BIOGRAPHICAL SKETCH

Senior Trainer

NAME: Jing Zheng

eRA COMMONS USER NAME (credential, e.g., agency login): jzheng30

POSITION TITLE: 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
Xiamen University, Fujian, P.R. China	BS	07/1982	Zoology
North Dakota State University, Fargo, ND	MS	07/1992	Reprod. Physiology
North Dakota State University, Fargo, ND	PhD	05/1995	Reprod. Physiology
University of Wisconsin-Madison	Postdoc	07/1997	Reprod. Physiology

A. Personal Statement

Major research interests of my lab is to reveal the ceullular and molecular mechanisms regulating fetal endothelial function. As a principle investigator, I have obtained steady NIH funding since 2000. Also as a Subsection PI, I oversaw an angiogenesis/cell & molecular core, which was funded by an NIH as P01 grant since 2000. Over the past 20 years, my laboratory has made significant contribution to our understanding of molecular and signaling mechanisms underlying placental angiogenesis and vasodilatation with more than 50 peer-reviewed publications. I have made significant efforts at mentor teaching, particularly with graduate students, MD/postdoctoral fellows, and junior faculty. In combination of our strength in endothelial biology and functional genomics, this current application will expand and solidify my future research directions to more comprehensively analyze cellular and molecular mechanisms underlying fetal and placental endothelial functions. Thus, with my expertise in fetal/placental endothelial biology and experience in grant management, I believe that I am highly qualified to serve as a mentor in this T32 application.

1. Li Y, Wang K, Zou QY, Jiang YZ, Zhou C**, Zheng** J. An endogenous aryl hydrocarbon receptor ligand suppresses angiogenic responses of human artery and vein endothelial cells: differential roles of AhR. Reprod Toxicol 2017; 74:181-188. PMC5718942
2. Zhou C, Yan Q, Zou QY, Zhong XQ, Tyler CT, Magness RR, Bird IM, **Zheng J**. Sexual dimorphism of preeclampsia-dysregulated transcriptomic profiles and cellular function in fetal endothelial cells. Hypertension (In Press). PMC In Process.
3. Zhou C, Zou QY, Li H, Liu AX, Wang RF, Magness RR, **Zheng J**. Preeclampsia down-regulates microRNAs in fetal endothelial cells: Roles of miR-29a/c-3p in endothelial function. J Clin Endocrinol Metab 2017; 102: 3470-3479. PMC5587062
4. Wang K, **Zheng J**. Signaling regulation of fetoplacental angiogenesis. J Endo. (Review) 2012; 212, 243-55. PMC3288248.

B. Positions and Honors

Positions and Employment

1982-1989 Assistant Lecturer and Researcher. Aquaculture Dept., Zhanjiang Fisheries College (Guangdong Ocean University now), Guangdong, P.R. China.

1989-1995 Graduate Research Assistant. Department of Animal and Range Sciences, North Dakota State University, Fargo, ND.

1995-1997 Postdoctoral Fellow. Dept. of Ob/Gyn., Univ. of Wisconsin, Madison, WI

1997-2001	Research Assistant Professor (Assistant Scientist). Dept. of Ob/Gyn., Univ. of Wisconsin, Madison, WI.
2001-2007	Assistant Professor. Dept. of Ob/Gyn., Univ. of Wisconsin Madison, WI.
2007-2014	Associate Professor with tenure. Dept. of Ob/Gyn., Univ. of Wisconsin, Madison, WI.
2014-	Professor with tenure. Dept. of Ob/Gyn., Univ. of Wisconsin, Madison, WI.

