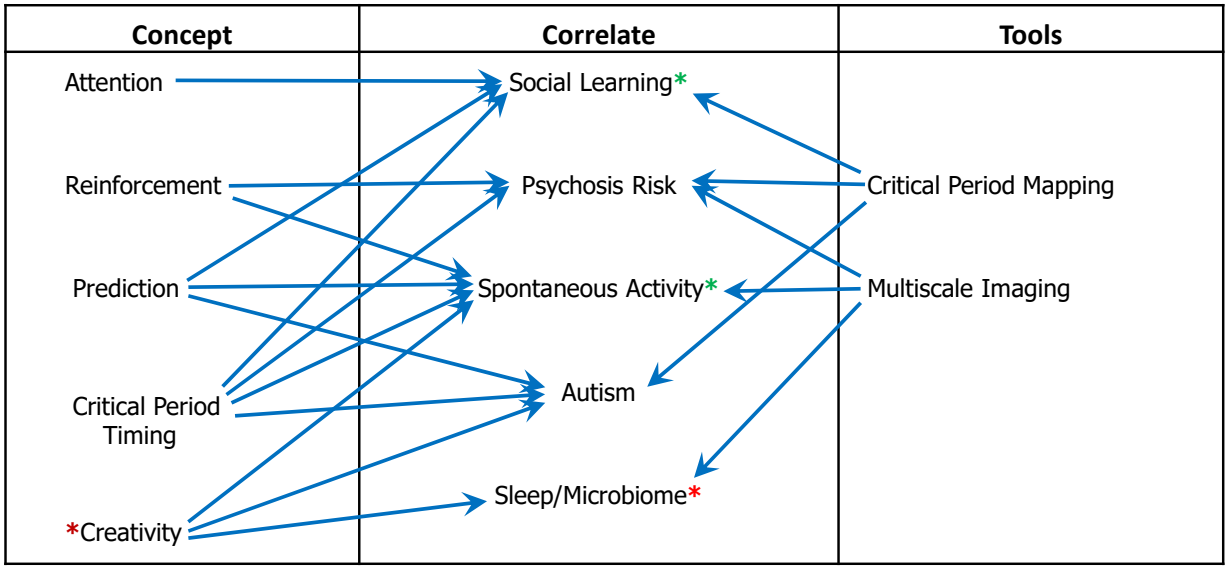
A third approach is development of new neural networks more dynamical than DNN and CNN. The Aihara lab proposed an asymmetrically connected recurrent neural network with ability of combinatorial optimization. This optimization neurodynamics can destabilize trapping local minima of the optimization function by extending the state space and outperform state-of-the-art solvers for some reference benchmarks in terms of the time-to-solution (Leleu et al. (2018), PCT/US2018/044469) (55). Future A.I. models will include further studies focusing on neuro-inspired H.I.

2. Generating Fused Disciplines

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

At IRCN, we have taken a trans-disciplinary "Team Science" approach focused on the computational implications of neuronal circuit development and its disorders. To coordinate this effort, a Synergy Office was created as of October 2019. This year, it promoted the integration of 12 new collaborative Teams (Table 1), whose focus falls into three categories: key concepts, neurological correlates, and new technologies. Not only does this structure facilitate flexible lateral thinking (meta-collaboration) by co-mentored postdocs across related teams, it also inspires innovative and fruitful fundraising and outreach efforts with the Sustainability and Community Offices, respectively.

Table 1. FY2019 IRCN Team Science Fusion



* Daikin support * Beyond AI (SoftBank) support

These twelve themes for FY2019 were chosen in a bottom-up manner by gathering proposals from all PIs to identify critical features of H.I. that are not yet fully explored in A.I. Each Team was required to incorporate PIs and AFs from at least three different domains (Human/Clinical, Development, Technology, Computation) with a budget request to enable their collaborative work, including reagents, equipment, personnel and training needs. Funding was set aside in our WPI budget, but also supported by generous corporate donations to UTokyo HQ (e.g. Daikin, SoftBank) awarded to specific team proposals. In addition to Teams, an IRCN Program Committee (IPC) was created to host brainstorming workshops to elaborate gaps between H.I. and A.I. which may seed near future Team Science. A brief synopsis of the Teams organized this year follows:

Attention (Aihara, Tsuji, Yazaki-Sugiyama, Takeuchi, Hensch)
Biological brains shift their processing resources to prioritize and isolate the information that is relevant at any given moment, rather than processing all input in parallel. Shining the "spotlight" of selective attention to ignore irrelevant objects has already contributed to enhancing A.I. By first understanding the neural mechanisms of attention and its modulation by developmental stage (critical periods) and environmental input (social and non-social contexts), we will further construct network models of excitatory and inhibitory neurons to analyse the opening/closing of brain plasticity. Nonlinear analyses of transitive dynamics without stable attractors would be important to understand the opening of CP. As our group spans cellular model systems to human infants and modeling, the goal is to establish a measure of attention/arousal that is comparable across species (human infant, songbird, mouse). Novel sensors will be developed to detect patterns of neuromodulation (ACh, NE) in freely behaving animals to be incorporated in the modeling. We will experimentally vary social and non-social contexts during learning and measure attention/arousal modulation. Possible applications include early detection of attention deficits in developmental disorders, reopening of critical periods (Lynx1), impact of stress or disease genes.

Reinforcement (H. Kasai, AF Ishii, Cai, AF Koike)
Reinforcement learning (RL) is a major tool of machine learning and is linked to brain function in the dopamine reward-prediction-error theory. IRCN research by Kasai / Ishii labs has clarified the underlying brain circuits and molecular mechanisms for RL (Yagishita et al., Science 2014; Iino et al., Nature 2020[1]). This put forward the over-generalization hypothesis of psychosis, as well as new features of extinction and possible working memory deficits in schizophrenia. We aim to

reconstruct the original RL theory and to develop innovative early diagnosis of schizophrenia in high risk subjects (EEG, fMRI). Technology improvement of learning circuit labeling (synaptic AS/BS probes) and presynaptic FRET probes is expected to visualize the reinforcement circuits. Ultimately, next-generation RL algorithms will implement new biological principles, such as developmentally determined generalization pathways, cross-talk between multiple monoamines, dichotomous operations in striatal pathways.

Prediction (Chao, AF Koike, Aihara, Ohki, AF Matsuzaki, Sugiyama, AF Nakayama, Nagai)
Current A.I. is limited in its ability to understand cause and effect. Predictive coding is a leading theory of animal and human behavior whose core tenet is that the brain is a biological prediction machine that balances internal expectations against external sensory information. We hypothesize that the brain has evolved a set of conserved neural circuit computations termed *motifs* for computing prediction and prediction-error signals in a hierarchical arrangement to minimize prediction error. Importantly, the identification and description of these neural circuit motifs remains elusive. Identifying such network structure and dynamics in the brain would provide a computational framework for general intelligence and its disorders in humans. We will use behavioral tasks and physiological and computational analyses that are cross-cutting between species and spatiotemporal scales to identify neurobiological markers for neural circuit motifs in mouse, marmoset, macaque, and human. Ultimately, such motifs will be implemented in neuromorphic AI and used as biomarkers to diagnose and treat psychiatric disorders involving prediction such as schizophrenia and autism.

Critical Period Timing (Hensch, Yazaki-Sugiyama, AF Cornelissen, AF Berde, AF Nelson)
Inhibitory interneurons determine windows of heightened brain plasticity and have rarely been considered in modern machine learning. Pioneering discoveries in the mouse have established the molecular triggers and brakes underlying critical period timing, revealing that timing is itself malleable with broad implications for human development. Our goal is to determine whether these principles generalize across species and how they impact intelligent behavior. For example, we have shown acceleration of songbird learning by premature GABA enhancement (with implications for human language learning) that mimics acceleration of mouse cortical development by repeated anesthetic exposure in early life (with recommendations for human infants). Use of EEG signal-to-noise ratio (transitions of E/I balance) to track developmental trajectories in human infants at-risk for autism, alongside parallel studies to rescue mouse models of autism by restoring E/I balance at strategic times in development will be pursued. Consequences of incomplete circuit pruning (synesthesia) or failure to close critical periods (schizophrenia) will be explored with IRCN partners (UBC, CIFAR, IIT, NCCR).

Creativity / Sleep (Nagai, Chao, Miyamoto, Hensch)
The flexible generation of new ideas or associations is considered a hallmark of H.I. that has eluded A.I. Often thought of as something internal that wells up ("gut feelings"), creativity can be heavily influenced by context as well. In partnership with Daikin, this team will explore environmental influences on 1) human psychophysical experiments of problem-solving insight and music, and 2) animal models of sleep and arousal to identify biomarkers and factors that enhance creativity. Human studies will focus on EEG signatures and animal studies will examine the role of the microbiome, which has emerged as critical to host physiology and development, impacting the inflammatory, immune, endocrine, metabolic and neural systems more broadly.

Social Learning (Yazaki-Sugiyama, Tsuji, Hensch, Aihara)
Unlike machines, living beings typically interact with each other and acquire knowledge from the experience of peers. How such collective intelligences emerge may hold the key for more efficient networks and super-additive effects. This team will track social behaviors in birds, mice and infants to establish EEG and other physiological signatures of socially interacting individuals. Computation

to integrate multimodal data of social networks in naturalistic home environments to investigate the influence of social group size and composition, as well as laboratory experiments of dyadic, bidirectional eye tracking of infants and caregivers will inspire infant-robot interaction paradigms (contingent reaction, human-like appearance, social contexts, etc) that test how the perception and action in humans is affected based on predictive processing. Our work will extend to an investigation of dynamical social networks between personal experience and social culture.

Psychosis Risk (K. Kasai, CM Okada, AF Koike, Hensch, Emoto, Kano, Aihara)
It is unclear under what conditions A.I. might suffer a "mental illness". Likewise, early detection and intervention of psychosis risk is crucial for preventing the development of cognitive disorders. Biomarkers for psychosis risk have not yet been fully developed or adopted in clinical settings. We thus aim to establish methods for early diagnosis, early intervention, and early recovery of psychosis through multidisciplinary approach including basic biology, genetics, neuroimaging, and computation. Here, we will explore novel biomarkers for psychosis risk through the detection of oxidative stress and perineuronal net (PNN) impairment in model animals and their translation to human diseases. A variety of biomarkers (whole-genome sequencing, skin advanced glycation end products, MMP9 assay, senescence-associated secretory phenotype, fMRI, EEG) as well as preclinical models (22q11.1DS, Setd1a, Fam107a, H2Bl, Glo1, Pcdh17) will be characterized together with global partners (Harvard, NCCR). Next, we will develop prediction methods of psychosis risk based on computational analysis of non-linear dynamics of EEG/neuroimaging data such as characteristic alterations in gamma-band activity in our human adolescent cohort and novel animal models using state-of-the-art algorithms and dynamic network biomarkers (DNB) analysis.

Spontaneous Activity (Ohki, Watanabe, Cai, Chao, AF Kuniyoshi, H. Kasai, Hensch, CM Fujiwara, Aihara)
The brain is never idle. Ever-changing spontaneous neural discharges propagate constantly shaping our thoughts and response to sensory input. Unlike programmed algorithms, it is these 'off-line' moments that likely underlie behavioral states, prediction, plasticity and creativity. We will measure and model the spatio-temporal patterns of activity patterns both in adulthood, development and disease. For example, we will consider coupled oscillator model bifurcation, predictive coding and reservoir computing, energy landscape analysis and the relationship between different models. What does spontaneous activity represent (past trials, internal states, prediction, mind wandering, attention)? How does it interact with sensory evoked response (additive, multiplicative, other)? In the developing brain, what is the source of spontaneous activity (peripheral, thalamic, cortical) and how does it drastically change in relation to emerging E/I balance, critical periods or disorders? We expect to find novel theories of learning and memory based on spontaneous activity, plasticity and intrinsic fluctuation, relearning by replay, avoiding overfitting/catastrophic forgetting which currently limit deep learning A.I.

Autism (Gotoh, Watanabe, Kano, AF Nelson, AF Fagiolini, Hensch)
Individual variability in human behavior is captured in the surge of autism spectrum disorders (ASD). Characterized by an E/I imbalance, these disorders are likely to reflect premature, delayed or incomplete circuit pruning during shifted critical periods of development. This team will focus on the overgrowth of prefrontal cortex and long-range disconnection from the cerebellum underlying abnormalities in social behavior. Electrophysiological and anatomical analyses of synapse pruning deficits will be measured across animal models (Fgf10, Kdmb6, Shank3). Computational methods to compare whole-brain functional imaging in humans (fMRI) and mice (fUS) will be developed to identify transitory global and local brain dynamics. Sex biases (vulnerability in males, resilience in females) as well as innovative social network analyses in group settings will be explored. In close collaboration with Boston Children's Hopsital, we will continue to leverage critical period biomarkers to predict at-risk subjects using deep neural networks trained on mouse data.

Critical Period (E/I) Mapping (Yazaki-Sugiyama, Hensch, Okada)
To reveal principles of critical periods across animal species, we will track developmental trajectories within 3D brain structures using state-of-the-art light-sheet microscopy and in vivo circuit tracing. We are constructing a standardized Zebrafinch 3D brain atlas, making a registration program, and tracing circuit rewiring during song learning. Likewise, whole-brain tracking of PNN development (marking critical period closure) in cleared wildtype and mutant mouse tissues will determine the relative timing of brain plasticity across regions underlying complex behaviors. Both datasets are expected to inform A.I. based on the integration of multiple modalities, such as song production or social interactions.

Multiscale Imaging (Ohki, Hensch, K. Kasai, Aihara)
A major challenge to understanding H.I. is the poor resolution of non-invasive imaging techniques. This team seeks to understand how neural activity is converted to hemodynamic signals, on the one hand, and cellular substrates of voxel-based patterns on the other, by simultaneous imaging of neuronal activity (wide field calcium imaging) and functional ultra sound (fUS) imaging in awake mice. We will assess physiological noise in hemodynamic signals and perform inverse modeling from hemodynamic signals back to neural activity. We expect these computational tools will contribute to various Teams, including the modeling of spontaneous activity patterns, prediction, creativity/sleep, and the search for biomarkers of psychiatric disorders in non-invasive imaging data from healthy and disease models (fUS) and patients (fMRI).

3. Realizing an International Research Environment

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

The Director has exceptionally strong global connections, and his continuous initiative has advanced the formation of an international network and research environment in the traditional UTokyo university setting. The following measures outline concrete steps for the Center's globalization:

International PI and researcher recruitment
The director has placed the highest priority on the recruitment of young foreign researchers with high ability and motivation. This focus on internationalization has rapidly increased the ratio of researchers coming from overseas: 24% (13% in FY2018) of PIs including two newly-hired PIs, 92% of postdocs, and 25% of other researchers. Through this policy, IRCN provided young PIs and researchers with independent positions, competitive compensation, and a start-up budget.

Improvement of PI gender balance
IRCN has exceeded the international standard on gender balance. After hiring two female PIs in FY2019, the percentage of female PIs has nearly doubled from 13% in FY2018 to 24% in FY2019. This is strikingly higher than the number of female PIs in the host UTokyo medical school (0%).

International collaboration
IRCN developed one of the strongest international collaboration programs for a Japanese research center. As shown in the table below, these partners were chosen strategically to complement the four research domains at IRCN. Over the past year, IRCN deepened the relationships with selected international Workshops at UTokyo, including "22q disorders" (with NCCR), "CDKL5 Disorder" (with Boston Children's Hospital), "Child Brain Development" (with CIFAR), and "Tracking Infant Brain Development" (with A*Star). In anticipation of reduced global travel in the post-pandemic world, regular videoconferencing seminars with these partners will be initiated to build international networks for trainee exchange.

