



# *Association of Korean Neuroscientists*



## **3<sup>rd</sup> AKN Research Symposium**

**Rutgers, The State University of New Jersey  
(Busch Campus)**

**August 26-27, 2022**



# Association of Korean Neuroscientists

## General Information

Hotel: Hyatt Regency New Brunswick, 2 Albany St, New Brunswick, NJ

Venue: Chemistry & Chemical Biology Building, 123 Bevier Rd, Piscataway, NJ

### Friday, Aug 26th

7:00-9:00

#### Welcome

Chemistry & Chemical Biology Building, 123 Bevier Rd, Piscataway, NJ

### Saturday, Aug 27th

Chemistry & Chemical Biology Building, 123 Bevier Rd, Piscataway, NJ

8:30-9:00

#### Registration

9:00-9:10

#### Opening

Dr. Daewoo Lee

#### Tong H. Joh Research Innovation Award

10:10-10:20

#### Announcement

Dr. Yongsoo Kim

10:20-10:50

#### Seminar

Dr. Seong Su Kang

"Locus-Coeruleus-induced Tau pathology and Follicle Stimulating Hormone in Alzheimer's Disease"

10:50-12:00

#### Research Presentation (Laboratory Introduction I)

Dr. Mi-Hyeon Jang

12:00-1:00

#### Lunch Break

1:00-2:00

#### Research Presentation (Laboratory Introduction II)

Dr. Alexa Woo

2:30-3:00

#### Coffee Break

3:00-4:30

#### Small Group Meeting

4:30-5:30

#### Post Meeting Discussion Closing & Group Photo

Dr. Yoon-Seong Kim

6:00-8:00

#### Dinner

Keum Ho Garden, 518 Old Post Rd, Edison, NJ 08817

# Research Presentation (Laboratory Introduction I)

Moderated by Dr. Mi-Hyeon Jang

	<b>Name</b>	<b>Affiliation</b>	<b>Topic Area</b>
1	Sunghee Cho	Cornell University	Stroke Brain Injury
2	Heh-In Im	KIST	Alzheimer's Disease Addiction and Depression
3	David Kang	Case Western Reserve University	Alzheimer's Disease Related dementias
4	Alexa Woo	Case Western Reserve University	Alzheimer's Disease Related dementias
5	Un Kang	New York University	Parkinson's Disease
6	Haesun Kim	Rutgers University	TBI and CMT
7	Taewan Kim	Memorial Sloan Kettering Cancer Center	hPSC Parkinson's Disease
8	Y. Hwan Kim	Delaware State University	Parkinson's Disease
9	Yong Kim	Rutgers University	Neurological Psychiatric disorders
10	Yongsoo Kim	Penn State University	Brain-wide network Brain mapping

# Research Presentation (Laboratory Introduction I)

Moderated by Dr. Alexa Woo

	<b>Name</b>	<b>Affiliation</b>	<b>Topic Area</b>
11	Yoon-Seong Kim	Rutgers University	Parkinson's Disease Related dementias
12	Mi-Hyeon Jang	Rutgers University	Aging, Adult neurogenesis
13	Yu shin Kim	UT Health Science Center at San Antonio	Chronic Pain and itch
14	Daewoo Lee	Ohio University	Parkinson's Disease Related dementias
15	KiBum Lee	Rutgers University	CNS injury and repair
16	In-Hyun Park	Yale University	IPSC Brain organoids
17	Youngjin Son	Temple University	CNS regeneration Spinal cord regeneration
18	Sehyoun Yoon	NorthwesternUniversity	Autism



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## Dr. Sunghee Cho

Burke Neurological Institute/Weill Cornell Medicine

### A. Research Interests

My lab investigates neuroimmunology of stroke pathology and repair mechanisms with a focus in translational studies. We specifically address on the role of immune receptor *CD36* that is highly expressed in monocytes/macrophages. Their role on stroke-induced inflammation and injury and how these immune cells interact with a neuronal system to influence stroke outcome and functional benefits are the main subjects.

#### **1. The role of *CD36* in stroke-induced inflammation/injury and recovery**

Since *CD36* is expressed in many different tissues and cell types, including peripheral monocytes/macrophages, we investigate the effect of *CD36* expressed in the peripheral organs including bone marrow, spleen, and blood. The major questions to address in this study are the recognition of peripheral immunity on CNS injury, validating *CD36* as a target in acute pathology, and characterizing a pharmacological agent that modulates *CD36* pathways.

#### **2. Comorbid-modified inflammation and brain injury in stroke**

The recurring failure to translate neuroprotective strategies in animal models into clinical settings prompted us to reevaluate existing preclinical stroke models. One major issue in preclinical studies has been the lack of inclusion of prevalent risk factors in animal models of stroke. We have been addressing this issue by including hyperlipidemia and diabetes, prevalent co-morbid conditions, in our experimental model of stroke. These studies will define if and how these risk factors modify peripheral immunity and influence stroke outcome and functional recovery and provide an importance of the inclusion of comorbidities in animal models of stroke.

#### **3. Stroke recovery mechanism/Genetics**

Because strategies that reduce acute stroke-induced injury and inflammation in preclinical studies have not successfully translated into clinical practice, studies to understand repair/recovery mechanisms that promote functional recovery has been emerged. Genetics is among several factors that influence stroke recovery. We address a role of the BDNF single nucleotide polymorphism (SNP) on stroke recovery, which is common in humans. Using mice that contain the human BDNF SNP variant, we investigate the impact of the BDNF SNP on stroke recovery and underlying event for functional recovery with BDNF SNP carriers, by dissecting structural and molecular plasticity in the brain in chronic stroke.

### B. Major techniques established in the lab.

#### **1. Animal model of stroke**

We generate animal model of stroke using an intraluminal thread method to occlude middle cerebral artery (MCAO). This is the most widely used animal model of stroke that produce injury in the striatum and part of cortex. The model has been used to study the pathology on acute (hours to days) and subacute (days to weeks) period and long-term recovery mechanisms (weeks and up 6 month).

#### **2. Behavior testing on motor/gait function and cognition.**

We have established comprehensive behavior testing modules for motor and cognitive function. The behavior tests include rotarod and gait functions by digitized Nordus Catwalk analyses system for stride length, walk speed, interlimb coordination, swing speed. For cognition, we use an automated system to record noble object recognition, Y-maze, elevated platform for anxiety test, and water maze for hippocampal memory.

#### **3. Flow cytometer determination of immune cell.**

We have established a protocol to isolate immune cells from CNS and periphery in normal and stroked animals. Flow cytometric measurement of immune cell population using 3-laser, 8-channel flow cytometer, this technique has been used to identify specific immune cell populations and sub-populations in the brain and peripheral organs.



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**Heh-In Im, D.V.M., Ph.D.**

**Principal Investigator** Brain Science Institute, KIST

**Visiting scholar** Institute for Neurological Therapeutics at Rutgers

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## **A. Research Interests**

We are very interested in how striatal dysfunction causes various kinds of brain diseases, called striatal dysfunction related diseases (SDD).