Other Experience and Professional Memberships

1990-	Society for the Study of Reproduction
1999-	Society for Reproductive (former: Gynecologic) Investigation
2000-	Perinatal Research Society (Honor Society)
2018-	American Heart Association
2006-2008	International Society for Stem Cell Research
2007	*Ad Hoc* Member, NIH Pregnancy & Neonatology Study Section
2009	*Ad Hoc* Member, NIH Special Emphasis Panel (ZRG1 EMNR-C (58)
2009	Member, NIH Special Emphasis Panel/ZES1 LKB-G (TW).
2010-2011	Editorial Board, Journal of Endocrinology.
2011, Spring & Fall 2014-	Member, American Heart Association, The Vascular Endothelial Biology and Function Committee 1.
2014-2018	Member, NIH Obstetrics and Maternal-Fetal Biology Subcommittee (CHHD-B Study Section).
2014, June & Nov	Member, NIH Obstetrics and Maternal-Fetal Biology Subcommittee (Special Panel).
2015 Nov	Member, NICHD Special Emphasis Panel: ZHD1 DSR-Z (CM).
2016 May	Member, NICHD Special Emphasis Panel for Human Placenta (omics) Project RFA.

Honors

1997	Perinatal Research Society NIH Young Investigator Travel Award.
2004-2006	Guest Professor, Zhanjiang Ocean University, Zhanjiang, China
2004	Invited speaker: FASEB Summer Research Conferences: Molecular and Cellular Signaling in the Perinatal Cardiovascular System, Tucson, AZ
2011-	Guest Professor, Guangdong Medical University, Zhanjiang, China

C. Contribution to Science

Roles of Aryl Hydrocarbon Receptors (AhR) in the Human Fetus, Placentas, Lung, and Ovarian Cancer: In addition to angiogenic factors, my lab has also opened a new research direction to determine the physiological role of AhR in fetoplacental endothelial functions. We have reported, for the first time, high AhR expression in human fetuses and placentas, primarily in trophoblast cells and endothelium of large blood vessels, in endothelium of human umbilical cord vessels, lung vessels, and in many human fetal organs. We also observed that exogenous (dioxin) and endogenous (ITE) AhR ligands at appropriate doses can suppress proliferation and/or migration of human umbilical vein and artery endothelial cells and human pulmonary artery endothelial cells. Recently, we also reported that AhR was widely present in many histotypes of ovarian cancer tissues, and both dioxin and ITE inhibited growth of a subset of ovarian cancer in vitro and in vivo. These data indicate that *ITE might potentially be used for therapeutic intervention for overgrowth of vascularity occurring in many severe vascular disorders such as pulmonary artery hypertension and placenta accrete as well as for a subset of human ovarian cancer.*

1. Jiang YZ, Wang K, Fang R, **Zheng J**. Expression of aryl hydrocarbon receptor in human placentas and fetal tissues. J Histochem Cytochem 2010 58: 679-86. PMC2907273.
2. Wang K, Li Y, Jiang YZ, Dai CF, Patankar MS, Song JS, **Zheng J**. An endogenous aryl hydrocarbon receptor ligand inhibits proliferation and migration of human ovarian cancer cells. Cancer Lett 2013; 340:63-71. PMC3781955
3. Wu YM, Chen X, Zhou Q, He QZ, Kang JH, **Zheng J**, Wang K, Duan T. ITE and TCDD differentially regulate the vascular remodeling of rat placenta via the activation of AhR. PLoS One 2014; 9: e86549. PMC3901702
4. Li Y, Wang K, Zou QY, Magness RR, **Zheng J**. 2,3,7,8-Tetrachlorodibenzo-p-dioxin differentially suppresses angiogenic responses in human placental vein and artery endothelial cells. Toxicology 2015; 336:70-78. PMC4593512.

Signaling Mechanisms in Feto-placental Angiogenesis: Upon joining the UW Dept. of Ob/Gyn, I developed a deep interest in the cellular and molecular mechanisms controlling angiogenesis and vasodilatation. We have shown that angiotensin II (AII) stimulated cell proliferation and increased eNOS and production of NO in fetoplacental artery endothelial cells. Thus, the high levels of AII in the fetal circulation may serve to modulate overall fetoplacental vascular resistance. *We have also reported that VEGFA and FGF2 regulate fetoplacental angiogenesis via an extremely complex signaling network involving multiple of protein kinases and phosphatases, NO as well as G-proteins. These proteins and vasodilators may be used as targets for regulating placental vascular growth, ultimately controlling blood flows to placentas and fetuses.*