Partner	Human/clinical	Development	Technology	Computation
A*Star (Singapore)	✓			
Hong Kong U Science & Technology	✓			
U British Columbia (Canada)	✓			
Asian Consortium MRI in Psychosis	✓			
NCCR Synapsy (Switzerland)	✓	✓		
Boston Children's Hospital	✓	✓		✓
Harvard Conte Center (CBS)	✓	✓	✓	✓
College de France		✓		
Chinese Academy of Sciences		✓		
Max-Planck Institute (Florida)		✓	✓	
Stockholm Trio (Karolinska, KTH, SU)		✓	✓	✓
CIFAR (Canada)		✓		✓
OIST		✓		✓
RIKEN (AIP, BDR)			✓	✓
Italian Institute of Technology				✓
Harvard Reischauer Inst / MIT MISTI	intern	intern	intern	intern

Frequent International Seminars/Symposia
In FY2019, a total of 66 (33 in FY2018) world-leading scientists from abroad visited IRCN to provide lectures/talks at seminars and workshops, which resulted in the enhancement of global research collaboration activities at IRCN. 20 international scientific events were held at IRCN in FY2019 consisting of 14 invited seminars and 6 international workshops. See Appendix 3-1-2 and 5 for details. We also welcomed sabbatical Prof Sarah Woolley (McGill U) as "UTokyo College" guest.

Neuro-Inspired Computation Course to attract excellent young global researchers
After the success of the FY2018 Neuro-Inspired Computation Course, IRCN had prepared the next lecture course in Neuro-Inspired Computation for October 2020, in collaboration with The International Symposium on Artificial Intelligence and Brain Science, organized by Dr. Doya (OIST) with IRCN as a co-sponsor. It was postponed to March 2021 because of the coronavirus pandemic.

Science Writing Core (SWC)
IRCN established the SWC to support manuscript and grant writing, oral presentation, and public-oriented writing for the purpose of publishing and promoting IRCN's research results to international journals, academies and societies, and the lay public. Charles Yokoyama (SWC core manager), a former Senior Editor at Cell Press, became a University Professor in preparation to expand support at the UTokyo-wide level. In addition, he organized an online course for Summer Semester 2020, "Scientific Writing, Publishing, and Communication", for the School of Science Graduate Program, Forefront of Physics and Mathematics Program to Drive Transformation (FoPM).

4. Making Organizational Reforms

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

Reorganizing the Management Structure
In direct response to the excellent WG suggestion, IRCN reorganized its management into three 'Offices': Sustainability Office, Synergy Office and Community Office. Each Office is led by a Deputy Director and designed to intersect the Director's top-down leadership and PIs' bottom-up proposals.

- Sustainability Office, led by Deputy Director Masanobu Kano, catalyzes support, infrastructure and personnel, including fundraising, building renovations for an 'under-one-roof' ecosystem, strategic recruitment with an emphasis on diversity, WPI budget, evaluation and related tasks.
- Synergy Office, led by Deputy Director Kazuo Emoto, promotes research fusion and team

science. It manages workshops, seminars, and salons proposed by the IRCN Program Committee to foster team science, and recommends the 'IRCN Director's Collaboration Awards'.

- Community Office, led by Deputy Director Kazuyuki Aihara, coordinates education and outreach activities. It offers academic courses for trainees, outreach events and workshops, and various learning opportunities within IRCN, and ensures logistical support for international researchers.

The Office for Research Strategy (ORS) encouraged fused research by building a 'research ecosystem', including Science Salons, PI Chalk Talks, the 2019 Annual Retreat, PI discussion meetings, and planning of the 3F Computation Wing. After these successful results, the ORS was reorganized into the Synergy Office and Community Office. The management structure was further strengthened with the appointment of Dr. Kazuyuki Aihara as a third Deputy Director on October 1 to accelerate and facilitate communication between the computation unit with other units, and his lab moved from Komaba campus to the Medical Department Building No. 1. He became a full-time Deputy Director with 100% effort from April 1, 2020. In addition, Maki Kubo joined as a Special Advisor to the Director to reform and internationalize the administration and was appointed as the Administrative Director after Dr. Tetsushi Kagawa resigned.

Involving researchers in IRCN activities in the Medical Building No.1
IRCN created a Deputy PI system to enable PIs whose main labs are located outside of the Medical Building No.1 to have a lab in the building, by assigning young researchers as their deputy lab heads. In FY2019, 4 PIs (Hensch, Takeuchi, Okada, and Konnerth) used this system to increase IRCN synergy under one roof. IRCN also launched an Associate Research Fellows program to involve younger researchers not only from other UTokyo campuses but also across UTokyo/non-UTokyo Graduate Schools in its activities, in addition to Affiliated Faculty.

Improving Core Facilities
With the addition of the Human fMRI core in FY2019, the five IRCN Core Facilities (ES-Mouse/Virus Core, Imaging Core, Data Science Core, Human fMRI core, and Science Writing Core) continue to provide inexpensive and rapid access to research materials and technologies by expert IRCN staff.

Supporting Graduate Student Education
IRCN joined the MEXT WISE Graduate Program 'Forefront of Physics and Mathematics Program to Drive Transformation', in which several IRCN PIs are organizing and teaching three courses: "21st Century Biology for Mathematicians and Physicists", "Scientific Writing, Publishing, and Communication" and "Introductory Course for Neuroscience and Neural Computation".
In addition, IRCN hosted eleven student interns from Harvard University and institutions in Europe and Canada. The planned expansion of the international student exchange to MIT in FY2020 was unfortunately canceled in FY2020 due to the pandemic situation.

Spreading IRCN international activities to UTokyo-wide
Charles Yokoyama became University Professor, and the IRCN Science Writing Core activities are being planned for expansion to UTokyo-wide support. IRCN has been supporting non-Japanese researchers for obtaining grants and starting research and life in Japan. Administrative activities are basically in English. In addition, IRCN launched an improvement of center's website for non-Japanese researchers in cooperation with UTokyo headquarters internationalization effort.

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

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

Upgrading the research roadmap
IRCN has upgraded the goals and the research roadmap leading to 'Neurointelligence' (See Summary of State of WPI Center Project Progress). In addition, IRCN developed fusion research by Director's pilot awards, a dozen inter-related teams and internal study sections on bridging neuroscience and AI. (See 2. Generating Fused Disciplines)

Improving PI balance
IRCN hired three PIs in the Computation unit and two PIs in the Human/Clinical unit (1 PI joined on April 1, 2020). As a result, the PI structure and balance across the four units of Neurodevelopment, Technology, Human/Clinical, and Computation was significantly improved. Dr. Aihara was appointed to Deputy Director on October 1, and moved his lab to the Faculty of Medicine Bldg.1, improving communication among the units in the 3F computation space. IRCN is currently searching internationally for an additional computational PI and several senior postdoctoral research fellows in to further collaborate with existing PIs in neuro-inspired computation/A.I. After pruning PIs who were unable to commit, the balance of PIs with 100% effort increased to five as of April 1, 2020.

Fostering young researchers
IRCN provided young researchers with independent positions, so the members of IRCN PIs with 100% effort are Associate Professors and Assistant Professors. UTokyo also supported IRCN through its Exceptional Young Faculty Program. In FY2019 an Excellent Young Researcher post was awarded for newly-hired junior PI (Dr. Tsuji) and Associate Research Fellow (Dr. A Hoshino) in Gotoh lab.

Increasing grants/cooperative research with private companies/donation
IRCN set up the Sustainability Office to ensure the mid and long-term viability of IRCN. IRCN made efforts to apply for grants with ORS/SWC and URA support for grant applications. The total amount of grants awarded for WPI related research is about ¥516 million (direct cost). IRCN has also been actively applying or preparing for large competitive grants, including the Grant-in-Aid for Transformative Research Areas and the government Moonshot Program. The planning of cooperative research with private companies is ongoing for the UTokyo Beyond AI Institute with Softbank and the Corporate Sponsored Research Program on Neuro-Creativity with Daikin. Regarding donations, IRCN created an endowment channel at the UTokyo Foundation, and has been negotiating with a major philanthropic institution based in the US. The Sustainability Office is currently preparing an outreach event at the UTokyo New York Office scheduled for November 2020.

Contribution of the host university
UTokyo has strongly supported and prioritized new space for IRCN. All core facilities and new PIs in the neurodevelopmental and computational units have newly renovated labs in the Faculty of Medicine Building 1, which is connected to the Faculty of Medicine Experimental Research Building that houses the fMRI core for private access by patients. The IRCN collaboration lounge, visiting faculty offices, teaching and gathering spaces, as well as satellite labs for PIs of the technology unit were also created. Appendix 3-1-4 Campus Map shows the IRCN 'Under One Roof' organization. UTokyo is also considering a new building for IRCN and other departments. The total amount of university support is ¥129,219,000 in FY2019, including support for PI / researcher compensation, international workshops, student exchange, graduate education, and fMRI lease.

6. Others

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

IRCN has developed a unique portfolio of outreach programs. Research experiments by two PIs (Dr. Tsuji and Dr. Nagai) involving babies and young children were selected as a 2019 Miraikan Open Lab, which fuses research and outreach activities. IRCN is also preparing a Miraikan Exhibition scheduled for FY2020 in cooperation with Nomura, an architectural space designer and constructor.
In addition, IRCN held events to provide lectures and lab tours for students from Super Science High Schools and other high schools. Some of those events were co-hosted with the local government.

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

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

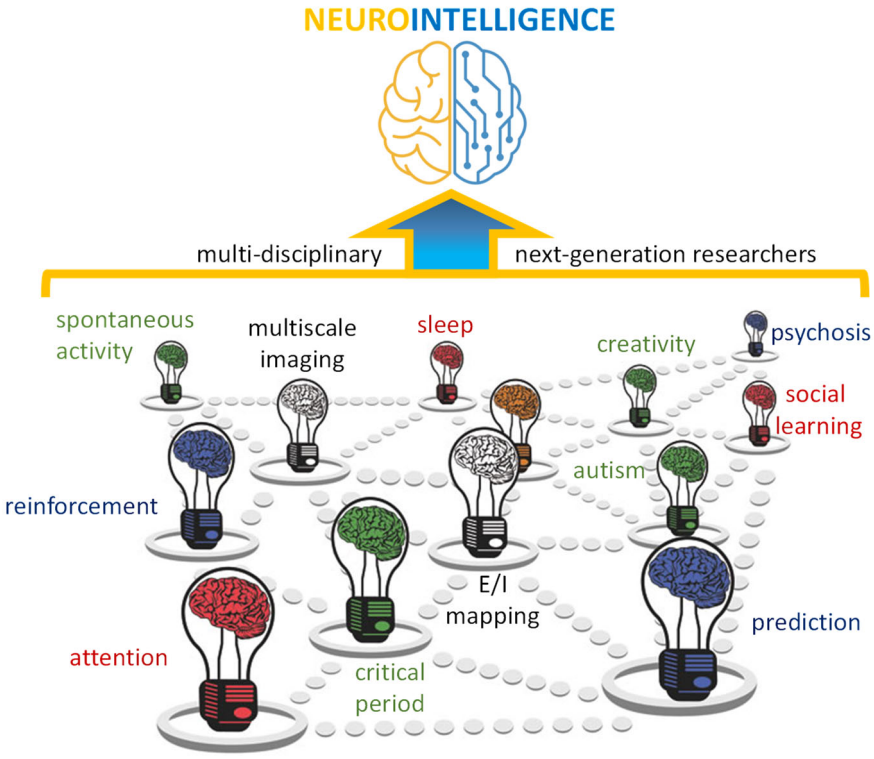
FY 2019 Follow-up of WPI Program

Q1: IRCN is still in the construction phase. The physical presence of Director Hensch at UTokyo

should build up to the level requested by the Program Committee.

A1: Since March 2019, Director Hensch has been on-site in Japan each month, except for his father's illness (August) and funeral (October). His extended sabbatical stay from the end of January 2020 was unfortunately cut short by global travel restrictions and laboratory closures due to the COVID-19 pandemic. Meanwhile, following the WG site visit recommendations (see point (3) below), he expeditiously reorganized IRCN management into a three 'Office' model, spanning Sustainability (fundraising), Synergy (research fusion) and Community (outreach/training). This structure complements the weekly Executive Board, bi-weekly Steering Committee and monthly PI meetings, which he leads by Zoom or in person. He also recruited a Special Advisor to the Director (SAD) with extensive administrative experience (MEXT, NSF, OIST) to help implement daily changes on the ground. With a variety of communication tools (Zoom, email, text message, Slack), Director Hensch directly instructs PIs and administrative staff with effective and efficient leadership even while overseeing the US satellite.

Q2: IRCN should develop a clear scientific strategy on how to incorporate findings from the neurodevelopmental unit into the computation unit to build neuro-inspired artificial intelligence. IRCN's long-term roadmap describing the Center's targets and milestones over the lifespan of the Center should be polished and explained at the next year's site visit.



A2: Team Science started in FY2018 through the Director's Science Salon Collaboration Awards, and was developed into a dozen integrated and inter-related Teams in FY2019. Workshops with strategic MOU partners helped to focus our research questions and collaborations. Further, internal study sections on bridging neuroscience and A.I. proposed by PIs and young researchers were started by the IRCN Program Committee. These activities are shaping IRCN's unique response to 'What is Neurointelligence?' (see '2. Generating Fused Disciplines') and are continually updating our long-term roadmap (see 'Summary of State of WPI Center Project Progress'). Notably, the majority of PIs and researchers in the computation unit were just newly hired or moved 'under-one-roof' into the Medical Department Building No.1 by winter 2019-20. Thus, collaboration between the computational unit and other units is ongoing. Moreover, we continue our commitment to open and transparent science by investigating the sources of questionable research practices (Tsuji et al. (2020) *Z. f. Psychologie*), and by publishing educational material for best research practices (e.g. pre-registration) (Havron et al. (2020) *Infancy*).

Q3: Next year, IRCN will need to focus on three topics: (i) long-term sustainability, (ii) further integration of individual research efforts, and (iii) establishing a stronger internal "esprit de corps" among IRCN researchers, staff and faculty, a sense of unique mission and brand. Carrying out these efforts will be challenging given the traditional department structure of the host university but will be essential in helping to establish an exciting new field and in making further scientific discoveries in areas of health and disease.

A3: In direct response to the excellent WG suggestion, IRCN reorganized management into three 'Offices': the Sustainability Office, Synergy Office and Community Office. Each Office is led by a Deputy Director and designed as an intersection of the Director's top-down leadership and PIs' bottom-up proposals. (See '4. Organizational Reforms')

Q4: UTokyo should work more proactively toward realizing an "under one roof" environment at IRCN and systematically providing positions to IRCN so that all the PIs can concentrate on their work at the Center. This will also be very important for the sustainability of IRCN beyond the WPI funding.

A4: UTokyo has strongly supported and prioritized space for IRCN. All core facilities and new PIs in the development and computation units have newly renovated labs in the Medical Department Building No.1, which is connected to the Experimental Research Building that houses the fMRI core for private access by patients. IRCN collaboration lounges, visiting faculty offices, teaching and gathering spaces, and satellite labs for technology unit PIs were also created. The Appendix 3-1-4 Campus Map shows the 'Under one roof' IRCN campus plan facilitated by generous support from UTokyo.