The striatum is a fascinating brain region that is known to orchestrate both emotion and cognition. Interestingly, in the event of striatal dysfunction or damage, this may lead to symptoms of anxiety, depression and/or even psychosis. On the other hand, if other regions of the striatum become affected by pathology, then it may cause severe cognitive deficits in neuropsychiatric and neurodegenerative diseases. These symptoms may be elicited collectively and cause other disorders such as addiction. However, the striatal regions nor the particular striatal neurons and molecular targets (e.g. epigenetic regulators) that play a role in these diseases and disorders are not yet clear. Therefore, we would like to do our best to explore the clues found in this phenomenon from the context of “striatal circuits and functions”.

**1. Research about adult striatal neurogenesis in the pathophysiology and treatment of striatal dysfunction related diseases (SDD).** Striatal neurogenesis constitutes the largest portion of adult neurogenesis in the brain, devoted to generation of functional interneurons in both the dorsal and ventral striatum. Our recent data revealed that SYNCRIP, a neuron-enriched RNA-binding protein that preferentially interacts with the mRNA markers of neurogenesis, is predominantly expressed in migrating striatal neural precursors. Through integration of single-nucleus omics and neuroscience techniques, we are investigating the physiological and pathophysiological roles of SYNCRIP in adult striatal neurogenesis.

**2. Cell-type-specific MeCP2 in the striatum in addiction and depression.** Methyl CpG-binding protein 2 (MeCP2) is an epigenetic regulator that binds to DNA and regulates the expression of a target gene. We have identified a decrease in dopamine D2 neuron-specific MeCP2 in the nucleus accumbens (NAc) of mice with cocaine addiction or depression-like symptoms. Using a virus, increasing the cell-type-specific MeCP2 in these mice alleviated symptoms of depression and cocaine addiction. We are investigating these disease-associated genes regulated by MeCP2 in the NAc.

**3. Developing de novo therapeutic striatal targets for Alzheimer’s disease: epigenetic regulation of MeCP2 in the pathogenesis of Alzheimer’s disease.** We recently investigated the mechanism of cognitive decline associated with the increase of MeCP2 in the striatal region of APP/PS1 mice. In addition, by screening small molecules that bind to the methyl-binding domain of MeCP2, novel epigenetic regulator drug candidates controlling the genome occupancy of MeCP2 are being developed.

**4. Study for investigating depression-induced early onset of Alzheimer’s disease through the brain-gut axis.** Depression is one of the most critical risk factors of AD. We have found that depression in amyloid-positive young adult mice can advance the timepoint of AD onset, and depression in normal young adult mice increase the possibility of dementia as they age. Via shotgun metagenomic sequencing, we have identified altered microbiota species that are responsible for depression-induced early onset of AD and dementia in later life.

## **B. Major techniques established in the lab.**

**1. Molecular biology and biochemistry:** qRT-PCR (miRNAs, mRNA from brain, blood, exosomes), miRNA-protein pull-down, HPLC, Western blotting, Immunohistochemistry, Cell culture

**2. Electrophysiology:** Multiple electrode array (MEA), In-vivo single unit recording

### **3. Animal behaviors**

- **(Cocaine/METH/Nicotine/Alcohol) Addiction:** Conditioned place preference, Drug self-administration

- **Depression:** Tail suspension test, Forced swim test, Sucrose preference test

- **Learning & memory:** Novel object recognition, Passive avoidance test, Water cross maze, Y-maze

- **Anxiety:** Elevated plus maze test, Light-dark box test, Marble burying test

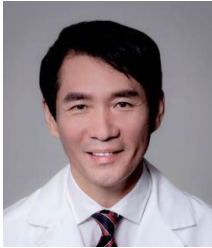
- **Schizophrenia & impulsivity:** Pre-pulse inhibition test, Three chamber test, Delayed discounting task

## **C. Techniques of interest**

Drug delivery technique for brain diseases, In-vitro & in-vivo light-induced gene expression system, single cell / single nucleus multiomics (ATAC+RNA seq), Spatial transcriptomics



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## David E. Kang, PhD

Howard T. Karsner Professor in Pathology  
Department of Pathology Case Western Reserve University  
Department of Pathology, School of Medicine  
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### A. Research Interests

Dr. Kang's research focuses on the molecular pathways underlying aberrant proteinopathy and neurotoxicity in Alzheimer's disease (AD) and Related Dementias (ADRDs), including Frontotemporal dementia (FTD)-Amyotrophic lateral sclerosis (ALS) spectrum disorders and Lewy body disorders (LBD). His laboratory takes an interdisciplinary approach to answer important questions pertinent to pathological brain aging in ADRDs. These include molecular, biochemical, cell biological, advanced imaging, and animal modeling (mouse & *C. elegans*) tools, the latter coupled with electrophysiology and behavior. Multiple proteinopathies arise in ADRDs, such as amyloid and tau in AD, TDP-43 or tau in FTD, TDP-43 in ALS, and alpha-synuclein in LBDs. All ADRDs also exhibit mitochondrial dysfunction and autophagy defects. Our goal is to gain insights from cutting-edge neuroscience investigations to advance translational and therapeutic strategies to treat or prevent ADRDs.

### B. Research Projects and established techniques

**1. Mechanisms of APP processing, A-beta production, and neurotoxicity:** Accumulation of the A-beta peptide, derived from the proteolytic processing of its precursor protein APP, is the primary hallmark of AD pathology. Our focus is on endocytic pathways and F-actin dynamics in regulating both the production of A-beta in neurons and its clearance by microglia. These pathways, particularly the RanBP9-SSH1-cofilin signaling axis, not only regulate the production and clearance of A-beta but also mediate the synergistic neurotoxic signaling between A-beta and tau.

**2. Role of autophagy in ADRDs:** Defects in autophagy and mitophagy, in large part, contribute to the accumulation of misfolded proteins and dysfunctional/toxic mitochondria in ADRDs. Our focus here is in the novel non-canonical role of SSH1 in the negative regulation of the autophagy cargo protein SQSTM-1/p62, an activity recently identified by the Kang lab. This SSH1 activity positively regulates tauopathy. We are also pursuing small molecule SSH1 inhibitors for potential therapeutic application.

**3. CHCHD10-mediated proteinopathy and mitochondrial dysfunction in ADRDs:** More than 30 mutations in the gene coding for the mitochondrial protein CHCHD10 are associated with familial and sporadic FTD-ALS spectrum disorders. Utilizing transgenic mice expressing wild-type or mutant versions of CHCHD10 generated by the Kang lab, we are characterizing novel pathological signatures of CHCHD10 dysfunction in ADRDs.

**4. Deubiquitinases (DUBs) in tau and TDP-43 pathogenesis:** Based on unbiased siRNA screens, the Kang lab has identified pathologically relevant DUBs playing significant roles in both tau and TDP-43 pathogenesis. Utilizing knockout animal models, cell biology, and proteomics, ongoing work aims to unveil mechanisms by which specific DUBs contribute to the pathogenesis of ADRDs. We are also interested in identifying small molecule inhibitors of specific DUBs for potential therapeutic application.

**5. Exosomes as ADRD biomarkers and agents of neurodegeneration:** The Kang lab has embarked on the study of extracellular vesicles (i.e. exosomes) as ADRD biomarkers and agents of neurodegeneration. We are profiling and validating the changes in the proteome of extracellular exosomes in response to AD pathogenic drivers (i.e. A-beta & tau). One of the goals is to identify a panel of brain-derived exosome biomarkers in blood plasma that could be used for the early detection of different ADRDs.

