BIOGRAPHICAL SKETCH

NAME: Bhandari, Ramji Kumar

eRA COMMONS USER NAME: BHANDARI2

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Bangladesh Agricultural University, Bangladesh	B.S.	06/97	Fisheries (Hons)
Bangladesh Agricultural University, Bangladesh	M.S.	12/98	Aquaculture
Hokkaido University, Sapporo, Japan	Ph.D.	03/02	Fish Biology
National Institute for Basic Biology, Japan	Postdoctoral Fellow	09/06	Developmental Plasticity/ Reproductive Biology
Washington State University, Pullman, WA	Postdoctoral Fellow	10/2011	Developmental Biology/ Environmental Epigenetics

A. Personal Statement

Nearly all diseases result from a complex interaction between an individual's genetic make-up and the environmental agents that he or she is exposed to (NIEHS, 2016). Some exposure effects appear as direct toxic effects, while others appear in subsequent generations due to past ancestral exposures. My research mission is to understand molecular underpinnings of environmentally induced developmental origins of adult onset and transgenerational health abnormalities. My laboratory takes comparative, molecular, cellular, and bioinformatics approaches and utilizes *in vitro* human cell co-culture (3D spheroids) and *in vivo* animal models. Together with Dr. Michael Skinner, we demonstrated transgenerational health effects in the offspring of rats several generations after exposure to pesticides had ceased and identified exposure-specific and disease-associated epigenetic mutations (epimutations) in the germ cells and sperm suggesting current health effects have epigenetic links to past ancestral exposures. Later, my laboratory demonstrated reproductive effects in fish in the third and fourth generation caused by ancestral exposure to bisphenol A (BPA) and birth control pill component (17α-ethinylestradiol, EE2). We are currently examining what epigenetic marks are established in germ stem cells by developmental BPA exposure and in what form these epigenetic marks (DNA methylation and miRNAs) are inherited by offspring across three generations. We are also focusing on whether these epigenetic marks can predict phenotypes with adverse health, such as infertility, altered mate preference, obesity, and tumorigenesis. We have identified unique epimutations that persist across three generations and transfer from germ cells to soma at F2 and F3 generations. We are also developing CRISPR-dCas9 tools to edit epimutations in transgenerational models.

As a PI, I have knowledge, training, expertise, and motivation necessary to successfully conduct environmentally induced transgenerational health research. My laboratory has equipment and resources to independently perform experiments on developmental biology, molecular biology, reproductive biology, environmental epigenetics, and transgenerational inheritance.

1. Skinner M.K., Haque M.M., Nilsson E., Bhandari R.K., McCarrey J.R. (2013). Environmentally induced transgenerational epigenetic reprogramming of primordial germ cells and the subsequent germ line. *PLoS One. 15;8(7):e66318* . PMID: 23869203
2. Bhandari, R.K., vom Saal, F.S., Tillitt, D.E. (2015). Transgenerational effects from developmental exposures to bisphenol A or 17α-ethinylestradiol in medaka, *Oryzias latipes*. *Scientific Reports.* 5: 9303. PMID: 25790734
3. Skinner, M.K., Bhandari, R.K., Haque, M.M., Nilsson, E.E. (2016). Environmentally induced epigenetic transgenerational inheritance of altered SRY genomic binding during gonadal sex determination.

Environmental Epigenetics. 2015:1-10. doi:10.1093/eep/dvv004

4. Bhandari, R.K. (2016). Medaka as a model for studying environmentally induced epigenetic transgenerational inheritance of phenotypes. Environmental Epigenetics. 2016, 1–9.