UTokyo also supported IRCN through its Exceptional Faculty programs, including a Special University Professorship for Deputy Director Kazuyuki Aihara, a President's discretionary Professorship to ED Charles Yokoyama, and Excellent Young Researcher posts for three newly-hired junior PIs (Drs Tsuji, Chao, Watanabe). (See '5. Efforts to Secure the Center's Future Development over the Mid- to Long-term')

Q5: The involvement of young students is essential for the development of IRCN. IRCN should develop its own PhD program.

A5: IRCN joined the graduate program 'Forefront of Physics and Mathematics Program to Drive Transformation' (WISE program), and IRCN PIs have organized and from April are teaching three courses: "21st Century Biology for Mathematicians and Physicists (PI Okada)", "Scientific Writing, Publishing, and Communication (ED Yokoyama)" and "Introductory course for neuroscience and neural computation (PIs Yazaki-Sugiyama, Chao, Cai and AF Morita) ". In addition, IRCN hosted student interns from Harvard University and institutions in Europe and Canada. The planned expansion of the international student exchange with MIT in FY2020 was postponed in response to the coronavirus pandemic.

Q6: The researcher lineup is now more balanced across the neural development, computation, and clinical aspects. It would be advisable to have one deputy director from computation side since the fusion of neuro and mathematical science is a very important mission of IRCN.

A6: Prof. Kazuyuki Aihara was appointed to Deputy Director on October 1, and his lab moved from the Komaba Campus to the Medical Department Building No. 1, where he will be a full-time IRCN PI with 100% effort from April 1, 2020.

<u>FY2019 Site Visit Report</u>

Q1: The researcher lineup is now more balanced across the neural development, computation, and clinical aspects. The 2 deputy PIs are still both from the biology/medicine side. It would be advisable to have one deputy from information/computation side since the fusion of neuro and mathematical sciences is a very important mission of IRCN.

A1: This is the same question as number (6) of the Follow-up Report. Please refer to our answer to (6).

Q2: Next year, IRCN will need to focus on three topics: (i) long-term sustainability, (ii) further integration of the individual research efforts to enhance synergy by encouraging more interactions at all levels—within and across disciplines, methods, species, and faculty, and (iii) establishing a

stronger internal "esprit de corps" among IRCN students, staff and faculty, a sense of unique mission and brand. Carrying out these efforts will be challenging given the traditional departmental structure of the host university but will be essential in helping to establish an exciting new field and in making further scientific discoveries in health and disease.
A2: This is the same question as number (3) of the Follow-up Report. Please refer to our answer to (3).

Q 3: The involvement of young students is essential for the development of IRCN. IRCN should develop its own PhD program with the assistance of UTokyo and MEXT. This is particularly important for young faculty members who are not affiliated with existing departments. They need PhD students to work with. This is also very critical to securing the future development of IRCN.
A3: This is similar question to number (5) of the Follow-up Report. Please refer to our answer to (5).

Q4: We recommend UTokyo to work more proactively toward realizing an "under one roof" environment at IRCN.
Q5: We recommend UTokyo to work toward systematically providing positions to IRCN so that all the principal PIs can concentrate on their work at the Center. This will also be very important for the sustainability of IRCN beyond the WPI funding.
A4 and 5: These questions are similar to number (4) of the Follow-up Report. Please refer to our answer to (4).

Q6: The physical presence of Director Hensch at UTokyo should build up to the level requested by the Program Committee.
A6: This is the same question as number (1) of the Follow-up Report. Please refer to our answer to (1).

Q7: To further promote collaboration at the non-PI level, it would be worthwhile to expand the Director's discretionary funds to cover collaboration between non-PI researchers in the different research fields.
Q9: IRCN's long-term roadmap describing the Center's targets and milestones over the lifespan of the Center should be polished and explained at the next year's site visit.
A7 and 9: These questions are similar to number (2) of the Follow-up Report. Please refer to our answer to (2).

Q8: It is necessary to define the function of the AFs and to specify the names of the AFs.
A8: AFs are not IRCN PIs but have responsibilities to actively join IRCN events, including international workshops, retreats, science talks by IRCN members (PILAF), and outreach activities. They also have access to IRCN core facilities and play important roles in joining and helping to advance Team Science research projects for advancing the mission of 'Neurointelligence'.

Appendix 1 FY 2019 List of Center's Research Results and Main Awards

1. Refereed Papers (PIs' co-authored publications)

- List only the Center's papers published in 2019. (Note: The list should be for the calendar year, not the fiscal year.)

A. WPI papers

(1) Original articles

1. Yoshida K, Kita Y, Tokuoka SM, Hamano F, Yamazaki M, Sakimura K, Kano M, Shimizu T: Monoacylglycerol lipase deficiency affects diet-induced obesity, fat absorption, and feeding behavior in CB_1 cannabinoid receptor-deficient mice. FASEB J 33:2484-2497, 2019. (DOI: 10.1096/fj.201801203R)

2. Sakai Y, Kassai H, Nakayama H, Fukaya M, Maeda T, Nakao K, Hashimoto K, Sakagami H, Kano M, Aiba A: Hyperactivation of mTORC1 disrupts cellular homeostasis in cerebellar Purkinje cells. Sci Rep 9:2799, 2019. (DOI: 10.1038/s41598-019-38730-4)

3. Nakao H, Kishimoto Y, Hashimoto K, Kitamura K, Yamasaki M, Nakao K, Watanabe M, Kano M, Kirino Y, Aiba A: mGluR1 in cerebellar Purkinje cells is essential for the formation but not expression of associative eyeblink memory. Sci Rep 9:7353, 2019. (DOI: 10.1038/s41598-019-43744-z)

4. Inoue M, Takeuchi A, Manita S, Horigane S-I, Sakamoto M, Kawakami R, Yamaguchi K, Otomo K, Yokoyama H, Kim R, Yokoyama T, Takemoto-Kimura S, Abe M, Okamura M, Kondo Y, Quirin S, Ramakrishnan C, Imamura T, Sakimura K, Nemoto T, Kano M, Fujii H, Deisseroth K, Kitamura K, Bito H: Rational engineering of XCaMPs, a multicolor GECI suite for in vivo imaging of complex brain circuit dynamics. Cell 177:1346-1360 e24, 2019. (DOI: 10.1016/j.cell.2019.04.007)

5. Tanigami H, Yoneda M, Tabata Y, Echigo R, Kikuchi Y, Yamazaki M, Kishomoto Y, Sakimura K, Kano M, Ohno-Shosaku T: Endocannabinoid signaling from 2-arachidonoylglycerol to CB1 cannabinoid receptor facilitates reward-based learning of motor sequence. Neuroscience 421:1-16, 2019. (DOI: 10.1016/j.neuroscience.2019.09.040)

6. Tsutsumi S, Hidaka N, Isomura Y, Matsuzaki M, Sakimura K, Kano M, Kitamura K: Modular organization of cerebellar climbing fiber inputs during goal directed behavior. eLife e47021, 2019. (DOI: 10.7554/eLife.47021)

7. Sakai H, Fujii Y, Kuwayama N, Kawaji K, Gotoh Y, Kishi Y. Plag1 regulates neuronal gene expression and neuronal differentiation of neocortical neural progenitor cells. Genes Cells, 24:650-666, 2019. (DOI: 10.1111/gtc.12718)

8. Tanaka H, Okazaki T, Aoyama S, Yokota M, Koike M, Okada Y, Fujiki Y, Gotoh Y. Peroxisomes control mitochondrial dynamics and the mitochondrion-dependent pathway of apoptosis. J Cell Sci 132, 2019. (DOI: 10.1242/jcs.224766)

9. Eto H, Kishi Y, Koseki H, Gotoh Y. The Polycomb group protein Ring1 regulates dorsoventral patterning of the mouse telencephalon. bioRxiv 2019. (DOI: 10.1101/639492)

10. Kawaguchi D, Gotoh Y. Neurexin nanoclusters: A novel structure at presynaptic terminals. J Cell Biol 218:2442-2443, 2019. (DOI: 10.1083/jcb.201907074)

11. Ukita J, Yoshida T, Ohki K. Characterisation of nonlinear receptive fields of visual neurons by convolutional neural network. Sci Rep 9:3791, 2019. (DOI: 10.1038/s41598-019-40535-4)

12. Matsui T, Murakami T, Ohki K. Neuronal origin of the temporal dynamics of spontaneous BOLD activity correlation. Cereb Cortex 29:1496-1508, 2019. (DOI: 10.1093/cercor/bhy045)

13. Nishiyama M, Matsui T, Murakami T, Hagihara KM, Ohki K. Cell-type-specific thalamocortical inputs constrain direction map formation in visual cortex. Cell Rep 26:1082-1088, 2019. (DOI: 10.1016/j.celrep.2019.01.008)

14. Moda-Sava RN, Murdock MH, Parekh PK, Fetcho RN, Huang BS, Huynh TH, Witztum J, Shaver DC, Rosenthal DL, Always EJ, Lopez K, Meng Y, Nellissen L, Grosenick L, Deisseroth K, Bito H, Kasai, H, Liston C Sustained rescue of prefrontal circuit dysfunction by antidepressant-induced postsynaptic spine formation. Science, 364: eaat8078, 2019. (DOI: 10.1126/science.aat8078)

15. Noguchi J, Nagaoka A, Hayama T, Ucar H, Yagishita S, Takahashi N, Kasai H. Bidirectional in vivo structural dendritic spine plasticity revealed by two-photon glutamate uncaging in the mouse neocortex. Sci Rep 9:13922, 2019. (DOI: 10.1038/s41598-019-50445-0)

16. Wang C, Taki M, Sato Y, Tamura Y, Yaginuma H, Okada Y, Yamaguchi S. A photostable fluorescent marker for the superresolution live imaging of the dynamic structure of the mitochondrial cristae. Proc Natl Acad Sci USA 116:15817-15822, 2019. (DOI: 10.1073/pnas.1905924116)

17. Lu CH, Tang WC, Liu YT, Chang SW, Wu FCM, Chen CY, Tsai YC, Yang SM, Kuo CW, Okada Y, Hwu YK, Chen P, Chen BC. Lightsheet localization microscopy enables fast, large-scale, and three-dimensional super-resolution imaging. Commun Biol 2:177, 2019. (DOI: 10.1038/s42003-019-0403-9)

18. Li J, Suda K, Ueoka I, Tanaka R, Yoshida H, Okada Y, Okamoto Y, Hiramatsu Y, Takashima H, Yamaguchi M. Neuron-specific knockdown of Drosophila HADHB induces a shortened lifespan, deficient locomotive ability, abnormal motor neuron terminal morphology and learning disability. Exp Cell Res 379:150-158, 2019. (DOI: 10.1016/j.yexcr.2019.03.040)

19. Hasegawa S, Sagawa T, Ikeda K, Okada Y, Hayashi K. Investigation of multiple-dynein transport of melanosomes by non-invasive force measurement using fluctuation unit χ. Sci Rep 9: 5099, 2019. (DOI:10.1038/s41598-019-41458-w)

20. Yokomizo A, Morimoto Y, Nishimura K, Takeuchi S. Temporal observation of adipocyte microfiber using anchoring device. Micromachines 10:358, 2019. (DOI: 10.3390/mi10060358)

21. Hirata Y, Morimoto Y, Nam E, Takeuchi S. Portable biohybrid odorant sensors using cell-laden collagen micropillars. Lab Chip 19:1971-1976, 2019. (DOI: 10.1039/c9lc00131j)

22. Larramendy F, Yoshida S, Maier D, Fekete Z, Takeuchi S, Paul O. 3D arrays of microcages by two-photon lithography for spatial organization of living cells, Lab Chip 19:875-884, 2019. (DOI: 10.1039/c8lc01240g)

23. Morimoto Y, Onoe H, Takeuchi S. Biohybrid device with antagonistic skeletal muscle tissue for measurement of contractile force. Adv Robotics 33:208-218, 2019. (DOI: 10.1080/01691864.2019.1567382)

24. Ikeda K, Takeuchi S. Anchorage-dependent cell expansion in fiber-shaped microcarrier aggregates. Biotechnol Prog 35:e2755, 2019. (DOI: 10.1002/btpr.2755)

25. Mori N, Morimoto Y, Takeuchi S. Perfusable and stretchable 3D culture system for skin-equivalent. Biofabrication 11:011001, 2019. (DOI: 10.1088/1758-5090/aaed12)

26. Okumura Y, Yamasaki S, Ando S, Usami M, Endo K, Hiraiwa-Hasegawa M, Kasai K, Nishida A. Psychosocial burden of undiagnosed persistent ADHD symptoms in 12-year-old children: a population-based birth cohort study. J Atten Disord 2019. (DOI: 10.1177/1087054719837746).

27. Murata Y, Fujii A, Kanata S, Fujikawa S, Ikegame T, Nakachi Y, Zhao Z, Jinde S, Kasai K, Bundo M, Iwamoto K: Evaluation of the usefulness of saliva for DNA methylation analysis in cohort studies. Neuropsychopharmacol Rep 39:301-305, 2019. (DOI: 10.1002/npr2.12075)

28. Zhao Z, Jinde S, Koike S, Tada M, Satomura Y, Yoshikawa A, Nishimura Y, Takizawa R, Kinoshita A, Sakakibara E, Sakurada H, Yamagishi M, Nishimura F, Inai A, Nishioka M, Eriguchi Y, Araki T, Takaya A, Kan C, Umeda M, Shimazu A, Hashimoto H, Bundo M, Iwamoto K, Kakiuchi C, Kasai K. Altered expression of microRNA-223 in the plasma of patients with first-episode schizophrenia and its possible relation to neuronal migration-related genes. Transl Psychiatry 9:289, 2019. (DOI: 10.1038/s41398-019-0609-0)

29. Ando S, Nishida A, Yamasaki S, Koike S, Morimoto Y, Hoshino A, Kanata S, Fujikawa S, Endo K, Usami S, Furukawa TA, Hiraiwa-Hasegawa M, Kasai K. TTC Scientific and data collection team: Cohort profile: The Tokyo Teen Cohort study (TTC). Int J Epidemiol 48:1414-1414g, 2019. (DOI: 10.1093/ije/dyz033)

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(2) Review articles

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None

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(2) Review articles

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111. Varhama K, Oda H, Shima A, Takeuchi S. Decellularized plant leaves for 3D cell culturing. Proceedings of the IEEE International Conference on Micro Electro Mechanical Systems (MEMS) 2019, pp.226-228, 2019.

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123. Nakajima S, Watanabe K, Sugiyama M. Variational Bayesian Learning Theory, 558 pages, Cambridge University Press, Cambridge, UK, 2019.

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

- List up to 10 main presentations during FY 2019 in order from most recent.
- For each, write the date(s), lecturer/presenter's name, presentation title, and conference name.