### C. Techniques of interest

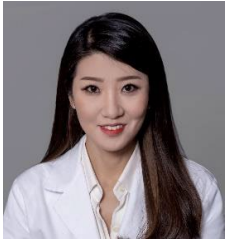
iPSCs, multi-omics, multi-photon imaging, Cryo-EM, Optogenetic tools

### D. NIH study section

CNN, CMND, NOMD, CDIN



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## **JungA 'Alexa' Woo, PhD**

Assistant Professor

Case Western Reserve University Department of Pathology,

School of Medicine

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### **A. Research Interests**

Tau pathology is a prevailing hallmark of Alzheimer's disease and multiple other neurodegenerative diseases. Our research focuses on understanding how beta-arrestins, proteins known to regulate various neuronal signaling receptors, contribute to neurodegeneration in Alzheimer's disease (AD) and related dementias (ADRD). My laboratory first identified beta-arrestin2 to be significantly increased in brains of FTD patients and functions as a key positive regulator of tau pathology. Her team also demonstrated that beta-arrestin2 oligomers but not monomers drive tauopathy in vivo.

### **B. Research Projects and established techniques**

#### **1. Molecular mechanisms and therapeutic targeting of beta-arrestins in ADRDs**

More than 50% of AD patients have comorbidities, including TDP-43 and Lewy body pathologies, which are hallmarks of FTD and PD, respectively. Beta-arrestin1 and beta-arrestin2 are ubiquitously expressed but show the highest expression in brain and spleen. While beta-arrestin1 and beta-arrestin2 share high sequence similarity (78% identical) and show functional overlap, significant differences exist. My lab is interested in further dissecting the molecular mechanisms by which beta-arrestin1 and beta-arrestin2 similarly or differentially drive multiple pathologies in ADRDs. We use interdisciplinary approaches from cell biology of neurons, live-cell imaging of genetically encoded fluorescent reporters, genetic models of AD/ADRD, recombinant AAVs, electrophysiology, and behavior to delve into an unexplored role of beta-arrestins in neurodegeneration in AD and ADRDs. Utilizing these state-of-art techniques, we aim to identify novel molecular insights to beta-arrestin1/2 activity, which enables us to find multiple ways target beta-arrestins to mitigate the pathogenesis in ADRDs. As oligomerized but not monomeric beta-arrestin2 drives tauopathy, one approach my lab is currently undertaking is the identification and characterization of small molecular inhibitors of beta-arrestin oligomerization as a therapeutic approach to mitigate tauopathy and possibly other signature brain pathologies.

#### **2. Mitochondrial protein CHCHD2 in Lewy body disorders**

Rare mutations in the gene coding for the mitochondrial protein CHCHD2 are associated with PD and other Lewy body disorders. Utilizing a multidisciplinary approach in vitro and in vivo, we aim to unveil how pathological CHCHD2 contributes to the pathogenesis of PD and other Lewy body disorders. In collaboration with the David Kang lab, we are also interested in identifying the similarities and differences between pathological CHCHD2 versus its homolog CHCHD10, the latter which is mutated in familial and sporadic FTD and ALS.

### **C. Techniques of interest**

Two-photon imaging, iPSCs, Human neuronal cultures, neural organoids, dopaminergic neuronal culture.

### **D. NIH study section**

CNN, CMND, NOMD, CDIN



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## **Dr. Un Jung Kang**

NYU Grossman School of Medicine

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### **A. Research Interests**

My research focuses on how brain circuitry is perturbed by dopamine loss and produces Parkinson's disease (PD) symptoms and how the compensatory plasticity contributes to the motor complications (including levodopa-induced dyskinesia [LID]) from pharmacological treatment of PD. Specific topics include (1) understanding the striatal circuit plasticity that underlies the long-duration response to dopamine replacement therapy (LDR), which is an ignored, but most beneficial component of the therapeutic effect of dopamine replacement, (2) the contribution of aberrant activity in the basal ganglia output nuclei, the substantia nigra reticulata (SNr) and globus pallidus internus (GPI) to LID, (3) how striatal cholinergic interneurons contribute to motor dysfunction and LID, and (4) the role of the pedunculopontine nuclei in gait abnormalities and freezing in PD. We address these questions at molecular, cellular, and circuit levels in mouse models, emphasizing the contribution of specific types of neurons. I am also interested in the molecular dysfunctions that contribute to neuronal dysfunction and loss in PD and translating this knowledge into PD-specific biomarkers that inform disease pathogenesis. These biomarkers may allow the earlier diagnosis of PD, better monitoring disease progression, and assessment of target engagement in therapeutic trials. Moreover, these studies allow us to understand the heterogeneity in PD pathogenesis, allowing us to better individualize therapeutic approaches. I work with international biomarker consortiums supported by MJFF and NIH for these studies.

### **B. Major techniques established in the lab**

As in C.

### **C. Techniques of Interest**

- Behavioral monitoring in PD rodent models
- Optogenetic and chemogenetic modulation of specific cell types in mouse brain
- In vivo multichannel electrophysiology recording and optic recording in mouse brain
- Single cell transcriptomics of human brain cells
- Biomarkers of human PD biofluids



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## **Haesun A. Kim, Ph.D.**

Professor

Department of Biological Sciences

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### **A. Research Interests**

#### **1. PNS myelination, maintenance, and repair**

One of the goals of my research program to define the mechanisms that underlie myelin abnormalities in the PNS. Using both cellular and animal models for peripheral neuropathies, we focus on understanding the genetic and intracellular signaling mechanisms that modulate Schwann cell myelination and myelin maintenance. Ultimately, we will use this information to design therapies to promote PNS recovery and function in diseases such as Charcot-Marie-Tooth (CMT) diseases, diabetic neuropathy and nerve trauma by promoting myelin repair and preventing myelin loss. Our extensive work on Schwann cells demonstrated an essential role for the external regulators such as growth factors and cell adhesion molecules in Schwann cell differentiation and myelination. We also demonstrated the importance of MAPK kinases in promoting Schwann cell plasticity, de-differentiation and myelin breakdown following PNS injury. We have considerable expertise in using both in vitro and in vivo genetic mouse models to study Schwann cell myelination.

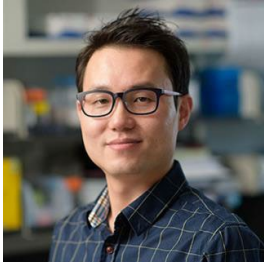
Currently, we are elucidating the role CTL1 (Choline Transporter-Like protein 1) in modulating Schwann cell myelination. We have shown that CTL1 loss in Schwann cells impacts the overall choline metabolism resulting in aberrant myelin formation. To this end, we are currently testing the hypothesis that CTL1 is a Schwann cell choline transporter. We are also investigating the role of choline metabolism in Schwann cell that modulates phospholipid signaling and epigenetic modification that are important for myelination. CTL1 is also highly expressed in oligodendrocytes of the CNS. Using Schwann cell- or oligodendrocyte-specific CTL1 knock out mouse models, we are investigating the role of CTL1 in myelin development, maintenance, and repair.