B. Positions and Honors

B1. Positions and Employment

2002-2003 Lecturer, University of the Ryukyus, Okinawa, Japan
2003-2006 Postdoctoral Fellow with Dr. Yoshitaka Nagahama, National Institute for Basic Biology, Japan
2006-2011 Postdoctoral Research Associate with Dr. Michael Skinner, Washington State University, Pullman, WA.
2011- 2012 Assistant Research Professor, Department of Physiological Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL.
2012- 2016 Assistant Research Professor, Division of Biological Sciences, University of Missouri-Columbia, Columbia, MO.
2012- Visiting Scientist, USGS Columbia Environmental Research Center, Columbia, MO.
08/2016 - Assistant Professor, Biology Department, University of North Carolina at Greensboro, NC.

B2. Other Experience and Professional Memberships

2001-2006 Member, Fisheries Society of Japan
2002-2007 Member, Zoological Society of Japan
2008- Member, Society for Study of Reproduction
2012- Member, Society for Developmental Biology
2014- Member, Society of Environmental Toxicology and Chemistry

B3. Honors

2018 Bernard and Glickman Dean's Professorship Award for Teaching & Research Excellence, UNCG
2007 Young Researcher Award | Zoological Society of Japan
2008 Lalor Foundation Merit Award | Society for Study of Reproduction
2011 Outstanding Postdoctoral Presentation Award | CRB | Washington State University
2011 Lalor Foundation Merit Award | Society for Study of Reproduction

C. Contribution to Science

1. **Epigenetic reprogramming of medaka embryo and its developing germ cells (*Current*)**: My laboratory is studying epigenetic programming of medaka embryo, especially DNA methylation dynamics, expression profile of DNA methyltransferases (*Dnmt*) and *Tet* genes, and miRNAs during early embryogenesis. We have identified DNA methylation reprogramming events in medaka embryo during early cleavage stage and in primordial germ cells during embryogenesis and post-empbryonic stages. This finding has allowed us to design studies concerning study stressor-induced epigenetic effects in germline and their transgenerational inheritance by future generations. We are unraveling epigenetic signatures that are established by BPA exposure on germ cells and examining whether these signatures can survive reprogramming events and be transgenerationally inherited by offspring. At the same time, we are also profiling circulating miRNAs to identify biomarkers of past BPA exposure and current reproductive impairment in adult males. Our ultimate aim from this project is to correlate transgenerational epimutations/miRNAs with history of past exposure to BPA and associated phenotypes and design epigenome editing tools to recover transgenerational healthy phenotype via removing epimutations *in vivo*.
    a. Wang, X., Bhandari, R.K. Global genome methylation changes during early embryonic development in medaka, *Oryzias latipes*. Cell Reports (*under peer-review*)
    b. Wang, X., Bhandari, R.K. Epigenetic reprogramming of primordial germ cells in medaka embryo. Molecular Cell (*under peer-review*).
    c. Cleary, J.C., Tillitt, D.E., vom Saal, F.S., Bhandari, RK. Transgenerational effects of developmental Atrazine exposure on reproductive axis of medaka fish. (Scientific Reports, *under peer-review*)
    d. Thayil, A., vom Saal, F.S., Tillitt, D.E., Bhandari, R.K. Environmentally induced transgenerational epimutations in germline and soma. (Epigenetics, *under peer-review*)

2. **Transgenerational inheritance of environmentally induced phenotypes**: Epigenetic changes control the way genetic information is expressed without altering genetic codes stored in DNA. Environmental exposures can induce epigenetic changes, but the extent of epigenetic damage depends on life history stages of the organism exposed. Our laboratory is trying to understand how environmental stressors (chemical or non-chemical) can induce epigenetic changes that result in adverse health outcomes or disease. Utilizing fish and rodents as models, we are trying to pinpoint the epigenetic changes that lead to harmful health effects.
    a. Bhandari, R.K. (2016). Medaka as a model for studying environmentally induced transgenerational inheritance phenotypes. Environmental Epigenetics 2:1-9.
    b. Bhandari R.K., vom Saal, F.S., Tillitt, D. E. (2015). Transgenerational effects from early developmental exposures to bisphenol A or 17α-ethinylestradiol in medaka, Oryzias latipes. Scientific Reports, 5 : 9303.
    c. Skinner, M.K., Bhandari, R.K., Haque, M.M., Nilsson, E.E. (2015). Environmentally induced epigenetic transgenerational inheritance of altered SRY genomic binding during gonadal sex determination. Environmental Epigenetics 1: 1-10. doi: 10.1093/eep/evv004
    d. Skinner MK, Guerrero-Bosagna C, Haque M, Nilsson E, Bhandari RK, McCarrey JR (2013) Environmentally induced transgenerational epigenetic reprogramming of primordial germ cells and the subsequent germ line. PLoS One. 8(7):e66318.