Date(s)	Lecturer/Presenter's name	Presentation title	Conference name
7.2.2020	Yasushi Okada	Live cell imaging technologies for single-cell analysis	The 29th Hot Spring Harbor International Symposium.
14.1.2020	Shoji Takeuchi	Emerging technology for Biohybrid Robotics	Gordon Conference on Robotics
28.11.2019	Haruo Kasai	The plasticity and fluctuations of dendritic spines and their behavioral consequences	Key note speaker, Workshop on the dynamic brain (Jerusalem, Israel).
19.11.2019	Kenichi Ohki	Robust representation of natural images by sparse and variable population of active neurons in visual cortex	2019 International Conference on Neural Cells, Circuits and Behavior (IDG / McGovern Institute, Beijing)
18.11.2019	Kazuyuki Aihara	Harnessing high-dimensionality of brain data	Neural Oscillation Conference 2019: Towards Integrative Understanding of Human Nature
19.10.2019	Yoko Yazaki-Sugiyama	Lessons from Songbirds and Scientists: Learning to Communicate More Effectively by Listening to Others	'Meet-the-Expert' at Society for Neuroscience
7.10.2019	Yukiko Gotoh	Regulation of adult neural stem/progenitor cell fate	The Notch Meeting XI
28.9.2019	Takao Hensch	Balancing brain plasticity / stability	Italian Neuroscience Society (SINS), Perugia
24.9.2019	Masanobu Kano	Neural mechanisms of synapse remodeling in the developing brain	The 10th IBRO World Congress of Neuroscience, Keynote lecture (Daegu, Korea)
12.7.2019	Yukie Nagai	Cognitive Development in Robots: A unified theory based on predictive coding	The 8th International Conference on Biomimetic and Biohybrid Systems

3. Major Awards

- List up to 10 main awards received during FY 2019 in order from the most recent.
- For each, write the date issued, the recipient's name, and the name of award.
- In case of multiple recipients, underline those affiliated with the center.

Date	Recipient's name	Name of award
23.3.2020	Yasushi Okada	34th Nakaakira Tsukahara Award
21.12.2019	Kazuyuki Aihara	MIMS Mimura Award
16.12.2019	Kazuyuki Aihara	2019 ICCM Best Paper Award
11.2019	Yukie Nagai	JSAI Annual Conference Award of the 33rd Annual Conference of the Japanese Society for Artificial Intelligence
17.4.2019	Shoji Takeuchi	UNESCO Netexplo Award 2019
1.4.2019	Sho Tsuji	The University of Tokyo Excellent Young Researcher

Appendix 2 FY 2019 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 or, for centers selected in FY2012 in the progress report for Extension application screening, attach a "Biographical Sketch of a New Principal Investigator" (Appendix 2a).

<Results at the end of FY2019> **Principal Investigators Total: 17**

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	53	Director, Project Professor International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Neurophysiology	80	October 2017	In FY2019, stayed at the center 69 days. Usually stays at Boston Children's Hospital satellite, and very often communicates by more than 10 emails per day and a few times a week by videoconferences. Promote IRCN's interests at universities, research institutions, and academic societies around the world.	Promotes and directs center's operations.
Masanobu Kano	64	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	Usually stays at the center and participates in the center's activities as Deputy Director and an Executive Board member.	
Kazuo Emoto	51	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 Networks	80	October 2017	Usually 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	65	Deputy Director, International Research Center for Neurointelligence, The University of Tokyo Institutes for Advanced Study Professor, Department of Informatics and Electronics, Institute of Industrial Science, The University of Tokyo	Ph.D. Biological Information Systems	80	October 2017	Usually stays at the Institute of Industrial Science and participates in the center's activities as a Steering Committee member.	
Haruo Kasai	63	Professor, Center for Disease Biology and Integrative Medicine, Graduate School of Medicine, The University of Tokyo	M.D. & Ph.D. Neurophysiology	80	October 2017	Usually stays at the center and participates in the center's activities as a Steering Committee member.	
Kiyoto Kasai	49	Professor, Department of Neuropsychiatry, Graduate School of Medicine, The University of Tokyo	M.D. & Ph.D. Neuroimaging and Early Intervention for Schizophrenia	80	October 2017	Usually stays at The University of Tokyo Hospital and participates in the center's activities as a Steering Committee member.	
Kenichi Ohki	48	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	Usually stays at the center and participates in the center's activities as a Steering Committee member.	
Arthur Konnerth	66	Director, Institute of Neuroscience, Technical University of Munich	M.D. & Ph.D. Neurophysiology	50	October 2017	Usually stays in TUM and participates in the center's activities on demand. Communication is done regularly by emails.	Sends a young scientist to the center. (1 post-doctoral fellow, entire FY2019)

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	Usually stays at the Graduate School of Pharmaceutical Sciences and participates in the center's activities.	
Yasushi Okada	51	Professor, Department of Physics, Graduate School of Science, the University of Tokyo	M.D. & Ph.D. Bioimaging	32	October 2017	Usually stays at the Graduate School of Science and participates in the center's activities.	
Shoji Takeuchi	47	Professor, Department of Mechano-Informatics, Graduate School of Information Science and Technology, and Institute of Industrial Science, the University of Tokyo	Ph.D. Biohybrid Systems	80	October 2017	Usually stays at the Graduate School of Information Science and Technology and participates in the center's activities.	
Masashi Sugiyama	45	Professor, Department of Complexity Science and Engineering, Graduate School of Frontier Sciences, the University of Tokyo	Ph.D. Statistical Machine Learning	16	October 2017	Usually stays at the Graduate School of Frontier Sciences or RIKEN AIP, and participates in the center's activities.	
Yoko Yazaki-Sugiyama	48	Project Associate Professor, International Research Center for Neurointelligence, The University of Tokyo Institutes for Advanced Study Associate Professor, Okinawa Institute of Science and Technology Graduate University	Ph.D. Biological Science	20	April 2018	Regularly stays at the center and participates in the center's activities, while sometimes commuting to OIST.	

Yukie Nagai	45	Project Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Engineering	100	April 2019	Usually stays at the center and participates in the center's activities.	
Sho Tsuji	35	Assistant Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Psycholinguistics	100	April 2019	Usually stays at the center and participates in the center's activities.	
Zenas C. Chao	44	Project Associate Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Biomedical Engineering	100	September 2019	Usually stays at the center and participates in the center's activities.	
Mingbo Cai	34	Project Assistant Professor, International Research Center for Neurointelligence,The University of Tokyo Institutes for Advanced Study	Ph.D. Neuroscience	100	December 2019	Usually stays at the center and participates in the center's activities.	

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

Principal investigators unable to participate in project in FY 2019

Name	Affiliation (Position title, department, organization)	Starting date of project participation	Reasons	Measures taken/Action
Kuniyoshi Sakai	Professor, Department of Basic Science, Graduate School of Arts and Sciences, The University of Tokyo	October 2017	Revision of time and effort commitment	Move from PI to an IRCN Affiliated Faculty position to continue research collaboration.
Hiroki Ueda	Professor, Department of Systems Pharmacology, Division of Functional Biology, Graduate School of Medicine, The University of Tokyo	October 2017	Revision of time and effort commitment	Move from PI to an IRCN Affiliated Faculty position to continue research collaboration.

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Yukie Nagai (45)**

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

Project Professor, International Research Center for Neurointelligence, The University of Tokyo

Academic degree and specialty

Ph.D. in Engineering, cognitive developmental robotics

Effort 100 %

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

Research and education history

2019-Present: Project Professor, IRCN, The University of Tokyo
2019-Present: Fellow, Center for Interdisciplinary Research, Bielefeld University
2018-2019: Guest Associate Professor, Osaka University
2017-2019: Senior Researcher, National Institute of Information and Communications Technology
2017-2018: Visiting Professor, Bielefeld University
2009-2017: Specially Appointed Associate Professor, Osaka University
2009-2016: Visiting Researcher, Bielefeld University
2006-2009: Postdoctoral Researcher, Bielefeld University
2004-2006: Postdoctoral Researcher, National Institute of Information and Communications Technology
2004: Ph.D. in Engineering, Osaka University
1999: M.E., Aoyama Gakuin University
1997: B.E., Aoyama Gakuin University

Achievements and highlights of past research activities

Dr. Yukie Nagai has been investigating underlying neural mechanisms for social cognitive development by means of computational approaches. She designs neural network models for robots to learn to acquire cognitive functions such as self-other cognition, estimation of others' intention and emotion, altruism, and so on based on the theory of predictive coding. The simulator reproducing atypical perception in autism spectrum disorder (ASD), which has been developed by her group, greatly impacts the society as it enables people with and without ASD to better understand potential causes for social difficulties. She serves as the research director of JST CREST Cognitive Mirroring since December 2016.

Achievements

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

a) Recipient of international awards

- Best Student Paper Award of the 5th HAI (2017)
- Babybot Challenge 1st Place Award of the 5th IEEE ICDL-EpiRob (2015)
- Best Paper Research Award of the RAAD Workshop (2013)
- Best Paper Award Finalist of the 16th Annual RoboCup (2012)
- Best Paper Award Finalist of the 16th IEEE RO-MAN (2008)

b) Member of a scholarly academy in a major country: NA

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

- Keynote speaker at CoRL2019, Autumn School of SPP 2019, Nature Conference 2019, LivingMachines 2019, Behaviors.ai 2019, UAE Symposium 2019, CRoNe 2018, etc.
- Invited speaker at IROS2019 WS, HAI2019 WS, ICDL-EpiRob2019 WS, RSS2019 WSs, HRI2019 WS, DWIH Symposium 2018, IROS2018 WSs, ICDL-EpiRob2018 WS, RSS2018 WS, ICDL-EpiRob2017 WSs, Lorentz Center WS 2017, IROS2016 WSs, ICDL-EpiRob2016 WS, EuroScience Open Forum 2016, HRI2016 WS, etc. (Total: 79 talks)
- General chair of HAI2020, HAI2017, HRI2016, ICDL-EpiRob2013
- Vise chair of AMD-TC, CIS IEEE

d) Editor of an international academic journal

- Special Issues Editor for ACM Transactions on HRI

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

- Evaluation panel of INRIA theme "Computational Neuroscience and Medicine"

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

CREST "Cognitive Mirroring: Assisting people with developmental disorders by means of self-understanding and social sharing of cognitive processes"

- Period: 2016FY – 2021FY
- Research director: Yukie Nagai
- Budget: 167,950,000 JPY (Total: 350,142,000 JPY)

KAKENHI Grand-in-Aid for Scientific Research on Innovative Areas "Modeling social cognitive development and designing support systems for developmental disorders"

- Period: 2012FY – 2016FY
- Principal investigator: Yukie Nagai
- Budget: 85,300,000 JPY (Total: 191,700,000 JPY)

KAKENHI Grand-in-Aid for Specially Promote Research "Constructive developmental science based on understanding the process from neuro-dynamics to social interaction"

- Period: 2012FY – 2016FY
- Principal investigator: Minoru Asada (Co-investigator: Yukie Nagai)
- Budget: 8,500,000 JPY

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

- P. Lanillos, D. Oliva, A. Philippsen, Y. Yamashita, Y. Nagai, and G. Cheng, "A review on neural network models of schizophrenia and autism spectrum disorder," Neural Networks, 122: 338-363, 2020. Cited 3 times.
- Y. Nagai, "Predictive learning: its key role in early cognitive development," Philosophical Transactions of the Royal Society B: Biological Sciences, 374(1771), 2019. Cited 5 times.
- T. Horii, Y. Nagai, and M. Asada, "Modeling Development of Multimodal Emotion Perception Guided by Tactile Dominance and Perceptual Improvement," IEEE Transactions on Cognitive and Developmental Systems, 10(3): 762-775, 2018. Cited 7 times.
- J. Baraglia, M. Cakmak, Y. Nagai, R. P. N. Rao, and M. Asada, "Efficient human-robot collaboration: When should a robot take initiative?," The International Journal of Robotics Research, 36(5-7): 563-579, 2017. Cited 21 times.
- T. Horii, Y. Nagai, and M. Asada, "Imitation of human expressions based on emotion estimation by mental simulation," Paladyn. Journal of Behavioral Robotics, 7(1): 40-54, 2016. Cited 12 times.
- J. Baraglia, Y. Nagai, and M. Asada, "Emergence of Altruistic Behavior Through the Minimization of Prediction Error," IEEE Transactions on Cognitive and Developmental Systems, 8(3): 141-151, 2016. Cited 10 times.
- H. Fukuyama, S. Qin, Y. Kanakogi, Y. Nagai, M. Asada, and M. Myowa-Yamakoshi, "Infant's action skill dynamically modulates parental action demonstration in the dyadic interaction," Developmental Science, 18(6): 1006-1013, 2015. Cited 24 times.
- E. Ugur, Y. Nagai, E. Sahin, and E. Oztop, "Staged Development of Robot Skills: Behavior Formation, Affordance Learning and Imitation with Motionese," IEEE Transactions on Autonomous Mental Development, 7(2): 119-139, 2015. Cited 61 times.
- Y. Nagai and K. J. Rohlfing, "Computational Analysis of Motionese Toward Scaffolding Robot Action Learning," IEEE Transactions on Autonomous Mental Development, 1(1): 44-54, 2009. Cited 75 times.
- Y. Nagai, M. Asada, and K. Hosoda, "Learning for joint attention helped by functional development," Advanced Robotics, 20(10): 1165-1181, 2006. Cited 90 times.
- Y. Nagai, K. Hosoda, A. Morita, and M. Asada, "A constructive model for the development of joint attention," Connection Science, 15(4): 211-229, 2003. Cited 211 times.

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

- Selected as "30 women in robotics you need to know about – 2019"
- Invited speaker at IJCAI-PRICAI2020, which is a major international conference on AI
- Invited speaker at Stockholm Tech Live 2020, which is the largest high-tech expo in the Nordics

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Sho Tsuji (35)**

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

Assistant Professor, IRCN, University of Tokyo

Academic degree and specialty

Ph.D., Psycholinguistics

Effort **100 %**

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

Research and education history

2019 - present	**Assistant Professor,** The University of Tokyo, International Research Center for Neurointelligence (IRCN)
2016 - 2019	**Postdoctoral researcher,** University of Pennsylvania, Department of Psychology and Laboratoire de Sciences Cognitives et Psycholinguistique (ENS, EHESS, CNRS)
2014 - 2016	**Postdoctoral researcher,** Laboratoire de Sciences Cognitives et Psycholinguistique (ENS, EHESS, CNRS)
2010 - 2014	**PhD in Psycholinguistics,** International Max Planck Research School (IMPRS) for Language Sciences & Radboud University
2009 - 2010	**Visiting researcher,** RIKEN Brain Sciences Institute, Laboratory for Language Development
2003 - 2008	**Diplom (MA equivalent) in Psychology**, Humboldt University Berlin

Achievements and highlights of past research activities

- Investigates through which mechanisms the social and linguistic environment supports early language learning, contributing to a quantitative account of the environment's role in acquisition
- Facilitates and promoting research transparency through meta-analysis of infant language acquisition research (www.metalab.stanford.edu)

Achievements

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

a) Recipient of international awards: NA

b) Member of a scholarly academy in a major country: NA

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

major international academic society in the subject field: NA

d) Editor of an international academic journal Advisory board, Meta-Psychology https://open.lnu.se/index.php/metapsychology/about/editorialTeam

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

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

2019-2021	The University of Tokyo Excellent Young Researcher Research Activity Start-Up grant JP¥ 6,000,000
2016-2019	ERC Horizon 2020 Marie-Skłodowska-Curie International Outgoing Fellowship €246,668 (Supervisors: Alejandrina Cristia and Daniel Swingley)

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

- **Tsuji, S.**, Jincho, N., Mazuka, R., & Cristia, A. (2020). Communicative cues in absence of a human interaction partner enhance 12-month-old infants' word learning. *Journal of Experimental Child Psychology, 191*, 104740. Preprint OSF page **cited 0 times**
- Bergmann, C., **Tsuji, S.**, Piccinini, P.E., Lewis, M.L., Braginsky, M., Frank, M.C., & Cristia, A. (2018). Promoting replicability in developmental research through meta-analyses: Insights from language acquisition research. *Child Development, 89*, 1996-2009. doi:10.1111/cdev.13079 Access here Reproducible analyses **cited 32 times**
- **Tsuji, S.**, Mazuka, R., Cristia, A., & Fikkert, P. (2015). Even at 4 months, a labial is a good enough coronal, but not vice versa. *Cognition, 134*, 252-256. doi:10.1016/j.cognition.2014.10.009. Access here **cited 18 times**
- **Tsuji, S.**, Bergmann, C., & Cristia, A. (2014). Community-Augmented Meta-Analyses:Toward Cumulative Data Assessment. *Perspectives on Psychological Sciences, 9*(6), 661-665. doi: 10.1177/1745691614552498**.** Access here InfantDBs **cited 34 times**

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

Engagement for Open Science:

Catalyst, Berkeley Initiative for Transparency in the Social Sciences, for promoting reproducible science.

