## BIOGRAPHICAL SKETCH

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NAME: Wang, Jinju

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

POSITION TITLE: Assistant Professor

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 |
|---|---|---|---|
| Nanhua University (Hunan, China) | B.S. | 07/2007 | Nursing |
| Wright State University (Dayton, OH) | M.S. | 08/2011 | Pharmacology & Toxicology |
| Wright State University (Dayton, OH) | Ph.D. | 06/2016 | Integrative Biology & Toxicology |
| Wright State University (Dayton, OH) | Post-doctoral | 06/2020 | Cerebrovascular Pharmacology |

### A. Personal Statement

I have a background and have a long-standing interest in vascular disease research. My research interest mainly focuses on establishing novel extracellular vesicle-based therapy for vascular diseases, especially in diabetes, hypertension, and its comorbidity ischemic stroke. I have almost 10 years' experience in exosome (EX) research. My graduate and postdoctoral work focusing on studying the role of exercise in progenitor cells and their derived exosomes in cerebrovascular diseases were supported by AHA predoctoral and postdoctoral fellowship awards. To specify the cellular origin of extracellular vesicles, I have established a novel approach to isolate and analyze specific extracellular vesicles from culture medium and biological fluid such as plasma. With this new methodology, we can conduct qualitative and quantitative assessments of specific extracellular vesicles, as well as biomarker discovery of diseases studies. In the short term, I put efforts on investigating the application of exosome-mediated intercellular communication in vascular injury in type 2 diabetes (T2D) and ischemic stroke.

Ongoing and recently completed projects that I would like to highlight include:
AHA Career Development Award
Wang (PI)
04/01/2022-03/31/2025
"The role of EPC exosomal communication in the beneficial effects of exercise on hypertension-associated ischemic stroke"

WVCTSI 2021 Pilot Grant
Wang (PI)
11/01/2021-04/30/2022
"MiRNA profiling of exosomes derived from perivascular adipocyte tissue in type 2 diabetic condition"

AHA postdoctoral fellowship award
Wang (PI)
07/01/2018-06/30/2020

"The regulatory effect of exercise on circulating EPC-EXs and its implication in ischemic stroke"

AHA predoctoral fellowship grant
Wang (PI)
07/01/2015-06/30/2016
"Co-transplantation of NPCs and EPCs derived from human iPSCs for treating ischemic stroke"

Citations:

1) Mattingly J, Li Y, Bihl J, **Wang J**[#]. The promise of exosome applications in treating central nervous system diseases. CNS Neurosci Ther. 2021;00:1–9. PMID: 34636491
2) **Wang J** *, Pothana K, Chen S, Sawant H, Travers J, Bihl J and Chen Y. Ultraviolet B Irradiation Alters the Level and miR Contents of Exosomes Released by Keratinocytes in Diabetic Condition. Photochemistry and Photobiology. 2021. PMID: 34931322
3) **Wang J** *, Polaki V, Chen S, Bihl J*. Exercise improves endothelial function associated with alleviated inflammation and oxidative stress of perivascular adipose tissue in type 2 diabetic mice. Oxid Med Cell Longev. 2020; 2020: 8830537. PMID: 33425218
4) **Wang J***, Liu H, Chen S, Zhang W, Chen Y, Yang Y*. Moderate exercise has beneficial effects on mouse ischemic stroke by enhancing the functions of circulating endothelial progenitor cell-derived exosomes. Exp Neurol. 2020 Apr 20; 330: 113325. PMID: 32325158

## B. Positions, Scientific Appointments, and Honors

### Positions and Scientific Appointments

2022.6 -: Assistant Professor (tenure-track), Department of Biomedical Sciences, Joan C. Edwards School of Medicine, Marshall University, Huntington WV
2021.1 - 2022.5: Research Assistant Professor (non-tenure track), Department of Biomedical Sciences, Joan C. Edwards School of Medicine, Marshall University, Huntington WV
2020. 7 - 2020.12: Research Assistant Professor, Department of Pharmacology & Toxicology, Boonshoft School of Medicine, Wright State University (WSU), Dayton OH
2016. 7 - 2020.6: Post-doctoral Researcher, Department of Pharmacology & Toxicology, Boonshoft School of Medicine, WSU, Dayton OH

2021- current: Member, Neuroscience Research Cluster (Marshall University)
2021- current: Member, Cardiovascular Disease Research Cluster (Marshall University)
2021- current: Member, West Virginia Clinical and Translational Science Institute (WVCTSI)
2017-current: Member, American Diabetic Association (ADA)
2014-current: Member, International Society for Extracellular Vesicles (ISEV)
2011-current: Member, American Heart Association (AHA)

### Honors

2021.10: Oral Presentation winner, 33rd Annual Health Science Research Day, Huntington, WV
2018 – 2020: Postdoctoral Fellowship Award, American Heart Association
2015 – 2016: Predoctoral Fellowship Award, American Heart Association
2012: Distinguished Master's Thesis Award Nominee

Professional services
Review Editor: Frontiers in Stroke
Reviewer for scientific journals: Cellular and molecular neurobiology, Oxidative medicine and cellular longevity, Scientific Reports, Neuropsychiatric Disease and Treatment, Journal of international medical research, Experimental Neurology, Toxicology, Metabolic Brain Disease, BMC in Genomics.

