BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Jang, Mi-Hyeon

eRA COMMONS USER NAME (credential, e.g., agency login): mjang2

POSITION TITLE: Associate Professor of Neurosurgery at Rutgers University

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Chungbuk National University, South Korea	BS	02/2000	Earth and Environmental Science
Kyung Hee University, South Korea	MS	02/2003	Physiology
Kyung Hee University, South Korea	PhD	02/2005	Physiology
Johns Hopkins University, Institute for Cell Engineering, Baltimore, MD, USA	Post-doc	02/2011	Regenerative Neurobiology

Personal Statement

The focus of research in my laboratory is to understand the underlying neurobiological mechanisms that promote regenerative processes of adult neurogenesis, oligodendrogenesis and remyelination (Jang et al., 2013, *Cell Stem Cell*; Ma et al., 2009, *Science;* Faulkner et al., 2008*, PNAS*). Ultimately, we hope to discover novel regenerative strategies for improving cognitive function in the context of brain aging (Choi et al., 2016, *Aging*, Yang et al., 2017, *Aging Cell*, Cho et al., 2018 *Aging Cell*;).

Building on my earlier work in brain aging, my laboratory pursues a new direction focused on chemobrain (chemotherapy-induced cognitive impairment; CICI), which resembles the accelerated brain aging process. Given that multiple molecular pathways contribute to the pathogenesis of CICI, the ***overarching goal*** of my research program is to uncover the molecular contributors driving CICI to direct development of rationally designed synergistic "*disease-modifying therapeutic strategies*" to ameliorate CICI, thus ultimately improving quality of life for cancer survivors. My laboratory's extensive repertoire of techniques together with well-established key collaborators have culminated in elucidation of mechanisms involved in the development of CICI and more importantly, our work has identified novel therapies to attenuate the inherent cognitive dysfunction engendered by this condition, which has been published in *Cancer Research* (2021), *Brain Plasticity* (2022) and *PNAS* (2022).

Over the past decade, I have studied the cellular, molecular and epigenetic mechanisms underlying neural stem cell development, adult neurogenesis, myelination, and cognitive function. I have extensive experience with biochemical/molecular biology, mouse genetics, viral-mediated single cell genetic manipulations, behavioral neuroscience, immunohistochemistry, stereological analysis, and multi-photon confocal imaging, and have developed effective methodologies for the proposed research. I am an active full member of the Cancer Pharmacology program at the Cancer Institute of New Jersey (CINJ). In addition, I am also a core member of the Rutgers Brain Health Institute (BHI). These affiliations will allow for fruitful collaboration, efficient use of resources, and ultimately a more productive and data-driven project. In summary, my expertise and experience are highly relevant to successfully performing the proposed study.

A. Ongoing projects that I would like to highlight include:

1) R01CA242158

Jang (PI)
08/08/2019-07/31/2024
PQ#12; Targeting Nampt-mediated NAD^+ metabolism in chemobrain.

2) **R01AG058560**
Jang (PI)
3/15/2018 - 12/31/2023
Role of BubR1 as a juvenile protective factor in hippocampal aging.

3) U.S. Department of Defense (DOD) – Has been recommended for funding.
Jang (PI) and KiBum Lee (Partnering PI)
7/01/2023 - 6/30/2027
Development of new therapeutic strategies of chemobrain for ovarian cancer survivors

Selected Citations (# means corresponding author; * means co-first author)

1. Oliveros A*, Yoo KH*, Rashid MA*, Corujo-Ramirez A, Hur B, Sung J, Liu Y, Hawse JR, Choi DS, Boison D, **Jang MH#**. Adenosine A2A receptor blockade prevents cisplatin-induced impairments in neurogenesis and cognitive function. ***PNAS***, 2022, 119(28):e2206415119. doi: 10.1073/pnas.2206415119. Epub 2022 Jul 7. PMID: 35867768.

2. Yoo KH*, Tang JJ*, Rashid MA*, Cho CH, Corujo-Ramirez A, Choi JH, Bae MG, Brogren D, Hawse JR, Hou X, Weroha SJ, Oliveros A, Kirkeby LA, Baur JA, **Jang MH#**. Nicotinamide mononucleotide prevents chemotherapy-induced cognitive impairments. ***Cancer Research*** 2021, canres.3290.2020. doi: 10.1158/0008-5472.CAN-20-3290. PMID: 33771896.