Governing board, MetaLab. Strategic and scientific development of project creating, sharing, and analyzing meta-analyses of child development.

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Zenas C. Chao (44)**

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

Project Associate Professor, IRCN, The University of Tokyo

Academic degree and specialty

PhD, Biomedical Engineering, Neuroscience

Effort 100 %

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

Research and education history

2019-Present: Project Associate Professor, IRCN, The University of Tokyo

2016-2019: Junior Associate Professor, Dept of Neuroscience, Kyoto University

2015-2016: Assistant Professor, Dept of Developmental Physiology, NIPS

2010-2015: Senior Research Scientist, RIKEN-BSI

2008-2010: Research Scientist, RIKEN-BTCC

2001-2007: Graduate Research Assistant, Georgia Institute of Technology, USA

2007: PhD, Dept of Biomedical Engineering, Georgia Institute of Technology, USA

1998: Dual BS, Dept of Life Science/Chemistry, National Tsing-Hua University, TAIWAN

Achievements and highlights of past research activities

Cognition is the foundation of the human brain's unique capacities. My research focuses on big-data analysis of cognition, which is often internal and has no direct behavioral correlates. To overcome this limitation, I combine large-scale broadband neuronal recording in human and nonhuman primates with big data-driven analysis to extract intrinsic structures in neuronal activity, called modules, where each module contains a unique fingerprint of network anatomy, dynamics, and function. This work pioneered the concept of the brain communication module, the modular information flows in brain networks that underlies cognition. This novel approach has to date led to the discovery of brain modules for motor planning, statistical learning, sequence processing, social cognition, and consciousness, and helped create testable hypotheses for neurological disorders such as depression, schizophrenia, and spinal cord injury. My most recent and ongoing work examines how brain modules interact with each other to learn and predict dynamic sensory inputs, and reveal a bidirectional cascade of neural oscillations, which use different frequency channels to support hierarchical and parallel computations of prediction and prediction error signaling. These findings raise novel neural principles of brain predictive coding, a theoretical framework that is a leading candidate for the grand unified theory of cognition.

Achievements

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

a) Recipient of international awards: NA

b) Member of a scholarly academy in a major country: NA

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

Invited talk at international conferences (over the past 5 years):

1. "Predictive-coding signals in primate brain." Tsinghua University Institute for Artificial Intelligence (THUAI) and International Research Center for Neurointelligence (IRCN) Workshop, Tokyo, Japan, December 2019.
2. "Searching for predictive-coding signals in primate brain." Neuroscience Program of Academia Sinica (NPAS) Seminar, Taipei, Taiwan, October 2019.
3. "Large-scale cortical networks for hierarchical prediction coding in the primate brain." Satellite Symposium for 29th Annual Meeting of the Society for Neural Control of Movement, Toyama, Japan, April 2019.
4. "Large-scale cortical networks for hierarchical prediction coding." International Research Center for Neurointelligence (IRCN) Seminar, Tokyo, Japan, December 2018.
5. "Dynamic reorganization of sensorimotor networks during recovery from spinal cord injury in monkeys." Yamada Symposium Neuroimaging of Natural Behaviors, Tokyo, Japan, October 2017.
6. "Dynamic reorganization of functional brain networks during recovery from spinal cord injury." 15th China-Japan-Korea Joint Workshop on Neurobiology and Neuroinformatics (NBNI), Busan, Korea, December 2015.

d) Editor of an international academic journal: NA

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

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

Kakenhi Kiban C (FY2019~2021): Hierarchical interactions of predictions and prediction errors in normal and schizophrenic brains

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

1. Chao ZC, Takaura K, Wang L, Fujii N, Dehaene S (2018). "Large-scale cortical networks for hierarchical prediction and prediction error in the primate brain." Neuron, 100, 1252-1266. Cited 31 times.
2. Chao ZC, Sawada M, Isa T, Nishimura Y (2018). "Dynamic Reorganization of Motor Networks

During Recovery from Partial Spinal Cord Injury in Monkeys." Cerebral Cortex, bhy172. Cited 5 times.

3. Chao ZC, Nagasaka Y, Fujii N (2015). "Cortical network architecture for context processing in primate brain." eLife 4: e06121. Cited 5 times.
4. Chao ZC, Nagasaka Y, Fujii N (2010). "Long-term asynchronous decoding of arm motion using electrocorticographic signals in monkeys." Frontiers in Neuroengineering 3:3. Cited 327 times.
5. Chao ZC, Bakkum DJ, Potter SM (2008). "Shaping embodied neural networks for adaptive goal-directed behavior." PLoS Computational Biology 4(3). Cited 70 times.
6. Chao ZC, Bakkum DJ, Potter SM (2008). "Spatio-temporal electrical stimuli shape the behavior of an embodied cortical network in a goal-directed learning task." J. Neural Eng. 5, 310-323. (The first two authors contribute equally) Cited 103 times.

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

NA

Appendix 2a Biographical Sketch of a New Principal Investigator

(within 3 pages per person)

Name (Age) **Mingbo Cai (34)**

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

Project Assistant Professor, International Research Center for Neurointelligence, The University of Tokyo

Academic degree and specialty

Ph.D., Neuroscience

Effort **100 %**

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

Research and education history

2019 – present: Project Assistant Professor, IRCN, The University of Tokyo

2015 – 2019: Postdoctoral Research Associate, Princeton Neuroscience Institute, Princeton University

2015: Ph.D. in Neuroscience, Department of Neuroscience, Baylor College of Medicine

2008: B.S.s in Electronics and Information Science and Technology & Psychology, Peking University

Achievements and highlights of past research activities

Studied illusions of human time perception and their computational mechanisms (2012, 2015a,b)

Developed Bayesian representational similarity analysis algorithm (2016, 2019)

Studied neural representation of task state space in orbitofrontal cortex (with Schuck et al., 2016)

Achievements

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

a) Recipient of international awards: NA

b) Member of a scholarly academy in a major country: NA

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

d) Editor of an international academic journal: NA

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

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

NA

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

Representational structure or task structure? Bias in neural representational similarity analysis and a Bayesian method for reducing bias. (2019) PLOS Computational Biology, cited 9 times

Human orbitofrontal cortex represents a cognitive map of state space. (second author) (2016) Neuron, cited 169 times

A Bayesian method for reducing bias in neural representational similarity analysis. (2016) Advances in Neural Information Processing Systems, cited 17 times

Perceived duration is reduced by repetition but not by high-level expectation. (2015) Journal of Vision, cited 22 times

Duration estimates within a modality are integrated sub-optimally. (2015) Frontiers in Psychology, cited 8 times

A neural model for temporal order judgments and their active recalibration: a common mechanism for space and time? (2012) Frontiers in Psychology, cited 66 times

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

NA

Appendix 3-1 FY 2019 Records of Center Activities

1. Researchers and center staff, satellites, partner institutions

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

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

Special mention

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

Strategic hiring in FY2019 led to the recruitment of PIs Yukie Nagai, Zenas Chao, Mingbo Cai and Takamitsu Watanabe - all of whom represent Computational Science with human subjects. In addition as a distinguished mentor, Dr Kazuyuki Aihara was appointed third Deputy Director and moved 'under-one-roof' into the first medical building on the Hongo campus (from Komaba campus) and named UTokyo University Professor. This powerful group spans many aspects of Neurointelligence research and is actively involved in Team Science. A fifth PI, Dr Sho Tsuji also successfully opened a human baby lab in the same building and has actively recruited subjects through public outreach events in the greater Tokyo area (Miraikan, city hall, etc). Finally, we started another international recruitment for further computational PI/senior postdoctoral fellows for FY2020.

For globalization, IRCN has continued to host interns from around the world (Harvard University, Italy, Germany, Canada, etc). In 2019, we also started sending UTokyo medical students out to Harvard University. Partner institutions also visited IRCN for targeted workshops to design collaborative research. One example is the NCCR Synapsy group from Geneva-Lausanne area. This Swiss WPI equivalent network has focused on schizophrenia and autism research, which is also a growing strength at IRCN. Together, we held a three-day meeting to explore "22q disorders" and brainstorm about researcher exchange and complementary work such as computational psychiatry or social robotics. A reciprocal visit by Dr Kiyoto Kasai to the NCCR retreat was planned for end of March 2020.

1-2. Satellites and partner institutions

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

<Satellite institutions>

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

Intelligence Project (AIP), RIKEN Center for Biosystems Dynamics Research (BDR)	Yasushi Okada	
National Centre Competence in Research (NCCR) Synapsy		
The Edwin O. Reischauer Institute of Japanese Studies at Harvard University		
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	newly added institution
Institute of Neuroscience (ION), Center for Excellence in Brain Science and Intelligence Technology, Chinese Academy of Sciences		newly added institution

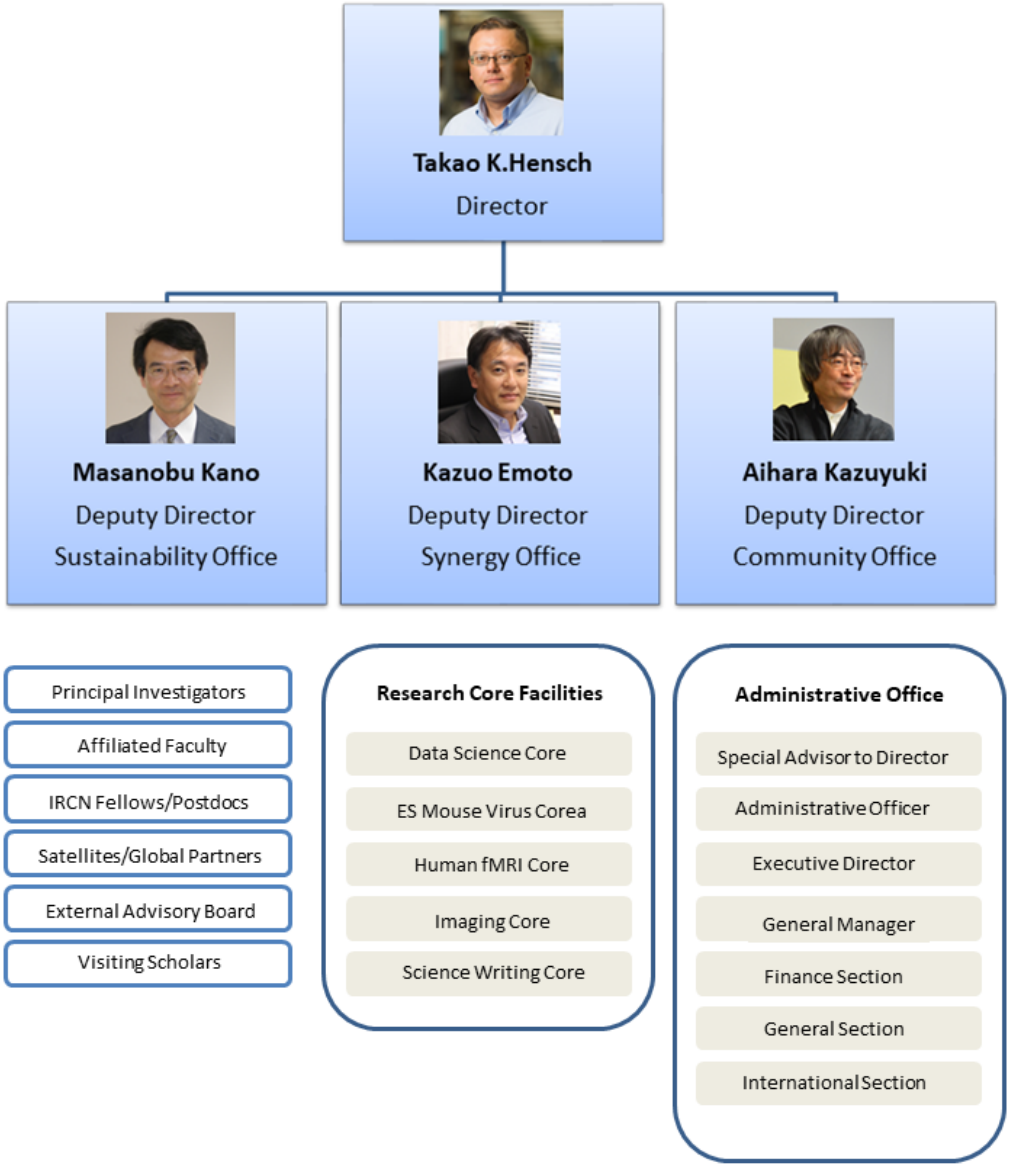
2. Holding international research meetings

- Indicate the number of international research conferences or symposiums held in FY2019 and give up to three examples of the most representative ones using the table below.