## C. Contributions to Science

1) I have actively participated in studying the role of extracellular vesicles in vascular diseases such as ischemic stroke, hemorrhagic stroke, hypertension, and diabetes. Exosomes (EXs) are small vesicles of cellular membrane released from almost all types of cells in response to physiological and pathological stimuli. Accumulating evidence suggest that EXs represent a novel way of intercellular communication by transferring their cargoes (proteins and miRs) to recipient cells and alter the function of the recipient cells. It is proposed that EXs could be the novel therapeutic target/approach for stroke; and could be the biomarkers for stroke patients. However, the EXs are nanoscale, accurate analysis of specific extracellular vesicles from biofluids is critical and challenging, which significantly hampers the advance of extracellular vesicle research over the past years. As inspired by the rapid development of nanoparticle tracking analysis tool and immunoassay techniques, I established a novel approach to isolate and analyze specific extracellular vesicles from culture medium and plasma. Notably, this method is not limited to ischemic stroke, but can readily be adapted to other systems, ranging from cardiovascular diseases to inflammatory to neoplastic disorders. I have investigated the role of EPC-derived EXs released under different stimuli on treating hypoxia/reoxygenation-injured endothelial cells. I have several co-authored peer-reviewed papers in these fields.

a. **Wang J**, Chen S, Ma X, Cheng C, Xiao X, Chen J, Liu S, Zhao B, Chen Y, "Effects of endothelial progenitor cell-derived microvesicles on hypoxia-reoxygenation induced endothelial dysfunction and apoptosis," Oxid Med Cell Longev, 2013, 2013: 572729. PMCID: PMC3830832.
b. Xiao X, Bi K, Liu Y, Fan R, Zhao Y, Ma X, **Wang J**, Zhao B, Chen Y, Chen J, "Cellular membrane microparticles: potential targets of combinational therapy for vascular disease," Curr Vasc Pharmacol, 2014: Oct 14. PMID: 25360845.
c. **Wang J**, Guo R, Yang Y, Jacobs B, Chen S, Iwuchukwu I, Gaines KJ, Chen Y, Simman R, Lv G, Wu K, Bihl JC. The Novel Methods for Analysis of Exosomes Released from Endothelial Cells and Endothelial Progenitor Cells. Stem Cells Int. 2016;2016: 2639728. PMID: 27118976.
d. Zhang C[+], **Wang J** [+], Ma X, Wang W, Zhao B, Chen Y, Chen C, Bihl J. ACE2-EPC-EXs protect ageing ECs against hypoxia/reoxygenation induced injury through the miR-18a/Nox2/ROS pathway. J. Cell. Mol. Med. Vol 22, No 3, 2018 pp. 1873-1882. PMID: 29363860.

2) I have been engaged in investigating the potential role of exosomal communications in exercise intervention-induced beneficial effects on vasculature. Exercise is a widely recognized non-pharmaceutical approach for vascular diseases, although the underlying mechanisms have not been well understood. EXs carrying bioactive molecules (miRs & proteins) mediate intercellular communication and are important players of tissue "microenvironment" that is involved in physiological processes and the development/progression of vascular diseases. Recently, emerging evidence indicated that exercise promotes the release of EXs into circulation and raises exosomal miRs level. However, the subpopulation and biological functions of EXs are unclear. I have further demonstrated that moderate exercise enhances the function of EPC-EXs on protecting endothelial cells (ECs) from hypoxia injury. The findings provide novel insights into the mechanism by which exercise elicits favorable effects on ischemic stroke. In addition, vascular disease is one of the major complications of diabetes, a disease affecting > 23 million people in the United States. Recent studies indicate that increased inflammation in perivascular adipose tissue (PVAT) contributes to endothelial dysfunction leading to ultimately vascular disease. I have recently shown that moderate exercise intervention can improve endothelial function associated with alleviated inflammation and oxidative stress of perivascular adipose tissue in type 2 diabetic mice. I have several co-authored and 2 corresponding-authored papers in this field.

a. Ma C, Ma X, **Wang J**, Liu H, Chen Y, Yang Y*. Physical exercise induces hippocampal neurogenesis and prevents cognitive decline. Behav Brain Res. 2017 Jan 15;317:332-339. PMID: 27702635.
b. Liu H, Lei H, Shi Y, **Wang J**, Chen N, Li Z, Chen Y, Ye Q, Yang Y. Autophagy inhibitor 3-methyladenine alleviates overload-exercise-induced cardiac injury in rats. Acta Pharmacol Sin. 2017 Jul; 38(7): 990–997. PMID: 28260802
c. **Wang J***, Liu H, Chen S, Zhang W, Chen Y, Yang Y*. Moderate exercise has beneficial effects on mouse ischemic stroke by enhancing the functions of circulating endothelial progenitor cell-derived exosomes. Exp Neurol. 2020 Apr 20; 330: 113325. PMID: 32325158
d. **Wang J** *, Polaki V, Chen S, Bihl J*. Exercise improves endothelial function associated with alleviated inflammation and oxidative stress of perivascular adipose tissue in type 2 diabetic mice. Oxid Med Cell Longev. 2020; 2020: 8830537. PMID: 33425218

