BIOGRAPHICAL SKETCH

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NAME: BIRD, IAN

eRA COMMONS USER NAME (agency login): **IMBIRD**

POSITION TITLE: Professor -OB/GYN

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Birmingham University, Birmingham	BS	07/1984	Medical Biochemistry
University of London, London	PHD	11/1987	Biochemistry
University of Edinburgh, Edinburgh	Fellow	01/1989	Biochemistry
University of Edinburgh, Edinburgh	Fellow	04/1991	Clinical Chemistry
University of Texas, Dallas	Fellow	01/1993	Reproductive Biology Sciences

A. PERSONAL STATEMENT

My training is as a biochemist, with further postdoctoral training in molecular endocrinology. While trained in basic science I have also spent my entire faculty career in OBGyn Departments with a focus on translational studies. This is a very realsitic goal for me since most small molecule drugs target the pathways I study. Many aspects of vascular dysfunction in pregnancy are known to relate to loss of vasodilatory function and are associated with elevated growth factors and cytokines. Our laboratory is focused on uterine vascular endothelial function in pregnancy and signaling function and dysfunction in response to growth factors and cytokines. In the context of this proposal, disorders of blood flow related to hypertension (including obesity and preeclampsia) are clearly associated with excess inflammatory mediators that target vascular endothelium. Whether these growth factors and cytokines are derived from the hypoxic placenta, endothelium itself, or an activated immune system, our work shows the common effect is inhibition of Cx43, so causing endothelial cell cell uncoupling and a loss of coordinated and sustained Ca2+ signaling that is otherwise necessary for optimal vasodilator production (NO and PGI2). We have published extensively that the most rapid inhibitory events are mediated by Cx43 phosphorylation via ERK and Src signaling. Our current studies and a growing body of preliminary data now shows longer term exposure to these same factors also leads to the ongoing destruction of the Cx43 microenvironment as junctional proteins that bind cells together are degraded. This process shares a common origin to acute Cx43 phosphorylation and closure since junctional proteins are also directly phosphorylated by ERK and particularly Src kinases, triggering internalization and accelerating destruction. Cytokines in particular also stimulate new mRNA expression and corresponding secretion of Matrix Metaloproteases (MMPS)that further degrade the extracellular domains of junctional protein that still remain on the plasma membrane surface. It is our experience and expertise in these combined areas that will guide our studies in Aim 4 of this proposal, to not only monitor these same Growth factor and Cytokine levels in human subjects under study but to also parallel those measures with monitoring of MMP isoforms in blood and urine. This will alliow us to clearly establish if different hypertensive/nonhypertensive conditions that may not appear different by imaging alone are still differentiated by unique endocrine and MMP profiles, and if smoking and obesity alter these responses further. Such knowledge will not only be necessary for analysis of this data as a whole, but will also lay the groundwork for future studies targeting specific diseases.

1. Bird IM, Zhang L, Magness RR. Possible mechanisms underlying pregnancy-induced changes in uterine artery endothelial function. Am J Physiol Regul Integr Comp Physiol. 2003 Feb;284(2):R245-58. PubMed PMID: 12529278.
2. Boeldt DS, Yi FX, Bird IM. eNOS activation and NO function: pregnancy adaptive programming of capacitative entry responses alters nitric oxide (NO) output in vascular endothelium--new insights into eNOS regulation through adaptive cell signaling. J Endocrinol. 2011 Sep;210(3):243-58. PubMed PMID: 21555345; PubMed Central PMCID: PMC4059042.

3. Bird IM, Boeldt DS, Krupp J, Grummer MA, Yi FX, Magness RR. Pregnancy, programming and preeclampsia: gap junctions at the nexus of pregnancy-induced adaptation of endothelial function and endothelial adaptive failure in PE. Curr Vasc Pharmacol. 2013 Sep;11(5):712-29. PubMed PMID: 24063383.
4. Boeldt DS, Hankes AC, Alvarez RE, Khurshid N, Balistreri M, Grummer MA, Yi F, Bird IM. Pregnancy programming and preeclampsia: identifying a human endothelial model to study pregnancy-adapted endothelial function and endothelial adaptive failure in preeclamptic subjects. Adv Exp Med Biol. 2014;814:27-47. PubMed PMID: 25015799.