1. Zou QY, Zhao YJ, Liu AX, Zhong XQ, Yan Q, Li Y, Zhou C, Yi FX, Bird IM, and Zheng J. G protein α subunit 14 mediates fibroblast growth factor 2-induced cellular responses in human endothelial cells. J Cell Physiol. 2018 Nov 1. doi: 10.1002/jcp.27688. [Epub ahead of print].
2. Zou QY, Zhao YZ, Li H, Wang XZ, Liu AX, Zhong XQ, Yan Q, Li Y, Zhou C, **Zheng J**. GNA11 differentially mediates fibroblast growth factor 2- and vascular endothelial growth factor A-induced cellular responses in human fetoplacental endothelial cells. J Physiol. 2018; 596(12):2333-2344. PMC6002203
3. **Zheng J**, Wen YX, Song Y, Wang K, Chen DB, Magness RR. Activation of multiple signaling pathways is critical for fibroblast growth factor 2- and vascular endothelial growth factor-stimulated ovine fetoplacental endothelial cell proliferation. Biol Reprod 2008; 78: 143-50. PMC2441762
4. Wang K, Song Y, Chen DB, **Zheng J**. Protein phosphatase 3 differentially modulates vascular endothelial growth factor and fibroblast growth factor 2-stimulated cell proliferation and signaling in ovine fetoplacental artery endothelial cells. Biol Reprod 2008; 79:704-10. PMC2574765

Fetoplacental Endothelial Adaptation to Physiological Chronic Low O2: Endothelial cells chronically reside in low-O2 environments in vivo (2%-13% O2), which are believed to be critical for cell homeostasis. To elucidate the roles of this physiological chronic normoxia in human fetal endothelial cells, we examined transcriptomes of human umbilical vein (HUVECs) and artery (HUAECs) endothelial cells, proliferation and migration of HUVECs. Immediately after isolation, HUVECs were cultured steadily under standard cell culture normoxia (SCN; 21% O2) or physiological chronic normoxia (PCN; 3% O2) up to 25 days. We found that PCN induced differential expression of an array of genes, 90% of which differed from those previously reported from HUVECs cultured under SCN and exposed to acute low O2. PCN also significantly enhanced FGF2- and VEGFA-stimulated cell proliferation and migration. Such O2 programmed cell responses were relatively stable, and were mediated via augmented activation of MEK1/MEK2/ERK1/ERK2 and/or PI3K/AKT1. Thus, PCN programs endothelial cells to undergo dramatic changes in transcriptomes and sensitizes cellular proliferative and migratory responses to FGF2 and VEGFA. These data prompt us to propose that *we may need to reexamine the current cellular and molecular mechanisms controlling fetoplacental endothelial (and many other cell types too) functions, which were largely derived from endothelial models established under ambient O2.*

1. Wang K, Jiang YZ, Chen DB, **Zheng J**. Hypoxia enhances FGF2- and VEGF-stimulated human placental artery endothelial cell proliferation: Roles of MAP2K1/2/MAPK3/1 and PI3K/AKT1 pathways. Placenta 2009; 30:1045-51. PMC2788063.
2. Jiang YZ, Wang K, Li Y, Dai CF, Wang P, Kendziorski C, Chen DB, **Zheng J**. Transcriptional and functional adaptations of endothelial cells to physiological chronic low oxygen. Biol Reprod 2013; 88:114. PMC4013893.
3. Jiang YZ, Wang K, Li Y, Dai CF, Wang P, Kendziorski C, Chen DB, **Zheng J**. Enhanced cellular responses and distinct gene profiles in human fetoplacental artery endothelial cells under chronic low oxygen. Biol Reprod 2013; 89:133. PMC4076354.
4. Jiang YZ, Li Y, Wang K, Dai CF, Huang SA, Chen DB, **Zheng J**. Distinct roles of HIF1A in endothelial adaptations to physiological and ambient oxygen. Mol Cell Endocrinol 2014; 391: 60-7. PMC4079002