FY 2019: 20 meetings	
Major examples (meeting titles and places held)	Number of participants
CDKL5 Workshop	From domestic institutions: 78 From overseas institutions: 25
Tsinghua AI Institute – IRCN joint workshop "Between artificial and human intelligence"	From domestic institutions: 34 From overseas institutions: 6
IRCN-Stockholm Trio Workshop "Neuronal Circuits and Intelligence"	From domestic institutions: 72 From overseas institutions: 11

3. Diagram of management system

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

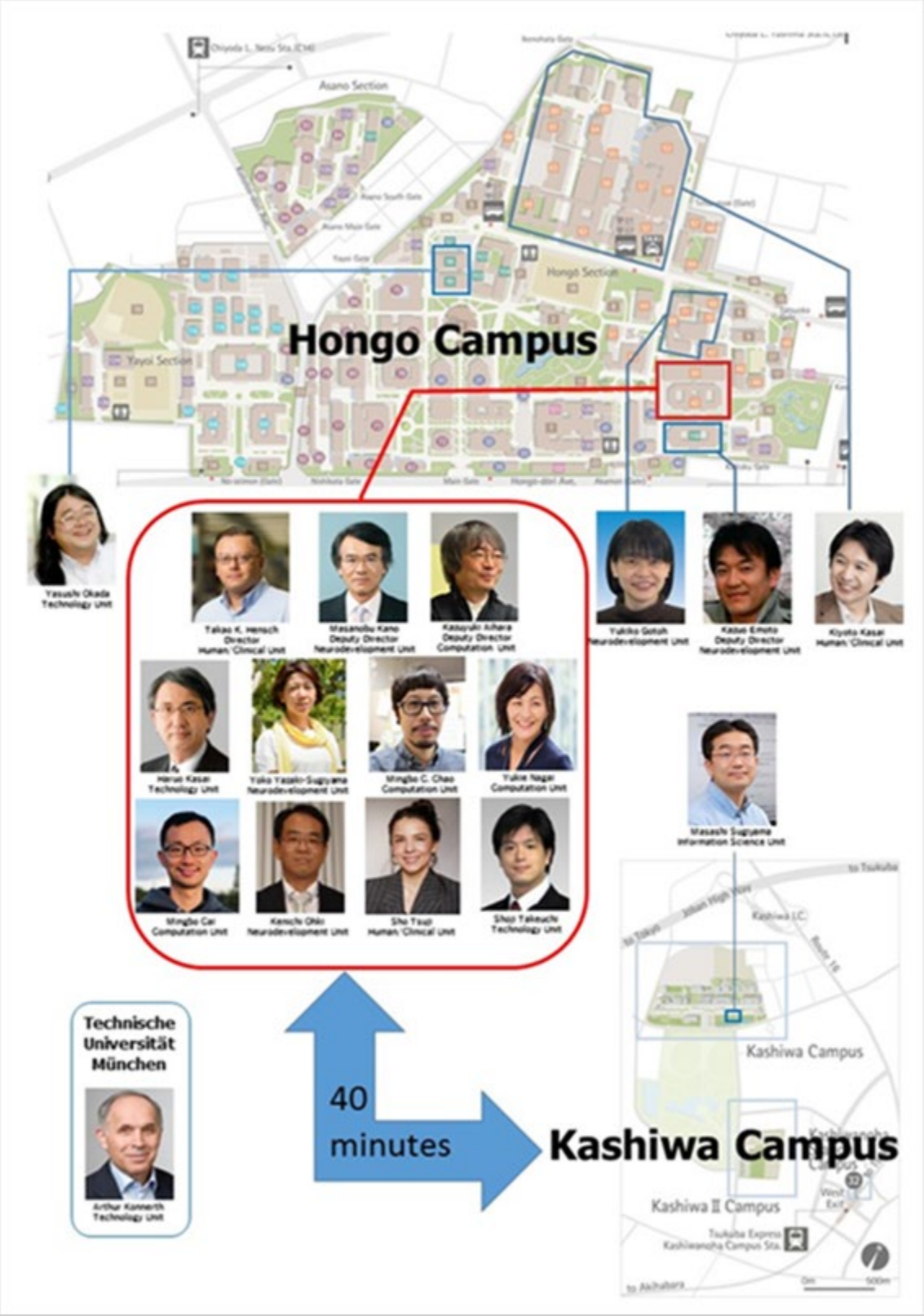


- Dr. Kazuyuki Aihara, Principal Investigator, was assigned as Deputy Director on Oct. 1, 2019.
- To promote bottom-up approach, three offices have been set up on Oct. 1, 2019: the **Sustainability Office**, the **Synergy Office**, and the **Community Office**.
- **Sustainability Office**, led by Deputy Director Masanobu Kano, catalyzes support, infrastructure and personnel, including fundraising, building renovations for 'under-one-roof' ecosystem, strategic recruitment with emphasis on diversity, WPI budget, evaluation and other related tasks.
- **Synergy Office**, led by Deputy Director Kazuo Emoto, promotes research fusion and team science. It suggests workshops, seminars, and salons proposed by the IRCN Program Committee to foster team science, as well as recommends 'Director's Prizes' to reward innovative collaborations and science salons.
- **Community Office**, led by Deputy Director Kazuyuki Aihara, coordinates education and outreach activities. It offers courses for trainees, outreach events or workshops, and various learning opportunities within IRCN, as well as logistical support for foreign researchers.

- Dr. Tetsushi Kagawa, Administrative Officer, had resigned on Feb. 29, 2020. Ms. Maki Kubo, Special Advisor to Director now serves as Administrative Officer.

4. Campus Map

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



5. Securing external research funding*

External research funding secured in FY2019

Total: 515,917,795 yen

- Describe external funding warranting special mention. Include the name and total amount of each grant.
* External research funding includes "KAKENHI," funding for "commissioned research projects," "joint research projects," and for others. (donations, etc.)

JSPS Grant-in-Aid for Scientific Research (S): 95,280,000 yen
Grant-in-Aid for Scientific Research (A): 21,232,000 yen

MEXT Grant-in-Aid for Scientific Research on Innovative Areas: 45,520,000 yen

JST CREST: 74,560,000 yen

AMED Strategic Research Program for Brain Science: 117,416,000 yen

AMED-CREST: 48,520,000 yen

Appendix 3-1a FY 2019 Records of Center Activities

Researchers and other center staff

Number of researchers and other center staff

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

a) Principal Investigators

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

(number of persons)

	At the beginning of project	At the end of FY 2019	Final goal (March 31, 2027)
Researchers from within the host institution	12	10	11
Researchers invited from overseas	2	4	4
Researchers invited from other Japanese institutions	0	3	2
Total principal investigators	14	17	17

b) Total members

	At the beginning of project		At the end of FY2019		Final goal (March 31, 2027)	
	Number of persons	%	Number of persons	%	Number of persons	%
Researchers	27		69		70	
Overseas researchers	3	11.1	25	36.232	19	27.14
Female researchers	4	14.8	12	17.391	17	24.29
Principal investigators	14		17		17	
Overseas PIs	2	14.3	4	23.529	4	23.53
Female PIs	1	7.14	4	23.529	2	11.76
Other researchers	13		40		40	
Overseas researchers	1	7.69	10	25	10	25
Female researchers	3	23.1	4	10	5	12.5
Postdocs	0		12		13	
Overseas postdocs	0		11	91.667	10	76.92
Female postdocs	0		4	33.333	5	38.46
Research support staffs	0		16		20	
Administrative staffs	3		13		10	
Total number of people who form the "core" of the research center	30		98		100	

Appendix 3-2 Project Expenditures

1) Overall project funding

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

(Million yens)

Cost items	Details (For Personnel - Equipment please fill in the breakdown of fiscal expenditure, and the income breakdown for Research projects.)	Total costs	Amount covered by WPI funding
Personnel	Center director and administrative director	36	36
	Principal investigators (no. of persons):17	131	29
	Other researchers (no. of persons):21	153	114
	Research support staff (no. of persons):14	57	42
	Administrative staff (no. of persons):15	99	32
	Subtotal	476	253
Project activities	Gratuities and honoraria paid to invited principal investigators (no. of persons):0	0	0
	Cost of dispatching scientists (no. of persons):2	2	2
	Research startup cost (no. of persons):21	40	40
	Cost of satellite organizations (no. of satellite organizations):1	89	89
	Cost of international symposiums (no. of symposiums):4	9	4
	Rental fees for facilities	56	49
	Cost of consumables	8	4
	Cost of utilities	5	0
	Other costs	78	78
	Subtotal	287	266
Travel	Domestic travel costs	5	4
	Overseas travel costs	14	14
	Travel and accommodations cost for invited scientists (no. of domestic scientists):9 (no. of overseas scientists):32	6	3
	Travel cost for scientists on transfer (no. of domestic scientists):4 (no. of overseas scientists):5	3	3
	Subtotal	28	24
Equipment	Depreciation of buildings		
	Depreciation of equipment		
	Subtotal	0	0
Research projects (Detail items must be fixed)	Project supported by other government subsidies, etc. *1	7	0
	KAKENHI	213	0
	Commissioned research projects, etc.	250	0
	Joint research projects	15	0
	Ohers (donations, etc.)	38	0
	Subtotal	523	0
Total		1314	543

Costs (Million yens)

WPI grant in FY 2019	0
Costs of establishing and maintaining facilities	12
Establishing new facilities (Number of facilities: , OO m²)	0
Repairing facilities (Number of facilities: , 149 m²)	12
Others	0
Costs of equipment procured	127
Ultrasonic Brain Function Measuring Device 1Set	43
Motion Capture System 1Set	5
Others	79

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

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

2) Costs of satellites

(Million yens)

Cost items	Details	Total costs	Amount covered by WPI funding
Personnel	Principal investigators (no. of persons):0		
	Other researchers (no. of persons):14		
	Research support staff (no. of persons):0		
	Administrative staff (no. of persons):0		
	Subtotal	44	44
Project activities	Subtotal	39	39
Travel	Subtotal	0	0
Equipment	Subtotal	6	6
Research projects	Subtotal	0	0
Total		89	89

Appendix 4 FY 2019 Status of Collaboration with Overseas Satellites

1. Coauthored Papers

- List the refereed papers published in FY 2019 that were coauthored between the center's researcher(s) in domestic institution(s) (include satellite institutions) and overseas satellite institution(s). List them by overseas satellite institution in the below blocks.
- Transcribe data in same format as in Appendix 1. Italicize the names of authors affiliated with overseas satellite institutions.
- For reference write the Appendix 1 item number in parentheses after the item number in the blocks below. Let it free, if the paper is published in between Jan.-Mar. 2020 and not described in Appendix 1.

Overseas Satellite 1 **Boston Children's Hospital** (Total: 7 papers)

1) (45) 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 2019. (DOI: 10.1073/pnas.1820847116)

2) (98) Picard N, Takesian AE, *Fagiolini M*, Hensch TK. NMDA 2A receptors in parvalbumin cells mediate sex-specific rapid ketamine response on cortical activity. Mol Psychiatry 24:828-838, 2019. (DOI: 10.1038/s41380-018-0341-9)

3) Chini M, Gretenkord S, Kostka JK, Pöpplau JA, *Cornelissen L, Berde CB*, Hanganu-Opatz IL, Bitzenhofer SH. Neural correlates of anesthesia in newborn mice and humans. Front Neural Circuits 13:38, 2019. (DOI: 10.3389/fncir.2019.00038)

4) 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 10:4188, 2019. (DOI: 10.1038/s41467-019-12202-9)

5) Wilkinson CL, Levin AR, Gabard-Durnam LJ, Tager-Flusberg H, *Nelson CA*. Reduced frontal gamma power at 24 months is associated with better expressive language in toddlers at risk for autism. Autism Res 12:1211-1224, 2019. (DOI: 10.1002/aur.2131)

6) Picard N, *Fagiolini M*. MeCP2: an epigenetic regulator of critical periods. Curr Opin Neurobiol 59:95-101, 2019. (DOI: 10.1016/j.conb.2019.04.004)

7) Patrizi A, Awad PN, Chattopadhyaya B, Li C, Di Cristo G, *Fagiolini M*. Accelerated hyper-maturation of parvalbumin circuits in the absence of MeCP2. Cereb Cortex 30:256-268, 2020. (DOI: 10.1093/cercor/bhz085)

2. Status of Researcher Exchanges

- Using the below tables, indicate the number and length of researcher exchanges in FY 2019. 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
FY2019	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
FY2019	0	7	0	0	7
	0	3	0	0	3

Overseas Satellite 2:

<To satellite>

	Under 1 week	From 1 week to 1 month	From 1 month to 3 months	3 months or longer	Total
FY2019	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
FY2019	0	0	0	0	0
	0	0	0	0	0

Appendix 5 FY 2019 Visit Records of Researchers from Abroad

* If researchers have visited/ stayed at the Center, provide information on them in the below table.

Total: 66

	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	Andrei S. Kozlov	55	Senior Lecturer, Department of Bioengineering, Imperial College London	UK	PhD	Wellcome Trust Investigators Award 2019	2019/4/10	IRCN Seminar speaker
2	Lorenzo Jamone	38	Lecturer, Queen Mary University of London	UK	PhD	Marie Sklodowska-Curie Grant (IEF)	2019/4/24	IRCN Seminar speaker
3	Mingbo Cai	33	Postdoctoral Research Associate, Neuroscience Center, Princeton University	US	PhD	Applying methods from probabilistic theory, psychology, neuroscience and machine learning to understand the computation performed by the human brain. Co-developer of BrainIAK	2019/6/8-9	Participation in IRCN Retreat
4	Shinsuke Shimojo	64	Gertrude Baltimore Professor of Experimental Psychology, The Division of Biology and Biological Engineering, Caltech	US	PhD	Toshihiko Tokizane Memorial Award 2004 Japanese Society of Cognitive Science, The "most creative study" award 2008 Nakayama Grand Prix 2008	2019/6/8-9	Participation in IRCN Retreat
5	John Hepburn	66	Vice-President, Research, CIFAR	Canada	PhD	Rutherford Medal in Physics 1993 Killam fellow Canada Council, 1995-1997 Member Fellow, Associated Press Sloan, 1988-1990	2019/6/11	Visit for seeking the opportunity of the research collaboration
6	Sarah C. Woolley	45	Assoc. Prof, Department of Biology, McGill University	Canada	PhD	National Science and Engineering Research Council Discovery Grant Neural mechanisms of social preferences 2018-2023	2019/6/22-7/22	IRCN Seminar speaker Tokyo college visiting scholar
7	Jon Tatsuya Sakata	46	Assoc. Prof, Department of Biology, McGill University	Canada	PhD	Natural Sciences and Engineering Research Council Discovery Grant Integration of brain circuits for the control and plasticity of vocal communication signals	2019/6/22-7/22	IRCN Seminar speaker
8	Alexandre Dayer	47	Director, NCCR Synapsy Professor, Psychiatry and Basic Neuroscience Departments, University of Geneva	Switzerland	MD	Collaborates with several clinical research groups in Child and Adult Psychiatry and has a particular interest in the developmental trajectories leading to stress-related disorders. Works as a senior clinician in the outpatient moods unit of the Service of Psychiatric Specialties of the University Hospital of Geneva and has a special interest in the treatment of patients with bipolar disorders.	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop
9	Stefan Eliez	51	Professor, Faculty of Medicine and Director of Child Psychiatry, Office Medico-Pedagogique and Fondation Pole Autisme Geneva	Switzerland	MD	Seeking to understand the cerebral, cognitive and psychiatric development of youths affected psychiatric disorders Foundedthe Fondation Pole Autisme in 2013 with donors and families of children with autism spectrum disorder. It is aiming at improving research, clinical training and care in the field of neurodevelopmental disorders.	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop
10	Alan Carleton	42	Associate professor, Faculty of Medicine, Department of Basic Neurosciences, University of Geneva	Switzerland	PhD	Study the mechanisms controlling sensory perception and how different senses may interact together.	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop
11	Marie Schaer	39	Assistant Professor, Department of Psychiatry, University of Geneva	Switzerland	MD/PhD	Brain imaging (MRI, EEG) and eye-tracking to quantify the outcome of preschoolers with autism who receive behavioral interventions.	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop
12	Camilla Bellone	46	Assistant Professor, Faculty of Medicine, Department of Basic Neurosciences, University of Geneva	Switzerland	PhD	Studying the neuronal mechanisms and the circuits underlying social interaction, and how deficits in specific circuits may lead to social dysfunctions in ASD. FENS-KAVLI network of Excellence 2015	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop
13	Guoping Feng	59	Poitras Professor of Neuroscience, McGovern Institute for Brain Research, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology	US	PhD	Understanding the mechanisms regulating the development and function of synapses in the brain and how synaptic dysfunction may contribute to psychiatric disorders. Using genetically engineered animal models, he combines cutting-edge technologies and multidisciplinary approaches to unravel the neurobiological mechanisms of neurodevelopmental and psychiatric disorders. Brain Research Foundation Scientific Innovations Award, 2015 Simons Foundation Autism Research Initiative (SFARI) grant award, 2014 – 2016	2019/7/6-7/8	Participation in NCCR-IRCN "22q" Workshop IRCN Seminar speaker
14	Dragomir Milovanovic	32	Professor, Departments of Neuroscience and Cell Biology, Program in Cellular Neuroscience, Neurodegeneration and Repair, Kavli Institute for Neuroscience, Howard Hughes Medical Institute, Yale University School of Medicine	US	PhD	Research on phase separation at the nerve terminal. Human Frontiers in Science Program Long-Term Research Fellowship 2016 - 2019	2019/7/31	IRCN Seminar speaker
15	Emre Ugur	38	Assist. Prof.,Dept. of Computer Engineering, Bogazici University	Turkey	PhD	Principle Investigator of IMAGINE project supported by European Commission, Horizon 2020 Programme	2019/8/8	IRCN Seminar speaker
16	Erhan Oztop	48	Prof, Computer Science Department, Ozyegin University	Turkey	PhD	Computational modeling of brain mechanisms of visuo-motor transformations, machine learning,robotics, and cognitive neuroscience. Outstanding Research Award, Advanced Telecommunications Research International (ATR) 2011	2019/8/8	IRCN Seminar speaker
17	Alessandro Gozzi	45	Senior scientist and group leader, Italian Institute of Technology	Italy	PhD	Focusing on the application of advanced MRI methods to investigate the large-scale neurofunctional architecture of the mouse brain, and describe its modulation by neurodevelopmental and pathological effectors.	2019/9/18-19	Participation in IRCN CDKL5 ASIA
18	Helen Leonard	73	Associate Professor, Telethon Kids Institute	Australia	MPH	National Health and Medical Research Council Senior Research Fellowship and is a Principal Research Fellow at the Telethon Kids Institute in Western Australia. Consumer and Community Participation Award Telethon Institute for Child Health Research 2012	2019/9/18-19	Participation in IRCN CDKL5 ASIA
19	Hisashi Umemori	55	Associate Professor, Principle Investigator, F.M. Kirby Neurobiology Center, Boston Children's Hospital, Harvard Medical School	US	MD/PhD	Aim to understand the principle of mammalian brain wiring and how the functional brain is built. The knowledge obtained will be applied to prevent or treat neurological and psychiatric disorders. Prizes from the Mallinckrodt, March of Dimes, Whitehall, and Simons Foundations	2019/9/18-19	Participation in IRCN CDKL5 ASIA