#### **2. Traumatic brain injury and oligodendrocyte myelin maintenance**

Chronic white matter atrophy or degeneration of myelinated axons is a common occurrence after repeated concussive injury, or mild TBI, which contributes to long-term functional deficits in the patients. In this project, we focus on elucidating the molecular mechanisms that contribute to myelin loss associated with mTBI. Specifically, we are testing the hypothesis that mechanical injury disrupts normal axon-to-oligodendrocyte signaling necessary for maintaining myelin homeostasis in the brain. We use both in vitro myelinated axon stretch injury model and in vivo rodent mTBI models (fluid percussion injury, FPI) to elucidate the signaling mechanism associated with the myelin loss.



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## **Taewan Kim, PhD**

Senior Research Scientist  
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Center for Stem Cell Biology  
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### **A. Research Interests**

Understand the fundamental molecular mechanisms of how cells gain pluripotency and how pluripotent cells are committed to specialized lineages. In particular, I am interested in how such mechanisms drive cell type-specific vulnerability to disease and impact disease initiation and progression. My research further exploits advances in stem cell biology to develop new classes of therapies, which include both drug and cell-based therapies, for debilitating neurodegenerative disease such as Parkinson's disease (PD).

### **B. Research Projects and established techniques**

#### **1. Improved derivation and purification of midbrain dopamine neurons (mDA) from human pluripotent stem cell (hPSC)**

Our first clinical grade mDA differentiation protocols may be sufficient to achieve functional improvement in animal models or even in PD patients. However, current strategies for generating mDA neurons from hPSC remain suboptimal as the final mature mDA neurons that persists often reflect only ~10% of the total cell population after transplantation. Additionally, there are currently no reliable purification methods available to enrich for post-mitotic mDA neurons. Therefore, I am further refining our current mDA differentiation strategy to obtain mDA neurons with improved molecular and functional properties, including more robust expression of EN1 and induction of the A9-related mDA neuron subtype marker ALDH1A1. To develop a sorting method for the routine purification of diverse hPSCs-derived post-mitotic mDA neurons, I have used high-throughput flow-based cell surface marker screen.

#### **2. Increased post-mitotic mDA neuron survival in vivo after transplantation**

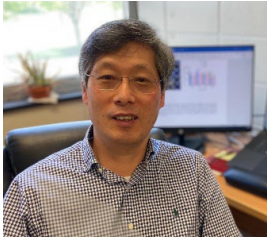
Another important challenge for cell-based therapy to PD patients is the limited cell survival of mDA neurons (~10% of grafted cells) after transplantation, which can cause variations in effective cell dosing and complicate the routine application of this technology for cell-based therapy. Thus, I have used in vivo CRISPR/Cas9 based loss-of-function (LOF) screen in purified mDA neurons to identify key restriction factors that limit in vivo survival of post-mitotic mDA neurons. Targeting those restriction factors and their upstream regulators will enable us to dramatically improve in vivo mDA neuron survival and provides important insights in the mechanism controlling cell survival post grafting.

### **C. Techniques of interest**

Two-photon imaging, Single-cell RNA/ATAC seq analysis, Proteomics, Metabolomics



# Association of Korean Neuroscientists



## **Y. Hwan Kim,**

Professor in dept of Biological Sci at Delaware State University

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### **A. Research Interests**

**1. Targeting cellular senescence markers for therapeutic intervention in PD pathology:** Our recent publication in collaboration with the Ko lab at Johns Hopkins suggests that  $\alpha$ -syn preformed fibrils (PFF)-induced pathology could lead to astrocyte and/or microglia senescence in PD brains, which may contribute to neuropathology in this model (Verma et al., 2021). Targeting senescent cells using senolytics could therefore constitute a viable therapeutic option for the treatment of PD. As a follow-up study, we test the hypothesis that cellular senescence processes result in the failure of maintaining the homeostasis in dopamine neurons or surrounding astrocytes/microglia, which is associated with PD pathology. With measuring the levels of senescence markers in the PD-related regions including the striatum and Substantia nigra from PFF-injected PD mouse model or human PD brains, we can determine the effects of cellular senescence in inducing dopaminergic neuronal loss and PD pathology and verify the validity of using senolytics in halting PD pathology. This study will allow us to understand the senescence aspects of neuropathology of PD, which may reveal potentially new therapeutic targets using senolytics for preventing neurodegeneration including PD.

**2. Oxidative stress increases the levels of deSUMOylation in PD related proteins for inducing PD pathology:** We turned our efforts to determine if higher levels of SUMO proteases (SENPs) play a critical role in inducing pathological conditions in the striatum and midbrain from human PD tissues, compared to age-matched normal brains. We found that the level of SENP1 in human PD patient brains was higher than that in age-matched controls (a manuscript in prep). Thus, we set up a hypothesis that SENP1 level and/or activity is stimulated by oxidative stress, which is a part of pathological mechanisms of PD. Our preliminary results demonstrated that MPTP- or PFF-induced oxidative stress removes SUMO1 from  $\alpha$ -synuclein in mouse striatum and midbrain, while SUMO conjugase, Ubc9 overexpression-mediated SUMOylation protects the dopaminergic neurons in the striatum and Substantia Nigra against the toxicities (Verma et al., eNeuro, 2020). In addition, we found that SENP1 inhibition protects dopaminergic neurons in the striatum and SNc in PFF-injected mice. We also expect to see that higher levels of SENP1 in the Lewy bodies than those in normal brainstem tissues. This approach will help us determine if stimulating SENP1 is related to induce the PD pathology in the human and mouse brains and blocking SUMO1 removal by SENP1 inhibition can be a novel therapeutic target in PD pathology.

**3. Assessing regulatory roles of SUMOylation in DAT, alpha-synuclein, and LRRK2 in Parkinson's disease pathology.**

**4. Developing neuroprotective compounds as potential therapeutics in Parkinson's disease mouse models.**

**5. Developing a combination therapy for halting PD pathology and identifying a biomarker from human PD patients' saliva.**

### **B. Common Lab techniques:**

Western blot, qRT-PCR, cell viability/cytotoxicity assays (MTT & LDH), ELISA, protein activity assays (including DAT, HAT & HDAC), ROS measurements, Protein aggregation (Thioflavin T) assay, primary neuron/astrocytes/microglia culture, microarray, Immunoprecipitation, immunohistochemistry, confocal microscopy, stereology, and Mass Spectrometry & MS imaging (collaboration).

### **C. Techniques of Interest**

Mass-Spectrometry brain imaging (Bruker), single-cell Seq or MS, and midbrain-derived organoids culture.

### **D. NIH Study section**

CMND, CDIN and NOMD.



# Association of Korean Neuroscientists



## Yong Kim, PhD

Associate Professor, Department of Neurosurgery

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### A. Research Interests

My lab is interested in the molecular and cellular compensatory mechanisms by which brain cells maintain homeostasis following exposure to brain injury or risk factors related to neurodegenerative or psychiatric disorders. Our long-term goal is to understand how brain-cell-type-specific natural compensatory mechanisms are altered in disorder conditions for the purpose of finding novel disease mechanisms and promising therapeutic targets or biomarkers.

**1. Ahnak pathways in endothelial cells and blood-brain barrier regulation.** Previously, we found Ahnak protein as one of key molecular factors regulating depression-like behavior or antidepressant actions. We have also found that chronic stress-induced divergent alterations of Ahnak in the brain are a critical determinant of behavioral susceptibility or resilience to chronic stress. Ahnak is highly expressed in cerebrovascular endothelial cells. The goal of current research is to find downstream molecules and pathways of Ahnak in endothelial cells and understand how Ahnak-mediated pathways in endothelial cells regulate transcytosis in the blood-brain barrier, neuronal circuit activities and depression or anxiety like behavior.