3. Cho CH, Yoo KH, Oliveros A, Paulson S, Hussaini SMQ, van Deursen JM, **Jang MH#**. sFRP3 inhibition improves age-related cellular changes in BubR1 progeroid mice. ***Aging Cell*** 2019 Jan 4:e12899. doi: 10.1111/acel.12899. PMID: 30609266.

4. **Jang MH*,#**, Bonaguidi MA*, Kitabatake Y*, Sun J*, Song J, Kang E, Jun H, Zhong C, Su Y, Guo JU, Wang MX, Sailor KA, Kim JY, Gao Y, Christian KM, Ming GL, Song H**#**. Secreted frizzled-related protein 3 regulates activity-dependent adult hippocampal neurogenesis. ***Cell Stem Cell*** 2013; 12(2):215-223. PMCID: PMC3569732.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2021-	Full member, Rutgers Cancer Institute of New Jersey (CINJ), NJ, USA
2021-	Core member, Brain Health Institute (BHI), Rutgers University, NJ, USA
2021-	Associate Professor with tenure, Dept. of Neurosurgery, Robert Wood Johnson Medical School, Rutgers University, New Brunswick, NJ, USA
2018-2021	Associate Professor, Dept. of Neurological Surgery, Mayo Clinic, Rochester, MN, USA
2012-2021	Member, Mayo Clinic Cancer Center
2012-2018	Assistant Professor, Dept. of Neurological Surgery, Mayo Clinic, Rochester, MN, USA
2011-2012	Research Associate, Institute for Cell Engineering, Johns Hopkins University, MD, USA
1999-2001	Research Assistant, Dept. of Physiology, Kyung Hee University, Seoul, South Korea

Other Experience and Professional Memberships

2021-	Associate Editor in Brain Disease Mechanisms, Frontiers in Molecular Neuroscience
2021-	Co-chair, eTALK series, Association of Korean Neuroscientists (AKN)
2020-	Council Member, Association of Korean Neuroscientists (AKN)
2013-	Editorial Board Member, Journal of Exercise Rehabilitation
2013-	Member, Sigma-Xi
2013-	Member, International Society for Stem Cell Research
2013-	Member, Society of Biological Psychiatry
2005-	Member, Society for Neuroscience

Honors & Awards

2022 Cancer Survivorship Research Center's Pilot Award from Rutgers CINJ
2019 Discovery Research Award from Regenerative Medicine Minnesota
2019 Eagles 5th District Cancer Telethon Funds for Cancer Research
2017 Research Award from Regenerative Medicine Minnesota
2017 Pilot Research Award from SPORE at Mayo Clinic Cancer Center
2014 Career Development Award in Regenerative Medicine and Science, Mayo Clinic Center for Regenerative Medicine
2013 Accelerated Regenerative Medicine Award, Mayo Clinic Center for Regenerative Medicine
2013 Travel Award for Mayo-Karolinska Institutet Annual Conference at Stockholm, Sweden
2013 Research Grant, Whitehall Foundation
2013 The Janet Rosenberg Trubatch Career Development Award for Society for Neuroscience
2012 Fraternal Order of Eagles Award, Mayo Clinic Cancer Center
2011 Travel Award for American College of Neuropsychopharmacology
2011 Hanmi Poster Award (1st place), Baltimore/Washington Metropolitan Area Life Scientists Poster Symposium
2010 NIH Pathway to Independence Award (K99/R00)
2010 The 4th Julius Axelrod Travel Award for Society for Neuroscience
2010 NARSAD Young Investigator Award
2009 Outstanding Poster Award, Baltimore Life Science Association Conference
2008 Best Poster Award, ICE Symposium 2008, Johns Hopkins University.
2005 Postdoctoral Fellowship Award from BME and ICE at Johns Hopkins University
2005 Kyung Hee University Medical School Award for the Best PhD Thesis
2004 Health Fellowship Award, Korea

Professional Services

Grant reviewer:

2022 Ad hoc reviewer (NIH/ZRG1 CVRS-S (55) R Special Emphasis Panel)
2021 Mail reviewer (NDPR study section)
2021 Ad hoc reviewer (NIH/ZAG1 ZIJ-8 [J1] Special Emphasis Panel)
2020 Ad hoc reviewer (NIH/ZRG MDCN-V (02) Special Emphasis Panel)
2018 & 2019 Ad hoc reviewer (NIH/NCF study section)
2013 & 2017 Ad hoc reviewer (NSF CAREER program)
2012 Ad hoc reviewer (Kansas NSF EPSCoR First Award program)
2012 Ad hoc reviewer (Austrian Science Fund)

Journal reviewer: JAMA Psychiatry, Stem Cell, Journal of Neuroscience, Aging Cell, Scientific Reports, Journal of Biological Chemistry, Neuroscience Letters, Fertility and Sterility, Brain and Development, Neural Plasticity, Journal of Nutritional Biochemistry, Plos One, and Molecular Brain.

C. Contributions to Science

1. Although cancer therapy-induced cognitive dysfunction becomes a significant medical concern with no known cure, the underlying pathophysiological mechanisms are unclear. Using CT-guided irradiation and cisplatin chemotherapy as a model system in mice in conjunction with human cortical neuron derived from induced pluripotent stem cells, we aim to elucidate druggable molecular pathways capable to prevent and/or reverse chemobrain. In particular, we aim to identify therapeutic approaches to prevent chemobrain should provide a secondary benefit of enhancing anti-tumor activity by chemotherapy, thus paving the way for development of novel strategies for chemobrain and cancer.
   a. Ford EC, Achanta PA, Purger D, Armour M, Reyes J, Fong J, Kleinberg L, Redmond K, Wong J, **Jang MH**, Jun H, Song HJ, Quinones-Hinojosa A. Localized CT-guided irradiation inhibits neurogenesis in specific regions of the adult mouse brain. ***Radiation Research*** 2011, 175(6): 774-783. PMCID: PMC3142866.

   b. Yoo KH*, Tang JJ*, Rashid MA*, Cho CH, Corujo-Ramirez A, Choi JH, Bae MG, Brogren D, Hawse JR, Hou X, Weroha SJ, Oliveros A, Kirkeby LA, Baur JA, **Jang MH**#. Nicotinamide mononucleotide prevents chemotherapy-induced cognitive impairments. ***Cancer Research*** 2021, canres.3290.2020. doi: 10.1158/0008-5472.CAN-20-3290. PMID: 33771896.

c. Oliveros A*, Yoo KH*, Rashid MA*, Corujo-Ramirez A, Hur B, Sung J, Liu Y, Hawse JR, Choi DS, Boison D, **Jang MH#**. Adenosine A_{2A} receptor blockade prevents cisplatin-induced impairments in neurogenesis and cognitive function. ***PNAS***, 2022, 119(28):e2206415119. doi: 10.1073/pnas.2206415119. Epub 2022 Jul 7. PMID: 35867768.

d. Rashid MA, Oliveros A, Kim YS, **Jang MH#**. Nicotinamide mononucleotide prevents cisplatin-induced mitochondrial defects in cortical neurons derived from human induced pluripotent stem cells. ***Brain Plasticity*** 2022, 8(2):143-152. doi: 10.3233/BPL-220143. PMID: 36721392

2. Aging is the greatest risk factor for neurodegenerative disorders with cognitive dysfunction. Evidence links age-related cognitive dysfunction to abnormalities in adult hippocampal neurogenesis and oligodendrocyte development. However, the molecular mechanisms governing these impairments are not well understood. Aided by animal genetics, shRNA-mediated retroviral approach, histological analysis, confocal imaging and animal behaviors, we identified two molecules BubR1 and IGF-1 as new critical factors controlling age-related neurogenesis. In addition, using animal genetics, histological analysis, confocal and electron microscopy and animal behavior studies, our group has further shown that BubR1 is required for maintaining oligodendrocyte progenitor proliferation, oligodendrocyte generation, and myelin production. Given that impairments in neurogenesis and myelination contribute to age-related cognitive dysfunction, identification of molecular factors that are capable of sustaining neurogenesis and myelination is critical to developing therapeutic strategies for brain aging.
   a. Yang Z, Jun H, Choi CI, Yoo KH, Cho CH, Hussaini SMQ, Simmons A, Kim S, van Deursen JM, Baker DJ, **Jang MH#**. Age-related decline in BubR1 impairs adult hippocampal neurogenesis. ***Aging Cell*** 2017; 16(3):598-601. PMCID: PMC5418205.