20	Marina Trivisano	38	Bambino Gesù Children's Hospital, Rome	Italy	MD/PhD	Main area of expertise is clinical and EEG characterization of rare genetic epilepsies as well as of other epileptic syndromes. Member of the Italian League Against Epilepsy	2019/9/18-19	Participation in IRCN CDKL5 ASIA
21	Maurizio Giustetto	50	Associate Professor of Anatomy Dept. of Neuroscience University of Torino	Italy	PhD	Study of the neurobiological bases of Rett syndrome, using both MeCP2 and CDKL5 mutant mice, with the longterm goal to serve this community of individuals and their families to find efficient and novel therapeutic approaches.	2019/9/18-19	Participation in IRCN CDKL5 ASIA
22	Michela Fagiolini	50	Associate in Neurology, Boston Children's Hospital Associate Professor of Neurology, Harvard Medical School	US	PhD	Studying experience-dependent brain development in mouse models of autism spectrum disorders (ASDs). Particularly focused on Rett Syndrome, a leading cause of intellectual disability with autistic features.	2019/9/18-19	Organize IRCN CDKL5 ASIA Visit as an affiliate Faculty of IRCN
23	Priscilla D. Negraes	41	Senior Scientist, R&D Department of StemoniX	US	PhD	Develop human models suitable for high throughput approaches that better reproduce the natural brain development but also in a disease context in order to speed up research and drug development.	2019/9/18-19	Participation in IRCN CDKL5 ASIA
24	Timothy Andrew Benke	55	Professor of Pediatrics, Pharmacology, Neurology, and Otolaryngology at University of Colorado School of Medicine	US	MD/PhD	Studies the mechanisms of early-life seizures to cause intellectual challenges and the role of CDKL5 on synaptic function. Board member of RMRA (Rocky Mountain Rett Association), advisor to LouLou Foundations and medical advisor to RSO (RettSyndrome.org)	2019/9/18-19	Participation in IRCN CDKL5 ASIA
25	Timothy Roberts	53	Professor, School of Medicine, University of Pennsylvania	US	PhD	Focuses on multimodal imaging and electrophysiology in pediatric disorders such as epilepsy and ASD. Authority on the use of magnetoencephalography (MEG) Oberkircher Family Endowed Chair in Pediatric Radiology	2019/9/18-19	Participation in IRCN CDKL5 ASIA
26	Tommaso Pizzorusso	53	Associate Professor, Department of Neurofarba, University of Florence	Italy	PhD	CDKL5 preclinical models: biomarkers and possible treatments IRP/IFP Schellenberg Prize, 2013	2019/9/18-19	Participation in IRCN CDKL5 ASIA
27	Vera Kalscheuer	55	Group Leader, RG Development & Disease, Max Planck Institute for Molecular Genetics	Germany	PhD	Elucidate the causative genetic defects of human disorders of the brain with a focus on intellectual disability (ID) and related neurological disorders by using state-of-the art genetics and genomics strategies, and to understand the functional relevance of pathogenic mutations and the cell protein signaling networks the respective proteins are embedded in.	2019/9/18-19	Participation in IRCN CDKL5 ASIA
28	Wenlin Liao	41	Associate Professor, Institute of Neuroscience, National Cheng-Chi University	Taiwan	PhD	Understanding the mechanisms regulating the psychomotor behaviors in neurodevelopmental and psychiatric disorders through phenotypic analysis of genetically engineered mouse models	2019/9/18-19	Participation in IRCN CDKL5 ASIA
29	Kim Noble	42	Associate Professor, Graduate School of Education, Health and Psycology, Columbia University	US	PhD	Fellow of the Association for Psychological Science, and was awarded the 2017 APS Janet Taylor Spence Award for Transformative Early Career Contributions. Her work linking family income to brain structure across childhood and adolescence has received worldwide attention in the popular press.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
30	Mike Kobor		Professor, Department of Medical Genetics, The University of British Columbia Senior Scientist, Centre for Molecular Medicine and Therapeutics at BC Children's Hospital Research Institute	Canada	PhD	Uingnderstang of the molecular mechanisms of epigenetic regulation in response to the environment. This is largely achieved through evaluating DNA methylation, histone variants, post-translational modification of histone, and nucleosome positioning. Additionally, genetic variation may interact with specific environments, imparting sensitivity or resilience, to ultimately alter epigenetics patterns and phenotypic outcomes.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
31	Sara Mostafavi	40	Assistant Professor, Department of Statistics, Department of Medical Genetics, The University of British Columbia	Canada	PhD	Develop and apply machine learning and statistical methods to study the genomics of complex diseases, with a particular interest in psychiatric disorders. Especially interested in developing models for combining association evidence across multiple types of genomic data, such as gene expression and genotype data, and modeling prior biological pathways and networks for disentangling spurious from meaningful correlations.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
32	Victoria Leong	35	Assistant Professor of Psychology, Nanyang Technological University (Singapore) Affiliated Lecturer, University of Cambridge	Singapore/UK	PhD	Developmental cognitive neuroscientist who is interested in neural synchrony between mothers and infants. Uses electroencephalgraphy (EEG) to study how mother-infant neural activity can become naturally synchronised during social interactions, and how this synchronisation could help babies to learn from their mothers.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
33	Paul Frankland	50	Associate Professor, Neuroscience Platform, Department of Physiology, University of Toronto	Canada	PhD	Understand how our brains normally encode, store and retrieve information.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
34	Joel Levine	53	Professor, Chair of Biology, University of Toronto	Canada	PhD	Current research focuses on the genetic basis of social interactions in Drosophila melanogaster.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
35	Candice Odgers	43	Professor, Psychological Science, University of California-Irvine Professor, Sanford School of Public Policy, Psych and Neuroscience, Duke University Co-Director, Child Brain & Development Program, CIFAR	US	PhD	Focuses on how social inequalities and early adversity influence children's future health and well-being, with an emphasis on how new technologies, including mobile phones and web-based tools, can be used to understand and improve the lives of young people.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
36	Ami Citri	53	Professor, The Safra Center for Brain Sciences and the life science institute, The Hebrew University of Jerusalem, CIFAR Azrieli Global Scholars	Israel	PhD	Deciphering the function of the claustrum & uncovering the molecular, synaptic and circuit mechanisms encoding experience. Adelis prize in Neuroscience 2015	2019/11/11-13	Participation in IRCN-CIFAR Workshop
37	Michael Meaney	68	James McGill Professor of Medicine at Douglas Mental health University Institute of McGill University Professor, Department of Neurology and Neurosurgery, McGill University Advisor to CIFAR	Canada	PhD	Margolese Brain Disorder Prize 2016 Understand how early experience exerts a sustained influence on neuronal function. Also interested in the development of individual differences in behavioural and endocrine responses to stress, and environmental and neuroendocrine mechanisms influencing maternal behaviour.	2019/11/11-13	Participation in IRCN-CIFAR Workshop

38	Tom Boyce	71	Professor Emeritus, University of California San Francisco Department of Pediatrics Advisor to CIFAR	US	MD	Leading expert on the interplay between neurobiological and psychosocial processes – an interplay that leads to socially partitioned differences in childhood health, development and disease. Distinguished Contributions to Interdisciplinary Understanding of Child Development Award 2015	2019/11/11-13	Participation in IRCN-CIFAR Workshop
39	Thomas McDade	50	Professor; Faculty Fellow, Institute for Policy Research; Director, Laboratory for Human Biology Research, Northwestern University Department of Anthropology Fellow of CIFAR	Canada	PhD	Current work focuses on the health impact of psychosocial stress and the long-term effects of early environments on inflammation. McDade has also developed 'field-friendly' methods for integrating biological measures into population-based social science research.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
40	Maria Aristizabal	38	Post Doctoral Fellow, Center for Molecular Medicine and Therapeutics - Kobor lab, The University of British Columbia	Canada	PhD	Expert in molecular biology with an emphasis on transcription regulation and epigenetic modifications. She has utilized yeast and flies to study mechanisms of transcription regulation in response to environmental perturbations.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
41	Anna Goldenberg	41	Varma Family Chair of Medical Bioinformatics and Artificial Intelligence, Associate Professor in the Department of Computer Science at the University of Toronto Fellow of CIFAR	Canada	PhD	Develops machine learning methods that combine diverse sets of biological and phenotypic measurements to refine the understanding of complex human diseases, identify the best treatments and individual patient outcomes, and guide decisions to improve the quality of life for patients.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
42	Rebecca Reh	35	CIFAR Postdoctoral Fellow	Canada	PhD	Focuses on how early life experience impacts brain development. In particular, the critical windows during development when the brain shows heightened sensitivity to environmental change.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
43	Ina Anreiter	29	Postdoctoral Researcher at Ontario Institute for Cancer Research	Canada	PhD	Wins prestigious Schmidt Science Fellowship for probing nature vs. nurture.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
44	Kieran O'Donnell	36	Assistant Professor, Department of Psychiatry, McGill University Fellow of CIFAR	Canada	PhD	Multidisciplinary research program combines psychiatric, genetic, epigenetic and epidemiological methods. His Epigenetics and Epidemiology lab seeks to better understand the biological embedding of early adversity and its association with altered child neurodevelopment.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
45	Daniel Ansari	42	Professor, Department of Psychology, University of Western Ontario, the Brain & Mind Institute and the Faculty of Education Fellow of CIFAR	Canada	PhD	Heads the Numerical Cognition Laboratory at Western University, where he and his research team use behavioural and neuroimaging methods to understand how numerical and mathematical skills develop. Advanced Research Fellowship, Klaus J. Jacobs Foundation 2018	2019/11/11-13	Participation in IRCN-CIFAR Workshop
46	Rachel Parker	45	Senior Director of CIFAR	Canada	PhD	Studied science policy and high-tech investments such as nanotechnology in China.	2019/11/11-13	Participation in IRCN-CIFAR Workshop
47	Michelle Kee	35	Research Fellow, Agency for Science, Technology and Research (A*STAR)	Singapore	PhD	Mapping Antenatal Maternal Stress (MAMS) Project	2019/12/16-17	Participation in IRCN-A*Star-IRCN @OIST Joint workshop
48	Tan Ai Peng	34	Consultant Neuroradiologist at the Department of Diagnostic Imaging, National University Hospital and National University Cancer Institute Singapore (NCIS) Assistant Professor, Yong Loo Lin School of Medicine, National University of Singapore	Singapore	MD	Her subspeciality interest is in the field of paediatric neuroradiology, with special interest in neurometabolic disorders, neonatal imaging, radiogenomics and congenital craniofacial malformations.	2019/12/16-17	Participation in IRCN-A*Star-IRCN @OIST Joint workshop
49	Evelyn Law Chung Ning	39	Consultant, Child Development Unit (Division of Developmental and Behavioural Paediatrics), Department of Paediatrics, Khoo Teck Puat - National University Children's Medical Institute, National University Hospital	Singapore	MD	Clinician scientist specialising in developmental and behavioural paediatrics	2019/12/16-17	Participation in IRCN-A*Star-IRCN @OIST Joint workshop
50	Laurel Gabard-Durnam	31	Postdoctoral Research Associate, Boston Children's Hospital, Hravard University	US	PhD	Developmental neuroscientist exploring how experiences shape our brains and behaviors Bill & Melinda Gates Foundation Neuroimaging Consortium Award 2018	2019/12/16-19	Participation in IRCN-A*Star-IRCN @OIST Joint workshop Participation in IRCN Mini Symposium
51	Patrick Purdon	45	Associate Professor, MGH Harvard Medical School	US	PhD	His research in neuroengineering encompasses the mechanisms of anesthesia, Alzheimer's disease and brain health, anesthesia and the developing brain, neural signal processing, and the development of novel technologies for brain monitoring. National Institutes of Health Director's New Innovator Award	2019/12/19	Participation in THUAI-IRCN Workshop
52	Maosong Sun	57	Professor, Department of Computer Science and Technology, Tsinghua University	China	PhD	Computational linguistics, information retrieval and social computation The National Excellent Scientific and Technological Workers Award 2016	2019/12/21	Participation in IRCN Mini Symposium
53	Jun Zhu	36	Professor, Computer Science Department Co-Director, TSAIL Group, Tsinghua University	China	PhD	Machine learning and applications in text and image analysis IEEE Intelligent Systems "AI's 10 to Watch" Award, MIT TR35 China, NSFC Excellent Young Scholar Award, CCF Young Scientist Award, and CCF first-class Natural Science Award. Supported by the National Youth Top-notch Talent Support program. Won several first-place awards in international competitions, including all the three tasks in NIPS 2017 adversarial attack and defense for deep learning and the intelligent decision task in ViZDoom 2018.	2019/12/21	Participation in THUAI-IRCN Workshop
54	Sen Song	41	Professor, Department of Biomedical Engineering, Tsinghua University	China	PhD	Working on brain-inspired artificial intelligence and solving the neural circuit basis for emotions and decision making. Also interested in medical problems, like depression and anxiety disorders, which challenges us and makes life difficult for many people.	2019/12/21	Participation in THUAI-IRCN Workshop
55	Ting Chen	48	Professor, Department of Computer Science and Technology, & Institute for Artificial Intelligence, Tsinghua University	China	PhD	Current research topics include (1) medical data analysis and intelligent medicine, (2) single-cell RNA sequencing data analysis, (3) diagnosis of rare diseases, and (4) human microbial interactions and functions. Sloan Research Fellowship 2004	2019/12/21	Participation in THUAI-IRCN Workshop