**2. Role of actin regulators in homeostatic control of neuronal activity and survival.** Initially, we discovered the heteropentameric WAVE1 protein complex as a binding partner of cyclin-dependent kinase 5. Our previous studies established WAVE1, a key component of the protein complex, as a neuronal activity-dependent regulator of actin polymerization in the brain. We have also suggested that a reduction of WAVE1 expression observed in Alzheimer's disease (AD) brains is a critical part of cellular compensatory mechanism to control amyloid  $\beta$  production. We are currently investigating the role of WAVE1 in Golgi-endosome-lysosomal dysfunction in AD mouse models and testing beneficial or detrimental effects of reduction or enhancement of WAVE1 function on tau or AD-relevant pathological features using human iPSCs-derived neuronal models and WAVE1 knockout or knock-in mouse models.

**3. Molecular and cellular pathways mediating comorbidities in neurological and psychiatric disorders.** Depression is the most common comorbid condition of epilepsy. Our previous studies indicate that parvalbumin (PV)-expressing GABAergic interneuron is a pivotal node controlling chronic stress-induced depression-like behavior. Alterations of PV interneurons are highly implicated in epilepsy as well. We have developed several PV interneuron-selective knockout mouse lines for depression research. We are currently using them as a tool to study common molecular pathways mediating epileptic seizures and depression comorbidities.

### B. Major techniques established in the lab:

**1. Translating Ribosome Affinity Purification (TRAP)/RNA-seq:** We have established parvalbumin expressing interneuron-selective TRAP/RNA-seq technique and endothelial cell-specific TRAP/RNA-seq technique to isolate and sequence cell-type-specific translating mRNAs in brain tissues.

**2. Multi-step in vitro fertilization and embryo transfer technique:** We are using various transgenic lines for the studies of key molecular factors in particular brain cell types. As a collaboration with the Genome Editing Shared Resource (GESR) facility at Rutgers, we are using multi-step in vitro fertilization (IVF) together with embryo transfer (ET) to surrogates in order to rapidly cross multiple transgenic lines and produce sufficient number of experimental mice with a minimal number of breeding cages. Multi-step IVF/ET circumvents fluctuations of breeding conditions and tedious work for the maintenance of breeding cages, uneven dates of birth of pups, and influence by any altered motherhood due to a phenotype of transgenic female mice. Fertilized embryos at any step can be cryopreserved and recovered for future experiments.

**C. Techniques of Interest**

Mass-Spectrometry brain imaging (Bruker), single-cell Seq or MS, and midbrain-derived organoids culture.

**D. NIH Study section**

CMND, CDIN and NOMD.



# *Association of Korean Neuroscientists*

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## **Dr. Yongsoo Kim**

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College of Medicine  
The Pennsylvania State University.  
Lab website: <https://kimlab.io/>

### **A. Research Interests**

Our main research interest focuses on understanding anatomical and functional organizational principle of different cell types in the brain in order to support normal cognitive function and its changes in brain disorders such as autism and Alzheimer's disease. The unique challenge to understand governing principles of the mammalian brain is that microscopic structures (e.g., cell bodies, axon) interact each other in macroscopic network (e.g., whole brain) to generate behavior. To overcome the challenge, we have been developing high-resolution 3D brain mapping methods to image and quantify fluorescently labeled neuronal and non-neuronal cell types as well as cerebrovasculature in the entire mouse brain, and their changes across the lifetime.

### **B. Major techniques established in the lab:**

To complement our anatomical mapping, we utilize many systems neuroscience tools (e.g., in vivo neural activity recording) to gain functional significance of specific cell types in a given circuit. Our current projects include oxytocin system mapping in the context of social behavior, neurovascular mapping linked with aging, and creating new digital 3D atlases of developing mouse brains. Leveraging our novel approaches, we strive to understand cell type specific organization of the nervous system to support cognitive functions



# Association of Korean Neuroscientists



## Dr. Yoon-Seong Kim

Institute for Neurological Therapeutics at Rutgers

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### A. Research Interests

- 1. The role of NADPH oxidases (NOXs)-mediated oxidative stress in the pathogenesis of Parkinson's disease.** In addition to mitochondria, we have identified NADPH oxidase 1 (NOX1) as a molecular source of ROS which is responsible for dopaminergic neuronal death. NOX1 is highly expressed in the intestinal epithelium, from where recent accumulating evidence suggests that  $\alpha$ -SYN aggregates progressively propagate to the brain parenchyma. Using Nox1 null mice, we are investigating gut microbiome-Nox1 activation- $\alpha$ -SYN pathogenesis axis in PD.
- 2. Contribution of transcriptional mutagenesis of oxidative DNA lesions to generating new mutant  $\alpha$ -SYN species and aggregation.** We have recently discovered that 8-oxo-dG, the most frequent oxidative DNA lesion, can generate mutant  $\alpha$ -SYN species by the intriguing mechanism called transcriptional mutagenesis. These mutant  $\alpha$ -SYN mRNA species were more frequently observed in the *substantia nigra* of PD patients compared to normal subjects. We are investigating how these mutant species contribute to the alpha-synucleinopathy.
- 3. Pum2-mediated translational regulation of alpha-synuclein mRNA on the outer surface of mitochondria.** Interplay between mitochondria and  $\alpha$ -SYN has been widely documented yet without clear molecular mechanism. We have found that  $\alpha$ -SYN mRNA is localized to the outer surface of mitochondria and its translation is initiated upon stimuli causing mitochondrial ROS. We have identified that Pum2, a translational repressor, binds to the 3'UTR of  $\alpha$ -SYN mRNA and it is released upon mitochondrial ROS, allowing translational initiation of  $\alpha$ -SYN near mitochondria. We are investigating the role of translational control of  $\alpha$ -SYN near mitochondria.
- 4. Chromatin landscape and epigenetic regulation of  $\alpha$ -SYN in PD.** In human, the  $\alpha$ -SYN gene (*SNCA*) contains high CpG rich region around transcription start site. We have found that CpGs in this region of dopaminergic neurons and human brain tissue are largely unmethylated in both control and PD conditions. Histone marks, however, demonstrate significant differences between them with for example much higher H3K4me3 levels in PD, supporting elevated  $\alpha$ -SYN levels. To modulate epigenetic marks in a precise target-specific manner, a CRISPR/dCas9-Suntag technique has been developed.

### B. Major techniques established in the lab

- 1. Multiomic analysis using single nuclei RNA-seq and snATAC-seq of postmortem brain.** We established this technique to investigate cell-type-specific transcriptomic and epigenomic profiles of single nuclei obtained from postmortem brain samples.
- 2. The CRISPR/dCas9-Suntag based target-specific epigenetic modifiers.** We recently established ten epigenetic modifying enzymes that modulate major histone marks including H3K4me3, H3K27me3, H3K9ac, H3K27ac and DNA methylation using CRISPR/dCas9-Suntag system. This epigenetic tool kit allows target-specific modulations of each genomic loci. In conjunction with sgRNA library spreading over the entire genome, this innovative technique can be applied to the identification of specific genes whose epigenetic modulations are critical for various disease conditions.
- 3. Single-molecule fluorescence in situ hybridization (smFISH) with human brain clearing technique.** To overcome strong auto-fluorescence from human brain tissue, especially dopaminergic neurons due to neuromelanin, we have established the technique to clear proteins/lipids after RNA-anchoring/gel embedding, enabling clear visualization of a single RNA. Together with the expansion microscope technique, subcellular localization of single RNA molecule can be visualized.