B. POSITIONS AND HONORS

Positions and Employment

1993 - 1994	Assistant Instructor, University of Texas Southwestern Medical Center, Dallas, TX
1994 - 1999	Assistant Professor -OB/GYN, University of Wisconsin, Madison, WI
1999 - 2003	Associate Professor with Tenure, University of Wisconsin, Madison, WI
2000 -	Affiliate Appointment -Pediatrics, University of Wisconsin, Madison, WI
2000 -	Chair and Director -Endocrinology Reproductive Physiology Graduate School Program, University of Wisconsin, Madison, WI
2003 -	Professor -OB/GYN, University of Wisconsin, Madison, WI
2013 -	Director Integrated Graduate Training -OB/GYN, University of Wisconsin, Madison, WI
2014 -	Vice Chair Integrated Graduate Training -OB/GYN, University of Wisconsin, Madison, WI

Other Experience and Professional Memberships

1986 - 1997	Member, Biochemical Society (UK)
1997 -	Member, Perinatal Research Society
1997 - 1997	Co-Organizer, No-Name Society Retreat
1997 - 1998	Associate Member, Society Gynecologic Investigation (USA)
1997 - 2006	Member, Endocrine Society (USA)
1998 -	Full Member, Society Gynecologic Investigation (USA)

Honors

1984	Science and Engineering Research Council, CASE Postgraduate Studentship
1988	Post-Doctoral Research Fellowship, Faculty of Medicine, University of Edinburgh
1990	Sir Stanley and Lady Davidson Lectureship and Research Award, Faculty of Medicine, University of Edinburgh
1991	Sir Stanley and Lady Davidson Lectureship and Research Award, Faculty of Medicine, University of Edinburgh
1991	Post doctoral Fellowship/Assistant Instructorship with JI Mason funded from NIH Training Grant to Cecil and Ida Green Center, UTSW Medical center, Dallas TX
1996	R13 Travel Grant Recipient, Perinatal Research Society, Napa Valley, CA
1999	Awarded Competitive SGI Medical Student Stipend for Research in Reproduction Award for further work on “Effects of betamethazone on adrenal function”, Student Jackie Cale, SGI
2001	Awarded Competitive SGI Medical Student Stipend for Research in Reproduction Award for further work on “zonal expression of eNOS in ovine adrenal”, Student Jane Peterson, SGI
2004	SGI Presidents presenters award and NICHD competitive Travel stipend to FuXian Yi, Postdoctoral Trainee, SGI, NICHD
2005	Nominated Perinatal Research Society (PRS) Council, PRS
2007	Elected PRS Council. Basic Science Representative, PRS
2009	Elected Secretary Treasurer Perinatal Research Society, PRS
2012	Established and R13 funded the NIH-Abbott Grants Writing Workshop for PRS Young Investigators, PRS
2014	President Elect Perinatal Research Society, active as President 2016 annual meeting, PRS