   b. Choi C, Yoo KH, Hussaini SMQ, Jeon BT, Welby J, Gan H, Scarisbrick I, Zhang Z, Baker DJ, van Deursen JM, Rodriguez M, **Jang MH#**. The progeroid gene BubR1 regulates axon myelination and motor function. ***Aging*** 2016; 8(11): 2667-2688. PMCID: PMC5191862.

   c. Cho CH, Yoo KH, Oliveros A, Paulson S, Hussaini SMQ, van Deursen JM, **Jang MH#**. sFRP3 inhibition improves age-related cellular changes in BubR1 progeroid mice. ***Aging Cell*** 2019 Jan 4:e12899. doi: 10.1111/acel.12899. PMID: 30609266.

   d. Ibrayeva A, Bay M, Pu E, Jörg D, Peng L, Jun H, Zhang N, Aaron D, Lin C, Resler G, **Jang MH**, Simons BD, Bonaguidi MA#. Early stem Cell aging in the mature brain. ***Cell Stem Cell*** 2021 28(5):955-966.e7. PMID: 33848469.

3. Focusing on risk factors for human psychiatric and neurological diseases, we began exploring how ongoing neurodevelopmental deficits were generated in the context of neuropsychiatric and neurological disorders. Using shRNA-mediated single-cell genetic retroviral manipulations combined with multi-photon confocal imaging and mouse genetics, we studied the molecular mechanisms that underlie synaptogenesis of adult-born neurons. We established that Disrupted in Schizophrenia-1 (DISC1), a susceptibility gene for mental disorders, was a key player for proper axonal targeting and synapse formation of adult-generated dentate granule neurons, suggesting novel roles for DISC1 in distinct processes during neuronal development.
   a. Terrillion CE, Abazyan B, Yang Z, Crawford J, Shevelkin AV, Jouroukhin Y, Yoo KH, Cho CH, Roychaudhuri R, Snyder SH, **Jang MH#**, Pletnikov MV#. DISC1 in astrocytes influences adult neurogenesis and hippocampus-dependent behaviors in mice. ***Neuropsychopharmacology*** 2017, 11:2242-2251. PMID: 28631721.

   b. Oliveros A, Cui A, Choi S, Lindberg D, Hinton D, **Jang MH**, Choi DS. Adenosine A2A Receptor and ERK Driven Impulsivity Potentiates Hippocampal Immature Neuron Proliferation. ***Translational Psychiatry*** 2017; 7(4):e1095. PMCID: PMC5416704.

   c. Kim JY, Duan X, Liu CY, **Jang MH**, Guo JU, Pow-anpongkul N, Kang E, Song H, Ming GL. DISC1 regulates new neuron development in the adult brain via modulation of AKT-mTOR signaling through KIAA1212. ***Neuron*** 2009; 63(6):761-773. PMCID: PMC3075620.

   d. Faulkner RL*, **Jang MH***, Liu XB*, Duan X, Sailor KA, Ge S, Jones EG#, Ming GL, Song H#, Cheng H-J#. Development of hippocampal mossy fiber synaptic outputs by new neurons in the adult brain. ***Proc Nat Acad Sci*** 2008; 105(37):14157-14162. PMCID: PMC2544594.