# Association of Korean Neuroscientists



## **Mi-Hyeon Jang, PhD**

Associate Professor Department of Neurosurgery  
Robert Wood Johnson Medical School  
Core Member, Brain Health Institute  
Full Member, Cancer Institute of New Jersey  
Rutgers, The State University of New Jersey  
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### **A. Research Interests**

My research is focused on investigating neurogenesis in the adult brain. Adult neurogenesis in the hippocampus is the process of generating functionally integrated neurons from neural stem cells (NSCs) for maintaining hippocampal function including learning and memory. Given that abnormalities in neurogenesis are thought to underlie the pathogenesis of synaptic and cognitive dysfunction, the ability to sustain or promote neurogenic processes holds significant implications for a broad range of brain disorders and future regenerative therapies.

### **B. Research Projects and established techniques**

#### **1. A new role for *BubR1* in brain aging:**

Aging is the most significant suppressor of adult hippocampal neurogenesis, synaptic plasticity and cognitive function. Given that *BubR1* expression in the brain is markedly reduced with aging, we sought to explore the impact of *BubR1* insufficiency in neurogenesis and cognitive function. Using adult- and dentate gyrus-specific *BubR1* knockdown and *BubR1*<sup>H/H</sup> mice, we identified a vital function of *BubR1* in controlling neurogenesis, dendrite morphogenesis of adult-born neurons, and mood and memory function. Strikingly, *BubR1* insufficiency accelerates age-dependent declines in neurogenesis, while a high level of *BubR1* promotes neurogenesis in aged mice. These novel discoveries for *BubR1* in maintaining normal hippocampal function may provide a genetic entry point to understand age-related changes in cognitive function.

#### **2. Targeting *Nampt*-mediated *NAD*<sup>+</sup> metabolic pathway as a therapeutic strategy for chemobrain:**

Chemotherapy-induced cognitive dysfunction (chemobrain) negatively impacts cancer survivors and has emerged as a significant medical problem. Using cisplatin as a model system for chemobrain, our group demonstrated that cisplatin causes impairments in adult hippocampal neurogenesis and prolonged cognitive function in mice. Mechanistically, such adverse cellular and behavioral effects of cisplatin are due to disruption of the nicotinamide phosphoribosyl transferase (*Nampt*)-mediated *NAD*<sup>+</sup> metabolic pathway, which is rescued via increasing *Nampt* and *NAD*<sup>+</sup> levels through the conditional mouse genetic and the dietary supplement NMN (nicotinamide mononucleotide, a *NAD*<sup>+</sup> precursor), respectively. Collectively, our results strongly suggest targeting *Nampt*-mediated *NAD*<sup>+</sup> metabolic pathway may serve as an effective new regenerative strategy for preventing chemobrain.

### **C. Techniques of interest**

Ca<sup>2+</sup> imaging, Electrophysiology, Single-cell RNA seq, ATAC-seq, Metabolomics



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## Dr. Yu Shin Kim,

University of Texas Health Science Center at San Antonio  
(UTHSA)

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### A. Research Interests

Our research focuses on the function and regulation of sensory modalities including pain, itch, and gentle touch. Special objectives in our research are to understand the cellular and molecular mechanisms of pain by studying neural circuit activities evoked by pain in basal and disease conditions. Inflammation and nerve injury can result in chronic pain that can seriously challenge daily activities. Pain is mainly mediated by a subset of primary sensory neurons known as nociceptors in Dorsal Root Ganglia (DRG) and Trigeminal Ganglia (TG). How DRG neurons function at a population level under physiological and pathological conditions is not known. Therefore, monitoring the activities of primary nociceptive neurons and axons is crucial to understanding pain mechanisms. Our research projects include **1)** identifying novel plasticity mechanisms underlying the transition from acute to chronic pain, **2)** examining the mechanism of Temporomandibular joint disorders (TMD), **3)** determining the mechanism of ongoing and evoked pain, **4)** characterizing the contributions of central terminal hypersensitivity of DRG neurons to chronic pain, and **5)** uncovering the mechanisms by which damages in skin nerve terminals contributes to chronic pain conditions **6)** mechanism of chemotherapy-induced peripheral neuropathy **7)** mechanism of incisional pain **8)** alcohol-associated headache mechanism **9)** mechanism of aging and learning and memory.

### B. Major techniques established in the lab

**1. In vivo Ca<sup>2+</sup>, cAMP and voltage sensing imaging in primary sensory and spinal cord cells, dura mater, brain (neurons, glia, immune cells).** The mechanisms by which heterogeneous primary sensory neurons encode different somatosensory inputs remains unclear. In vivo intact dorsal root ganglia (DRG) imaging using genetically encoded Ca<sup>2+</sup> indicators (GECIs) using **GCaMP** stands out among the available methodologic advances providing an unprecedented spatial and populational resolution with simultaneous imaging of in vivo TG (>2800 neurons/TG), dura mater, and DRG (>1800 neurons/DRG) in live mice. Additionally, genetically encoded voltage indicators (GEVIs) that reveal subthreshold electrical activity and resolve fast spike timing with subcellular resolution offer numerous advantages during in vivo potential imaging with high temporal resolution. The **ASAP4** or **Marina** is sufficiently bright and fast enough to optically characterize individual neuron coding dynamics. Finally, we found that a combination of cAMP sensor, **Pinkflamingo** imaging with other sensor imaging such as GCaMP or ASAP4 empowered in vivo optical studies of sensory signal processing and integration mechanisms with optimal spatiotemporal analysis.

**2. In vivo imaging of different types of cells in primary sensory, spinal cord, and brain in freely moving animals.** We established in vivo imaging in freely moving animals using miniscope and small sensor imaging.

**3. Electrophysiologic recording in primary sensory neuron in culture and in situ and spinal cord slice.** We perform intra and extracellular electrophysiologic recording in culture, in situ sensory tissue and spinal cord.

**4. Mouse genetics, behavioral assays (pain & learning and memory), viral-mediated cell transformation and transduction.** We developed specific promoter site to generate mouse KI/KO transgenic mice lines. We perform pain & other learning and memory live animal behavioral assays associated with viral-mediated cell transformation and transduction.

### C. Techniques of Interest

High-Throughput Screening of small molecule libraries, Methods to identify and optimize small molecules interacting with proteins or RNAs, RNAScope, Multielectrode array for neural activity.

### D. NIH Study section

NPI, SAT, NRTC, Heal Initiative,



# Association of Korean Neuroscientists



**Dr. Daewoo Lee,**  
Neuroscience Program, Dept. of Biological Sciences,  
Ohio University  
Email: leed1@ohio.edu

## A. Research Interests

Our Main Research Interest is to understand pathogenic mechanisms underlying neurodegenerative diseases (NDs). In particular, we are interested in prion-like propagation of pathogenic proteins such as  $\alpha$ -Synuclein ( $\alpha$ -Syn) and microtubule associated protein tau (MAPT).