3) I lead research to investigate that whether co-transplantation of endothelial progenitor cells (EPCs) and neural progenitor cells (NPCs) has synergistic effects on treating ischemic stroke. Ischemic stroke resulting in brain cell (neurons, glial cells and ECs) death and focal tissue loss is one of the most severe health problems in the world. In general, the therapies for treating ischemic stroke are quite limited. Administration of thrombolytic agents is effective but is limited by a narrow therapeutic window and the risk of hemorrhagic complication. Cell transplantation has been suggested as a promising therapeutic strategy for stroke. However, there are still many problems that need to be solved, such as the proper type of cells for cellular grafts. Although NPCs and EPCs have been documented to be effective for ischemic stroke, it is not known whether there is a synergistic effect if they are co-transplanted. Therefore, I proposed to test the hypothesis that co-transplantation of NPCs and EPCs augments the therapeutic efficacy of progenitors for ischemic stroke. I focused on evaluating the therapeutic efficacy of NPCs and EPCs by measuring ischemic injury (infarct volume, neurological deficit) and tissue repair (microvascular density, angiogenesis and neurogenesis). The possible mechanisms of VEGFR2/PI3K and TrkB/PI3K pathways were explored by using PI3K inhibitor Ly294002 and determined by assessing the levels of VEGFR2 and TrkB in brain tissue.

a. **Wang J,** Chen Y, Yang Y, Xiao X, Chen S, Zhang C, Jacobs B, Zhao B, Bihl J, Chen Y. Endothelial progenitor cells and neural progenitor cells synergistically protect cerebral endothelial cells from Hypoxia/reoxygenation-induced injury via activating the PI3K/Akt pathway. Mol Brain. 2016 Feb 3;9:12. PubMed PMID: 26842559.
b. Chen Y, Lu B, **Wang J**, Chen S, Lin Z, Ma X, Liu Y, Zhao B, Chen Y. Circulating CD133+ CD34+ progenitor cells and plasma stromal-derived factor-1alpha: predictive role in ischemic stroke patients. J Stroke Cerebrovasc Dis. 2015 Feb;24(2):319-26. PMID: 25444027.
c. Liu H, Li G, Ma C, Chen Y, **Wang J**, Yang Y. Repetitive magnetic stimulation promotes the proliferation of neural progenitor cells via modulating the expression of miR-106b. Int J Mol Med. 2018 Dec;42(6):3631-3639. PMID: 30320352.

4) I have also participated in several other projects revolving around defining the protective role of ACE2/Ang-(1-7)/Mas in ischemic stroke. The renin angiotensin system participates in the pathogenesis of stroke, primarily through the actions of the vasoactive peptide Ang II and its pathway ACE/Ang II/AT1. ACE2/Ang-(1-7)/Mas, a newly identified member of RAS, has been demonstrated to counteract the effects of ACE/Ang II/AT1. ACE2 is a homologue of ACE that is abundantly expressed in the cardiovascular-related areas of the brain and blood vessels. The primary function of ACE2 is to metabolize the deleterious Ang II into Ang-(1-7), a heptapeptide with vasoprotective actions. Therefore, ACE2 might represent a novel target and strategy for treating strokes. We recently published data that demonstrate ACE2 protects brain from ischemic stroke, and how ACE2 improves the therapeutic efficacy in ischemic stroke.

a. Chen J, Zhao Y, Chen S, **Wang J**, Xiao X, Ma X, Penchikala M, Xia H, Lazartigues E, Zhao B, Chen Y, “Neuronal Over-expression of ACE2 protects brain from ischemia-induced damage,” Neuropharmacology, 2014, 79: 550-558. PMCID: PMC 3992949.
b. Zheng JL, Li GZ, Chen SZ, **Wang J**, Olson JE, Xia HJ, Lazartigues E, Zhu YL, Chen YF. Angiotensin converting enzyme 2/Ang-(1-7)/mas axis protects brain from ischemic injury with a tendency of age-dependence. CNS Neurosci Ther. 2014 May;20(5):452-9. PubMed PMID: 24581232.
c. Xiao X, Zhang C, Ma X, Miao H, **Wang J**, Liu L, Chen S, Zeng R, Bihl J[#], Chen Y[#], “Angiotensin-(1-7) counteracts angiotensin II-induced dysfunction in cerebral endothelial cells via modulating Nox2/ROS and PI3K/NO pathways”, Exp Cell Res, 2015, Jun 19. PMID: 26101159.

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https://www.ncbi.nlm.nih.gov/myncbi/1fuddaqj3sm5j/bibliography/public/