3. **Molecular mechanism of sex determination in mammals:** I studied molecular mechanisms of fetal gonad development in the rat. I took a ChIP-on-chip promoter tiling array approach to identify targets of sex determining factor proteins in fetal rat Sertoli cells. Several direct and indirect target genes of sex determining factors, SRY and SOX9, were identified in the developing rat testis. Among them were some basic helix-loop-helix (bHLH) transcription factors. Further investigation of their roles in gonadogenesis revealed their ability to promote Sertoli cell differentiation in the testis, *in vitro*. Germline mutation led to female-to-male sex reversal and loss of kidneys.
    a. Bhandari R.K, Haque M.M. & Skinner M.K. (2012). Global genome analysis of the downstream binding targets of testis determining factor SRY and SOX9. *PLoS One. 2012;7(9):e43380*
    b. Bhandari, R.K., Schinke, E.N., Haque, M.M., & Skinner, M.K. (2012). SRY-induced TCF21 genome- wide targets and cascade of bHLH factors during Sertoli cell differentiation and male sex determination in the rat. *Biology of Reproduction, 87: 131-136.*
    c. Bhandari, R.K., Clement, T., Sadler-Riggleman, I. & Skinner, M.K. (2011). Basic helix-loop- helix transcription factor Tcf21 is a downstream target of male sex determining gene Sry. *PLoS One,* 6(5): e19935. pp1-11.
    d. Clement, T*., Bhandari, R.K*., Riggleman, I. & Skinner, M.K. (2011). *Sry* directly regulates Neurotrophin-3 promoter during male sex determination and testis development (*Equally contributing first authors). *Biology of Reproduction.* 85: 277-284.

Complete List of My Published Work
Pubmed: http://www.ncbi.nlm.nih.gov/pubmed/?term=Ramji+Bhandari

D. Research Support

NIH R21 Exploratory/Developmental Research Grant (ICER)
(*1R21ES027123*) 04/01/2017-03/31/2019
"Germline transmission of epigenetic alterations to offspring induced by bisphenol A exposure".
This research concerns epigenetic reprogramming of early medaka embryo and their germ cells. Additionally, it will identify epigenetic signatures established by developmental exposure to BPA that escape epigenetic reprogramming in germ cells across three generations.
Role: PI

US Geological Survey- Cooperative Ecosystem Studies Units
(*G15AS00092*) 08/15/2015-12/31/2018
Transgenerational effects of atrazine exposure in medaka, *Oryzias latipes*.

This research concerns the long-term, transgenerational effects of developmental exposure to atrazine (broadleaf herbicide) on reproduction, histone proteins, and miRNA in medaka germ cells across four generations.
Role: PI

Mizzou Advantage Fund, University of Missouri
Mizzou Advantage Grant 07/01/2014-3/15/2019
Endocrine disruption of the epigenome across taxa
This research concerns the effects of bisphenol A on brain and spermatogonial stem cell transcriptome and epigenome in three classes of vertebrates: fish, turtles, and mice.
Role: Co-PI (*Dr. Cheryl Rosenfeld, PI*)

Faculty Startup Package
University of North Carolina Greensboro 08/01/2016-12/31/2018
This start up package supports facility, equipment, personnel salary, and lab supplies.