**1. Cell-to-cell propagation of  $\alpha$ -Syn:** Abundant neuronal protein  $\alpha$ -Syn is a pathogenic protein to form abnormal protein aggregates, called Lewy body (LB) and causes several NDs including Parkinson's disease and LB dementia (LBD). Prion-like spreading of  $\alpha$ -Syn is an exciting new discovery in the progression of NDs. However, there are critical gaps in our understanding of  $\alpha$ -Syn spreading. We study how  $\alpha$ -Syn is released, taken up, and thus spreads between neurons. We are particularly interested in  $\alpha$ -Syn released by neuronal activity as known PD risk factors such as traumatic brain injury (TBI) and sleep deprivation increase neuronal activity and levels of extracellular  $\alpha$ -Syn. In addition, hyperexcitability and seizures are known to be associated with pathological progression of LBD. Our goal is to study how neuronal subtypes,  $\alpha$ -Syn mutants, and functional/molecular factors affect pathological transmission of  $\alpha$ -Syn.

**2. Mechanisms underlying activity-dependent human tau release:** Tau is an intracellular protein but also released to the extracellular fluid. Studies have shown that a prion-like mechanism involving the transfer of hyperphosphorylated tau between synaptically connected neurons underlies the seeding and spread of tau pathology throughout the brain. Interestingly, neuronal excitability increases during the early stages of AD and tau release can be enhanced by the excitability. A better understanding of activity-dependent tau release is a key to uncover mechanisms underlying cell-to-cell propagation of tau. It is not known the role of phosphorylation in activity-dependent tau release and proteins interacting with tau have yet to be identified for their role in mediating tau release. We have developed a tractable and highly reproducible method of studying activity-dependent tau release in *Drosophila* primary neuronal culture & neuromuscular junction, and a human neural progenitor cell line (ReNcell), which form the experimental framework of this study. Optogenetic method has been also used to induce activity-dependent tau release.

**3. Dopamine signaling and Parkinson's disease:** We have studied neurodegenerative and neuroprotective role of dopamine signaling in PD. Dysregulation of dopamine homeostasis causes selective neurodegeneration while activation of D2 receptors is neuroprotective.

**4. Biogenic amine signaling and olfactory learning:** The main goal of this project is to investigate functional role of dopamine and serotonin receptors in synaptic plasticity and olfactory learning. We also study their downstream G-protein signaling mechanisms and the role of DA autoreceptors in modulating excitability and synaptic inputs.

## B. Major techniques established in the lab

Electrophysiology (patch clamp, amperometry), Primary neuronal culture, Human neural cell line (ReNCell), Cellular imaging/analysis, Western blot. ELISA, Confocal microscopy, Optogenetics & chemogenetics, *Drosophila* genetics (mutant & transgenic approaches), Behavioral assays (learning & locomotion)

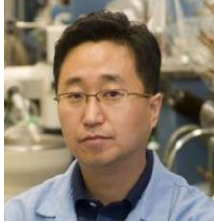
## C. Techniques of Interest:

Protein Interactome, APEX Proximity Labeling, NGS/RNA-Seq.

**D. NIH Study section:** CMND, SYN



# Association of Korean Neuroscientists



## Dr. KiBum Lee

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### A. Research Interests

#### **1. Promoting Axonal Regeneration in the injured CNS using a Non-viral Gene Manipulation method.**

Given the intrinsically limited regenerative potential of the central nervous system (CNS) and the complex inhibitory environment, there is an urgent need for effective strategies towards robust axon regeneration and neurite outgrowth of neurons to re-establish the damaged neural circuitry. In this project, we plan to integrate several fields of research, Nanotechnology, Biomaterials, Chemical Biology, Neuroscience, and Stem Cell Biology, to develop a novel nanomaterial-based platform that induces axon regeneration and neurite outgrowth, which are safe, effective, and innovative for in vivo transplantation and potential clinical applications.

#### **2. In Vivo Cell Reprogramming of Reactive Astrocytes into Neurons for Enhancing CNS Repair.**

Reactive astrogliosis has been considered a major hurdle in the recovery after CNS injuries. Reactive astrocytes can, therefore, be a good target for therapy to both suppress the secondary injury as well as provide a means of neuron replacement therapy. To this end, we are developing a non-viral transcription factor (TF) method to in vivo reprogram reactive astrocytes to neurons.

**3. Advanced Stem Cell Therapies for CNS injuries and Advanced in vivo Drug/Gene Delivery using Bioinspired Hybrid Nanoscaffolds.** Stem cell transplantation, as a promising treatment for central nervous system (CNS) diseases, has been hampered by crucial issues such as low cell survival rates, incomplete differentiation, and limited neurite outgrowth in vivo. We designed and developed a biodegradable hybrid inorganic (BHI) nanoscaffold-based method to improve the transplantation of human patient-derived neural stem cells (NSCs) and to control the differentiation of transplanted NSCs in a highly selective and efficient way. [Nature Communications, 2018]. The development and the use of biomaterials for stem cell-based tissue engineering to treat CNS diseases/injuries to date have focused on: (i) providing favorable microenvironments for endogenous and exogenous cellular regeneration and (ii) serving as a spatiotemporally controlled drug release platform to regulate pro-neuroregenerative signaling pathways. In summary, our work [Nature Communications, 2018] is based on the development of a biodegradable hybrid inorganic nanoscaffold and its utilization for the enhanced transplantation of stem cells into SCI sites. Our demonstrated nanoscaffold technology platform [Advanced Materials, 2021] can further be combined with other neurogenic drugs, as well as stem cell therapeutic efforts currently in development.

### B. Major techniques established in the lab

1. Nanoparticle-based Artificial Transcription Factor (NanoScript) for Effective Gene Regulation in Cellular Reprogramming.
2. Integrating Epigenetic Modulators into Non-viral gene delivery.
3. Nanotechnology Approaches to Advance CRISPR-Cas-based Gene Therapies.
4. Developing hybrid RNAi-Nanoparticle-based gene therapy to enhance cellular reprogramming in vivo: We are developing a novel platform technology to design and synthesize RNAi (siRNA) nanoparticles using the rolling circle transcription (RCT) process. The key concept of this method is to develop a naturally biodegradable multigene regulator by integrating several different types of RNAi approaches (dsRNA and ssRNA) onto a single nanoplatform to control a transcriptional cascade for the targeted cell reprogramming.

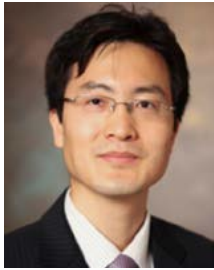
### C. Techniques of Interest:

MEA/NEA for neural activity, In Vivo Molecular Imaging, and Gene/Drug Delivery



# Association of Korean Neuroscientists

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**Dr. In-Hyun Park,**  
Associate Professor of Genetics,  
Yale Stem Cell Center  
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## **A. Research Interests**

My research interest is to use human pluripotent stem cells (hPSCs) to investigate the human brain development and diseases.

### **1. Generation of human brain organoids.**

We established methods to generate human dorsal or ventral cortical forebrain regions. These methods are useful to study human cortical development and developmental disorders.