C. Contribution to Science

1. My studies of endothelial adaptation to pregnancy began in 1994. The major breakthrough was the direct result of establishing the uterine artery endothelial cell (UAEC) culture model. While we initially observed that pregnancy altered the expression of key proteins responsible for vasodilator synthesis in uterine artery endothelium in vivo, the finding that these differences in expression were lost in primary culture, yet differences in vasodilator production still remained lead us to realize this was associated with additional pregnancy specific differences in cell signaling.
    a. Bird IM, Sullivan JA, Di T, Cale JM, Zhang L, Zheng J, Magness RR. Pregnancy-dependent changes in cell signaling underlie changes in differential control of vasodilator production in uterine artery endothelial cells. Endocrinology. 2000 Mar;141(3):1107-17. PubMed PMID: 10698187.
    b. Di T, Sullivan JA, Magness RR, Zhang L, Bird IM. Pregnancy-specific enhancement of agonist-stimulated ERK-1/2 signaling in uterine artery endothelial cells increases Ca(2+) sensitivity of endothelial nitric oxide synthase as well as cytosolic phospholipase A(2). Endocrinology. 2001 Jul;142(7):3014-26. PubMed PMID: 11416023.
    c. Gifford SM, Cale JM, Tsoi S, Magness RR, Bird IM. Pregnancy-specific changes in uterine artery endothelial cell signaling in vivo are both programmed and retained in primary culture. Endocrinology. 2003 Aug;144(8):3639-50. PubMed PMID: 12865347.
2. Further investigation revealed that pregnancy altered both kinase signaling and Ca2+ signaling. Further, Ca2+ signaling was more sustained in duration and took the form of successive Ca2+ bursts (mediated via TRPC under the permissive control of Cx43). As a result, pregnancy literally recruited more cells into a synchronous response, and then sustained that response for much longer.
    a. Gifford SM, Yi FX, Bird IM. Pregnancy-enhanced Ca2+ responses to ATP in uterine artery endothelial cells is due to greater capacitative Ca2+ entry rather than altered receptor coupling. J Endocrinol. 2006 Aug;190(2):373-84. PubMed PMID: 16899570.
    b. Gifford SM, Yi FX, Bird IM. Pregnancy-enhanced store-operated Ca2+ channel function in uterine artery endothelial cells is associated with enhanced agonist-specific transient receptor potential channel 3-inositol 1,4,5-trisphosphate receptor 2 interaction. J Endocrinol. 2006 Aug;190(2):385-95. PubMed PMID: 16899571.
    c. Yi FX, Boeldt DS, Gifford SM, Sullivan JA, Grummer MA, Magness RR, Bird IM. Pregnancy enhances sustained Ca2+ bursts and endothelial nitric oxide synthase activation in ovine uterine artery endothelial cells through increased connexin 43 function. Biol Reprod. 2010 Jan;82(1):66-75. PubMed PMID: 19741206; PubMed Central PMCID: PMC2802114.
3. Our development of a simultaneous imaging method for Ca2+ and NO and its application to endothelium still on the lumenal surface of intact vessels allowed us to directly observe that pregnancy enhanced Ca2+ bursts actively drive pregnancy enhanced NO output in ovine uterine artery. This adaptive response is exactly paralleled in Human Umbilical Vein Endothelium. We have more recently shown that growth factors and cytokines inhibit endothelial Cx43 function and so Ca2+ bursts and associated NO down to a level of nonpregnancy or preeclamptic vessel dysfunction in both vessel types, and the two dysfunctional states are indistinguishable.
    a. Yi FX, Magness RR, Bird IM. Simultaneous imaging of [Ca2+]i and intracellular NO production in freshly isolated uterine artery endothelial cells: effects of ovarian cycle and pregnancy. Am J Physiol Regul Integr Comp Physiol. 2005 Jan;288(1):R140-8. PubMed PMID: 15297265.
    b. Yi FX, Boeldt DS, Magness RR, Bird IM. [Ca2+]i signaling vs. eNOS expression as determinants of NO output in uterine artery endothelium: relative roles in pregnancy adaptation and reversal by VEGF165. Am J Physiol Heart Circ Physiol. 2011 Apr;300(4):H1182-93. PubMed PMID: 21239633; PubMed Central PMCID: PMC3075018.
    c. Krupp J, Boeldt DS, Yi FX, Grummer MA, Bankowski Anaya HA, Shah DM, Bird IM. The loss of sustained Ca(2+) signaling underlies suppressed endothelial nitric oxide production in preeclamptic pregnancies: implications for new therapy. Am J Physiol Heart Circ Physiol. 2013 Oct 1;305(7):H969-79. PubMed PMID: 23893163; PubMed Central PMCID: PMC3798749.

D. RESEARCH SUPPORT

Ongoing Research Support

2015/04/01-2019/06/30
R13 HD036244, NIH
BIRD, IAN (PI)
Perinatal Research Society Annual Meeting
Role: PI

2014/05/01-2019/04/30
T32 HD41921, NIH
BIRD, IAN (PI)
Endocrinology and Reproductive Physiology Training Grant
Role: PI

2013/07/01-2018/06/30
P01 HD38843, NIH
Magness, Ronald R (PI)
Importance of Endothelial Cell-Cell Communication at the Maternal Fetal Interface
Project Leader Project 1 Director Core C
Role: CPI

2013/07/01-2018/06/30
R13 HD079163, NIH
BIRD, IAN (PI)
Perinatal Research Society YI Grants Writing Workshop
Role: PI

2012/05/01-2017/04/30
T32 HD049302, NIH
Gloria Sarto (PI)
Health Disparities Research Scholars
Role: Co-Investigator

2012/02/01-2017/01/31
R25, NIH
Mary Carnes (PI)
Training and Education to Advance Minorities in Science (TEAM-Science)
Role: Co-Investigator

2011/05/01-2016/04/30
R01 HL079020, NIH
BIRD, IAN (PI)
Pregnancy/NO Induced Changes in UAE Ca2+ Signaling
Role: PI

Completed Research Support

2009/07/01-2014/06/30

R01 HL093282, NIH
Murphy, William L (PI)
Biomaterials for local regulation of growth factor signaling
Role: Co-Investigator

2009/05/01-2014/04/30
T32 HD41921, NIH
BIRD, IAN (PI)
Endocrinology and Reproductive Physiology Training Grant
Role: PI

2011/07/01-2013/06/30
R21 HD069181, NIH
BIRD, IAN (PI)
Vascular Endothelial Dysfunction in Preeclampsia
Role: PI

2007/07/01-2012/06/30
RO1 HL087144, NIH
Magness, Ronald R (PI)
Physiologic Cardiovascular and Uterine eNOS responses: Role of Endogenous Estrogen in Pregnancy
Role: Co-Investigator

2007/04/01-2012/03/31
P01 HD38843, NIH
Magness, Ronald R (PI)
Mechanisms of Endothelial and Embryonic Stem Cell Regulation in Pregnancy
Project Leader project 1 Co-Director Core C
Role: CPI