56	Xiaolin Hu	41	Associate Professor, State Key Laboratory of Intelligent Technology and Systems, Department of Computer Science and Technology, Tsinghua University	China	PhD	Main research interests include developing brain-inspired computational models and revealing the visual and auditory information processing mechanism in the brain.	2019/12/21	Participation in THUAI-IRCN Workshop
57	Guoqi Li	37	Associate Professor, Institute of Instrument Science and Technology, Tsinghua University	China	PhD	Brain-inspired computing, Machine learning, Neuromorphic computing Complex systems	2019/12/21	Participation in IRCN Mini Symposium
58	Jens Hjerling Leffler	40	Associate Professor and Group Leader, Department of Medical Biochemistry and Biophysics, Karolinska Institutet	Sweden	PhD	Interested in the genetic and cellular mechanisms of the development and function of the brain's inhibitory system. He applies advanced mouse genetics in combination with electrophysiology and modern molecular methods.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
59	Arvind Kumar	43	Associate Professor, Divison of Computational Science and Technology, KTH Royal Institute of Technology	Sweden	PhD	Computational neuroscientist studying the dynamics and information processing properties of neuronal networks.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
60	Johan Lundström	46	Director, Brain Imaging Center, Stockholm University	Sweden	PhD	Determine the neural and behavioral function of the olfactory system, and how it interacts with the other senses, to interpret our environment in health and disease.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
61	Karima Chergui	53	Senior Lecturer, Group Leader of Molecular neurophysiology, Department of Physiology and Pharmacology, Karolinska Institutet	Sweden	PhD	Parkinson's disease, synaptic plasticity, novel treatment targets	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
62	Christian Broberger	48	Professor, Dept. of Biochemistry and Biophysics, Stockholm University	Sweden	MD/PhD	Interested in the central control of basic survival functions such as reproduction, the control of energy balance and transitions between sleep and arousal.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
63	Marie Carlén	42	Associate Professor and group leader, Department of Neuroscience Karolinska Institutet	Sweden	PhD	Investigated how the activity of inhibitory interneurons expressing parvalbumin (PV) relates to cortical oscillatory activities and cognitive functions.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
64	Pawel Herman	44	Associate Professor, Divison of Computational Science and Technology, KTH Royal Institute of Technology	Sweden	PhD	Biophysically detailed cortical network models	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
65	Mia Lindskog	45	Assiociate Professor, Dept. Neurobiology, Care sciences and Society, Karolinska Institutet	Sweden	PhD	Depression has been linked to dysfunctional glutamatergic neuronal networks and therapeutic effect of antidepressant drugs has been associated with increased synaptic remodeling. Using animal models of depression the group performs electrophysiological recordings in brain slices as well as biochemical analysis and behavior.	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop
66	Konstantinos Meletis	41	Senior researcher, Department of Neuroscience Karolinska Institutet	Sweden	PhD	Provide a detailed understanding of circuit function as determined by activity of GABAergic interneurons, ultimately providing us with a rational basis to develop new pharmacotherapies for mood disorders. William K. Bowes Jr. Foundation Associate Professor Award 2015	2020/1/27-28	Participation in IRCN-Stockholm Trio Workshop

Appendix 6 FY2019 State of Outreach Activities

* Fill in the numbers of activities and times held during FY2019 by each activity.
* Describe the outreach activities in the "6. Others" of Progress Report, including those stated below that warrant special mention.

Activities	FY2019 (number of activities, times held)
PR brochure, pamphlet	1 (IRCN pamphlet revised – both English and Japanese versions)
Lectures, seminars for general public	8
Teaching, experiments, training for elementary, secondary and high school students	10 (cumulative total number – 5 high schools and 2 other parties)
Open houses	1 (Open Campus of The University of Tokyo)
Participating, exhibiting in events	3 (WPI: Super Science High School Event and Science Symposium, The University of Tokyo: Komaba Festival)
Press releases	12
Publications of the popular science books	12 (excluding magazine – details are described separately)
Others（Open Lab Experiments）	12 (at Miraikan) *Details are described separately.
Others（Workshops）	3 (Workshops on ASD VR Simulator) *Details are described separately

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

Outreach Activities and Their Results

List the Center's outreach activities carried out in FY 2019 that have contributed to enhancing the brand or recognition of your Center and/or the brand of the overall WPI program, if any, and describe its concrete contents and effect in narrative style. (Where possible, indicate the results in concrete numbers.)

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

【Fusion of Research and Outreach Activities】

Miraikan Open Lab

Miraikan Open Lab is an initiative by the Miraikan Museum to host on-site experiments that fuse research and outreach activities, and collecting opinions and viewpoints derived from bidirectional communication between researchers and visitors. From September 2019, research experiments involving babies and young children were conducted by two IRCN Principal Investigators, Drs. Sho Tsuji and Yukie Nagai. They succeeded to acquire data from 288 visitors for 12 open lab days through February 2020. As a result, the number of registered subjects for Dr. Tsuji's IRCN Baby Lab were significantly increased.

【Collaboration with Local Governments】

- Teaching Events for High School Students

  26 high school students from **Saitama Prefecture** who were selected as members of the "Project for Developing Next-Generation Science-talented Students" visited IRCN. The event involved a core facilities tour (which is a distinctive feature of IRCN) and a lecture by Principal Investigator Shoji Takeuchi. In addition, a lecture on how to deliver effective scientific presentations was given to students who were going to be dispatched overseas for a science event.

  On August 22 and 23, IRCN co-hosted an event, "1st IRCN-Tokyo Metropolitan Government Event ~Meet a Young Scientist/Research Experience for High School Students~" with the **Tokyo Metropolitan Government**. Co-hosting events with Tokyo Metropolitan Government usually requires a three-year process, but IRCN succeeded to co-host an event in the first year. A total of 38 high school students visited IRCN. The event program emphasized interactions with

young researchers such as postdoctoral fellows and a tour of the core facilities.

- Public Event for Babies and Mothers (Collaboration with IRCN Baby Lab) at **Minato City, Tokyo**
  Minato City has the second highest birth rate among the 23 wards in Tokyo. The Outreach Team collaborated with the IRCN Baby Lab to organize two mini-lectures at the Minato Children and Families Support Center (November 18, 2019 and February 12, 2020). These mini-lectures will continue and will be held every two or three months.

【Workshops on a Simulator of ASD Visual Perception as a Social Contribution】

The research team led by Principal Investigator Yukie Nagai developed an ASD Visual Perception Simulator in March 2015. This simulator is a head-mounted display system that enables wearers to experience atypical visual perception. Dr. Nagai's research team computationally analyzed how atypical perception is elicited in social contexts, and their experimental results revealed several common atypical patterns such as high contrast, intense brightness, colorless, and blurring caused by movement. In FY2019 Dr. Nagai held workshops with patient groups using this simulator to reduce the stigma of ASD. In addition, public workshops were held in Miyagawa Juvenile Medical Reformatory and the Board of Education of Tsukuba City (Ibaraki Prefecture).

【Collaboration with Other Disciplines】

- With Music
  A music composer, Ms. Misato Mochizuki, Professor of Artistic Disciplines at Meiji Gakuin University, participated in the 1st IRCN Public Event, "Brain Prediction and Brain Development" on July 13, 2019. IRCN invited her because she had composed a song called "Brain" which was inspired by a discussion about the brain with IRCN Affiliated Faculty Yuji Ikegaya,. At the event, Ms. Mochizuki moderated a roundtable discussion with 3 IRCN principal investigators providing an opportunity for visitors to hear about brain research, including the involvement of brain prediction in art, music and science. (221 participants)

- With Philosophy
  On February 16, 2020, IRCN, Kavli Institute for the Physics and Mathematics of the Universe (IPMU) of The University of Tokyo and the Earth-Life Science Institute (ELSI) of Tokyo Institute of Technology held the 5th joint public lecture, "A Question of Origins." With the origins of human intelligence, universe, earth and life as themes, scientists from all 3 institutes gathered to give presentations about cognitive science, biogeochemistry, and cosmology. A discussion about the study of scientific origins was moderated by Associate Professor Takayuki Suzuki, an expert in philosophy of mind followed to further explore connections between the fields. (152 participants / 51 participants via live streaming)

【App Development】

Affiliated Faculty Kuniyoshi Sakai and Global Vision Technology Co., Ltd. began joint research to develop a "World 1st" English training app, which would be based on brain science research. With this app, users can learn a foreign language easily like their native tongue by employing a new learning method based on grammar. The effectiveness of this app will be scientifically verified by conducting comparative studies using fMRI imaging of users.

【Relationship Development with a Super Science High School】

Toshimagaoka-jyoshigakuen High School was selected as a Super Science High School (SSH) from the FY2018. A teaching event at IRCN (May 15, 2019) was held with advice for how to make effective presentations in preparation for a SSH Event. Although it was cancelled due to the COVID-19 epidemic, Dr. Kuniyoshi Sakai would have attended the Toshimagaoka-jyoshigakuen SSH Presentation Event as a keynote speaker and advisor for the students' presentations.

【General Public Books Published in FY2019】

- AI事典 第3版 (AI Encyclopedia Edition 3)
  Yukie Nagai (Principal Investigator)
  "8.8 予測符号化に基づくロボットの認知発達" pp. 222-224
  (Article about "Cognitive development of robots based on predictive coding" pp. 222-224)
  Kindai Kagakusha Co., Ltd. (Published on 2019/12/21)

- メンタルローテーション "回転(ローテーション)脳"を鍛える ("Mental Rotation – Training for Brain Rotation")
  Yuji Ikegaya (Affiliated Faculty)
  Fusosha Publishing Inc. (Published on 2019/6/21)

- 生きているのはなぜだろう。("Why are we living?") (Picture Book)
  Yuji Ikegaya (Affiliated Faculty)
  Hobonichi Co., Ltd. (Published on 2019/5/15)

- 脳はなにげに不公平 パテカトルの万能薬 (文庫版) ("Are brains unfair inadvertently?")
  Yuji Ikegaya (Affiliated Faculty)
  Asahi Shimbun Publications Inc. (Published on 2019/5/13)

- モンテカルロ統計計算 (データサイエンス入門シリーズ) ("Monte Carlo Statistics Methods" – Data Science Introduction Series)
  Fumiyasu Komaki (Affiliated Faculty)

Kodansha Ltd. (Published on 2020/3/27)

- 最適化手法入門 (データサイエンス入門シリーズ) (“Optimization Methods” – Data Science Introduction Series)
  Fumiyasu Komaki (Affiliated Faculty)
  Kodansha Ltd. (Published on 2019/8/31)

- 小児の医療倫理 ケーススタディ (“Case Studies – Medical Ethics for Children)
  Akira Oka (Affiliated Faculty)
  Medical Science International Ltd. (Published on 2020/1/16)

- ADHDと多動性障害~ADHDと多動性障害の臨床像・ 診断評価・治療のハンドブック~ (“ADHD and Hyperactivity Disorder ～Handbook for Clinical, Diagnosis and Treatment～)
  Akira Oka (Affiliated Faculty)
  Nihon Shoni Iji Publications (Published on 2019/4/25)

- ことばと心 (”Language and Consciousness”)
  Kazuo Okanoya (Affiliated Faculty)
  Tamagawa Academy & University Publications (Published on 2019/11/20)

- 本棚から読む平成史 (“History of Heisei Era, Reading from Published Books”)
  Kazuo Okanoya (Affiliated Faculty)
  Kawade Shobo Shinsha Publishers (Published on 2019/6/25)

- チョムスキーと言語脳科学 (インターナショナル新書) (“Chomsky and Neuroscience of Language”)
  Kuniyoshi Sakai (Affiliated Faculty)
  Shueisha International Inc. (Published on 2019/4/5)

- 乳幼児の発達と保育: 食べる・眠る・遊ぶ・繋がる (“Development and Care for Infants: Eat, Sleep, Play and Communicate”)
  Gentaro Taga (Affiliated Faculty)
  Asakura Publishing Co., Ltd. (Published on 2019/8/7)

Appendix 7 FY 2019 List of Project's Media Coverage

* List and describe media coverage (e.g., articles published, programs aired) in FY2019.

	Date	Types of Media (e.g., newspaper, magazine, television)	Description
1	2019/4/4	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"
2	2019/4/8	Asahi Shinbun (website)	**【Takeuchi】** Article includes the explanation about the sensor for human sweat which is developed by Takeuchi "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"
3	2019/4/9	Radio Nikkei (radio)	**【KKasai】** Radio Program about Research of 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）"
4	2019/4/16	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"
5	2019/5/4	Yomiuri Shinbun (newspaper)	**【Aihara】** "AI takes over a designer?"
6	2019/5/27	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"
7	2019/5/29	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"
8	2019/6/3	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"
9	2019/6/3	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"
10	2019/7/11	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"
11	2019/7/14	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"
12	2019/7/18	Financial Times (website)	**【Sugiyama】** "Japan falling behind in artificial intelligence, warns SoftBank founder" (Sugiyama's comment included)
13	2019/7/25	Nikkei Shinbun (website)	**【Okada】** "Nagoya Univ, UTokyo & RIKEN - Develop Photostable Fluorescent Marker for Super-Resolution Live Imaging of the Dynamic Structure of the 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"
14	2019/8/4	Interesting Engineering (website)	**【Hensch】** "AI Algorithm Might Detect Autism Early Using Pupil Dialation, Heart Rate"
15	2019/8/7	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"
16	2019/8/16	Nikkei Sangyo Shinbun (newspaper)	**【Okada】** "Super-Resolution Live Imaging of the Dynamic Structure of the Mitochondrial Cristae" "ミトコンドリア内部生きたまま観察"
17	2019/8/18	Yakuji Nippo (newspaper)	**【Okada】** "Live-Imaging of Cell Structure" "生きたまま細胞の構造観察"
18	2019/8/20	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"
19	2019/9/4	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"
20	2019/9/21	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"
21	2019/9/23	AERA (magazine)	**【Aihara】** Article about AI and Fashion "AIソールは靴ずれ知らず"
22	2019/10/5	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"
23	2019/10/8	robohub (website)	**【Nagai】** "30 women in robotics you need to know about – 2019"
24	2019/10/10	nexus experiments (website)	**【Nagai】** "SARE UND YUKIE NAGAI"
25	2019/10/10	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"
26	2019/11/14	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"
27	2019/11/19	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"
28	2019/11/29	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"
29	2019/12/2	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"
30	2019/12/4	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」
31	2019/12/6	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"
32	2019/12/14	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"
33	2019/12/27	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"
34	2019/12/27	Japan Times (newspaper)	**【Nagai】** "VR builds bridge between staff and young detainees with developmental disorders in Japan"
35	2020/1/27	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"

36	2020/1/30	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"
37	2020/2/13	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"
38	2020/2/19	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"
39	2020/3/13	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"
40	2020/3/20	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=IwAR0ifif44047hxEeYzf52qE1uZDUiPDqXUbiQiWvcb01Rz6icSAHOdz--B4
41	2020/3/22	Jiji Tsushin (website)	**【HKasai】** "Discrimination in Learning in Brain - Delution of Schizophrenia" "脳で訂正機能が低下か　統合失調症の妄想―東大"
42	2020/3/27	Kagaku Shinbun (newspaper)	**【HKasai】** "Elucidation of the Mechanism of Antipsychotics and Delusion" "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"
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