### **2. Investigate the function of MeCP2**

We engineered human embryonic stem cells (hESC) to introduce mutations in MeCP2 gene. These hESCs are useful to study Rett syndrome.

### **3. Investigate the X chromosome status in human pluripotent stem cells.**

MeCP2 is present on X chromosome. In hESC, X chromosome status is unstable. My lab investigates X chromosome status in hESC and iPSCs.

### **4. Study the mechanism of epigenetic reprogramming**

My lab also investigates how human or murine somatic cell reprogramming is established at epigenetic level.

## **B. Major techniques established in the lab**

The followings are major techniques established in my lab.

### **1. Differentiation of hESCs into neuronal cells and brain organoids**

We use hESC and can differentiate neuronal lineages.

### **2. Genomics tools.**

We perform and analyze RNA-seq, ChIP-seq, ATAC-seq, RRBS, and HiC, and use the data to study transcriptome, epigenome, and global chromatin status.

### **3. scRNA-seq**

My lab can perform and analyze the scRNA-seq using 10XGenomics of Chromium.



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## **Dr. Young-Jin Son,**

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Lewis Katz School of Medicine at Temple University,  
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### **SPINAL CORD AND PERIPHERAL NERVE REGENERATION**

The long-term goals of my research are to elucidate the mechanisms that govern maintenance and regeneration of synaptic connections in the spinal cord and muscle, particularly those associated with glial cells, and to use this knowledge to promote repair of spinal cord-muscle connections in patients with injury, disease, disuse or aging.

#### **A. Research projects (current)**

##### ***1. Oligodendrocyte progenitor cells as a novel inhibitor of CNS regeneration.***

We are testing if Dorsal root axons fail to regenerate into the spinal cord by forming aberrant synapses with OPCs (or NG2 glia).

##### ***2. Coactivation of BRAF and mTOR signaling to promote spinal cord regeneration.***

We have found that concurrent activation of BRAF and inhibition of PTEN induces unprecedented robust regeneration of dorsal root axons into the spinal cord after dorsal root injury. We are extending the finding to test further the strategy can lead to robust regeneration of primary sensory axons after direct SCI.

##### ***3. Novel Spinal cord ischemic stroke induced by spinal root injury.***

We are studying unexpectedly robust ischemic damage dorsal root injury can elicit in the spinal cord and related mechanisms.

##### ***4. Role of YAP and TAZ in Schwann cell myelination and nerve repair.***

We are studying the roles of Hippo signaling and the oncoproteins, YAP/TAZ in the development and maintenance of peripheral nerve myelination, Schwann cell plasticity and nerve repair.

##### ***5. Enhancing peripheral nerve regeneration.***

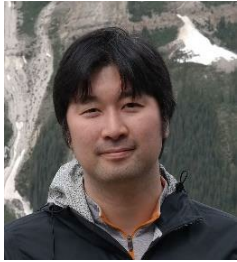
We are manipulating BRAF, PTEN, ErbB2 signaling in motor and sensory axons, and/or Schwann cells to facilitate nerve regeneration after peripheral nerve injury (proximal and chronic injury models).

#### **B. Research methods**

We primarily use mouse to study these projects. Our techniques include transgenic and knockout mice, cell type specific conditional and inducible gene or cell manipulation, in vivo time-lapse imaging, TEM, mouse microsurgery for spinal cord and DRG neurons, virus injection and transduction of DRG and sciatic nerve (AAV and lentivirus), tissue clearing, in vitro co-culture of DRG neurons, OPCs, and/or Schwann cells, and other standard molecular, cellular, and behavioral analyses.



# Association of Korean Neuroscientists



## Sehyoun Yoon, PhD

Research Assistant Professor

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### A. Research Interests

Changes in spine number and morphology, along with the glutamate receptor content of synapses, contribute to functional connectivity in synaptic circuits. Altered spine density in cortical pyramidal neurons has been observed in postmortem studies of patients with schizophrenia (SZ), bipolar disorder (BD), autism spectrum disorder (ASD), and intellectual disability (ID). Recent genome-wide association, whole-genome sequencing, and whole-exome sequencing studies have extensively highlighted genes encoding for ankyrins, ANK3, ANK2, in the neurodevelopmental and psychiatric disorders, ID, ASD, ADHD, SZ, and BD. While conventionally AnkG and -B have been seen as playing roles mainly at the axon initial segment, the mechanisms by which it promotes dendritic spine stability and its global function in maintaining the synaptic proteome have not yet been fully investigated. Recently I have found the homeostatic regulation of ankyrin repeat domain-containing proteins by Usp9X, and occurred in response to TGF $\beta$ , as upstream signaling. Also, the postsynaptic role of ankyrin-G and Homer1b/c and DAGL $\alpha$  interaction had been reported.

### B. Research Projects and established techniques

#### 1. *Molecular Mechanisms of USP9X in Neurodevelopment and Autism*

One major challenge for research into ASD and ID is that the causes of these disorders are extremely heterogeneous. Genetic heterogeneity makes personalized medicine development and clinical trial design difficult. However, a solution may be to target genetically defined subgroups by understanding and manipulating the etiological mechanisms for specific high-risk genes and syndromic factors. Recent studies support a role in dysregulation of the ubiquitin system pathway in ID and ASD, suggesting that protein turnover may play an essential role in neurodevelopmental disorders (NDDs). USP9X is a deubiquitylating enzyme with relatively narrow substrate specificity, which displays an extraordinarily high level of sequence conservation from *Drosophila* to mammals. Little is known about how synaptic targets of USP9X and deubiquitylation of synaptic proteome affect synaptic plasticity and contribute to NDD pathogenesis. Altered synapses are believed to cause changes in the activity of neuronal circuits, which ultimately drive impaired behaviors in ASDs. Understanding the underlying USP9X mechanisms that cause alterations in synaptic protein composition and function in ASDs offers a significant advancement toward the identification of new targets for effective drug therapy.

#### 2. *Molecular Mechanism of Ankyrin-B in Autism Spectrum Disorder*

According to a Centers for Disease Control and Prevention report, 1 in 44 children in the US have been diagnosed with autism spectrum disorders (ASDs). Among over 1,200 risk genes from the Simons Foundation Autism Research Initiative (SFARI), ANK2 (encoding ankyrin-B; AnkB) is specifically interesting because mutations resulting in an ASD diagnosis are mostly non-syndromic and are less compatible with intellectual ability. I will investigate how AnkB affects the expression of other genes and their proteins to alter the synaptic function and cause behavioral disturbances. To accomplish these goals, I will use conditional knockout mice, behavioral analyses, neuroproteomics, bioinformatics, and calcium imaging with two-photon microscopy, to investigate the synaptic functions of AnkB's protein partners in the dendrite. From our results, we may determine how disrupted synaptic transmission affects abnormal social behaviors and understand the protein networks that drive a key pathological ASD mechanism. Furthermore, future therapeutic targeting of these newly identified protein networks may provide a new and effective strategy for individual ASD patients.



### **3rd AKN Research Symposium Committee**

- Dr. Yoon-Seong Kim at Rutgers University (Chair)
- Dr. Mi-Hyeon Jang at Rutgers University (Co-chair)
- Dr. Alexa Woo at Case Western Reserve University
- Dr. Yongsoo Kim at Penn State University
- Dr. Daewoo Lee at Ohio University (President)