Corporal Luteal and Placental Angiogenesis: During my early training, my research aimed to investigate angiogenesis in ovary and placentae My studies showed that luteal vascularity increased in the estrous cycle in association with increase in FGF1 and FGF2. I have also demonstrated that both FGF2 expression and endothelial mitogenic activity in fetoplacentomas increase in late pregnancy. More importantly, we showed that endothelial mitogenic activity of fetal placentas is associated with FGF2 levels. In addition, I have also shown that that mRNA expression of VEGF, a potent regulator of endothelial cells was increased in preeclamptic vs.

normal placentas and that expression of VEGFR-1 mRNA, but not EG-VEGF and the three other VEGF receptors studied, is elevated in preeclamptic vs. normal placentas. These observations *advance our understanding of luteal and placental angiogenesis, which will aid us to control blood flows to these tissues. More importantly, the observations on VEGFA and its receptors in placentas are significant since endothelial dysfunction is a key factor associated with many severe diseases such as preeclampsia. I served as the primary investigator or co-investigator in all of these studies*.

1. **Zheng J,** Redmer DA, Reynolds LP. Vascular development and heparin-binding growth factors of the bovine corpus luteum at several stages of the estrous cycle. Biol Reprod 1993; 49:1177-89.
2. **Zheng J**, Fricke PM, Reynolds LP, Redmer DA. Evaluation of growth, cell proliferation and cell death in bovine corpora lutea throughout the estrous cycle. Biol Reprod 1994; 51:623-32.
3. **Zheng J**, Vagnoni KE, Bird IM, Magness RR. Expression of basic fibroblast growth factor, endothelial mitogenic activity, and angiotensin II type-1 receptors in the ovine placenta during the third trimester of pregnancy. Biol Reprod 1997; 56:1189-97.
4. Chung JY, Song Y, Wang YP, Magness RR, **Zheng J**. Differential expression of VEGF, EG-VEGF, and VEGF receptors in human placentas from normal and preeclamptic pregnancies. J Clin Endocrinol Metab 2004; 89:2484-90. PMC3282114

Complete List of Published Work in MyBibliography: http://www.ncbi.nlm.nih.gov/sites/myncbi/1D1_ij8K-nq/bibliography/9696726/public/?sort=date&direction=ascending

D. Research Support

Ongoing:

PI and CoI	Source	Years	Title
Jing Zheng (PI in Proj III and Co-PI in Cellular Core).	NIH P01 HD38843	09/01/13-08/31/19 (no cost extension)	Importance of Endothelial Cell-Cell Communication at the Maternal Fetal Interface.
Project III is to study the role of G protein α subunit 11 and 14 in human endothelial function.			

J Zheng (PI)	NIH P01 HD038843-14S1	07/01/16-06/30/18 (no cost extension)	Importance of Endothelial Cell-Cell Communication at the Maternal Fetal Interface

This is an Administrative Supplements for Research on Sex/Gender Differences (NIH PA-16-066Admin Supp.), aiming is to increase the sample size of primary HUVECs preparations from both male and female subjects and use RNAseq to compare/characterize the expression profiles of all human miRNAs between NT and PE HUVECs from male and female subjects.
No Overlap.

J Zheng (PI)	Retention grant	07/01/15-

This is a retention grant from Department of Ob-Gyn, School of Medicine and Public Health, and Graduate School, UW-Madison to Zheng's research. .

Completed for the past three years:

PI and CoI	Source	Years	Title
RR Magness (PI) **J Zheng** (CoI)	NIH R01 HL117341	09/01/13-08/31/17	Endothelial Function in a Model of IUGR Induced by Uterine Space Restriction

This grant proposes to use a sheep uterine space restriction model to examine changes in uterine and placental blood flow, the role of vasodilatory (NO) and angiogenic influences on its development, and the postnatal outcome of intrauterine programming due to space restriction.

J Zheng (PI) Chi Zhou (Co-I)	Dept. R& D pilot grant	07/01/15-06/31/17	Utero- and feto-placental arteries' miRNAs expression in uterine space restriction induced intra uterine growth restriction

This pilot proposes to analyze transcriptomic profiles in ovine uterus- and feto-placental arteries using Next Generation Sequencing.