4. In an attempt to determine an epigenetic mechanism of activity-induced adult hippocampal neurogenesis, I began studying molecules differentially induced by electroconvulsive therapy (ECT) within the hippocampus and neurogenesis process. By using shRNA-mediated single-cell genetic manipulations with retroviral and lentiviral systems, mouse genetics, and stereological analysis, I identified a molecule called Gadd45b that is induced by ECT in dentate granule neurons and involved in DNA-demethylation in the specific promoter regions of critical growth factors, including BDNF and FGF1. This work demonstrated Gadd45b's essential role in ECT-induced adult hippocampal neurogenesis and helped us better understand how transient neuronal activation could achieve long-lasting effects in neural plasticity and memory owing to an epigenetic mechanism.
   a. Ma DK*, **Jang MH***, Guo JU, Kitabatake Y, Chang ML, Pow-anpongkul N, Flavell RA, Lu B, Ming GL, Song H. Neuronal activity-induced Gadd45b promotes epigenetic DNA demethylation and adult neurogenesis. ***Science*** 2009; 323 (5917): 1074-1077. PMCID: PMC2726986.
   b. Guo JU, Ma DK, Mo H, Ball MP, **Jang MH**, Bonaguidi MA, Balazer JA, Eaves HL, Xie B, Ford E, Zhang K, Ming GL, Gao Y, Song H. Neuronal activity modifies the DNA methylation landscape in the adult brain. ***Nat Neurosci*** 2011; 14(10): 1345-1351. PMCID: PMC3183401.
   c. Jun H, Hussaini SMQ, Cho CH, Welby J, **Jang MH#**. Gadd45b mediates electroconvulsive shock induced proliferation of hippocampal neural stem cells. ***Brain Stimul*** 2015; 8(6):1021-1024. PMCID: PMC4656097.
   d. Jun H, Hussaini Q, Rigby MJ, **Jang MH#**. Functional role of adult hippocampal neurogenesis as a novel strategy for mental disorders. ***Neural Plasticity*** (Invited Review) 2012:854285. PMCID: PMC354953.
5. Previous research showed that hippocampal neurogenesis is increased after exercise and antidepressant use; however, no mechanism linking these paradigms had been determined. I studied Wnt pathway inhibitor secreted frizzled-related protein 3 (sFRP3) in mouse models and ran parallel collaborative studies to understand the pharmacogenetic association of the human sFRP3 (*FRZB*) gene in patients with clinical depression and latency to antidepressant response. By using clonal analysis, histology, shRNA-mediated single-cell genetic manipulations, mouse genetics, confocal imaging, and animal behavior testing, I found that sFRP3 regulates multiple stages of adult neurogenesis and mediates fluoxetine antidepressant action in an activity-dependent fashion in mice. In addition, our human pharmacogenetic association analysis revealed that polymorphisms in *FRZB* contribute to a faster response to antidepressant action in clinical cohorts. Considering that current antidepressant efficacy is hampered by the slow onset of clinically appreciable improvement, our discovery may provide a framework for development of more effective drugs.
   a. **Jang MH*,#**, Bonaguidi MA*, Kitabatake Y*, Sun J*, Song J, Kang E, Jun H, Zhong C, Su Y, Guo JU, Wang MX, Sailor KA, Kim JY, Gao Y, Christian KM, Ming GL, Song H**#**. Secreted frizzled-related protein 3 regulates activity-dependent adult hippocampal neurogenesis. ***Cell Stem Cell*** 2013; 12(2):215-223. PMCID: PMC3569732.
   b. **Jang MH**, Kitabatake Y, Kang E, Jun H, Pletnikov MV, Christian KM, Hen R, Lucae S, Binder EB, Song H, Ming GL. Secreted frizzled-related protein 3 (sFRP3) regulates antidepressant responses in mice and humans. ***Mol Psychiatry*** 2013; 18(9):957-958. PMCID: PMC3970729.
   c. Hussaini SMQ, Choi CI, Cho CH, Kim HJ, Jun H, **Jang MH#**. Wnt signaling in neuropsychiatric disorders: ties with adult hippocampal neurogenesis and behavior (Review). ***Neurosci Biobehav Rev*** 2014; 47:369-383. PMCID: PMC4258146.
   d. Sun J, Bonaguidi MA, Jun H, Guo JU, Sun GJ, Will B, Yang Z, **Jang MH**, Song H, Ming GL, Christian KM. A septo-temporal molecular gradient of sfrp3 in the dentate gyrus differentially regulates quiescent adult hippocampal neural stem cell activation. ***Mol Brain*** 2015; 8(1):52. PMCID: PMC4559945**.**

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/mi-hyeon.jang.1/bibliography/43380897/public/?sort=date&direction=descending