BIOGRAPHICAL SKETCH

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NAME: Moshmi Bhattacharya

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

POSITION TITLE: Associate Professor of Medicine

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
The University of the West Indies, Trinidad	B.Sc.	05/92	Natural Sciences
McGill University, Montreal, Quebec, Canada	Ph.D.	02/2000	Pharmacology & Therapeutics
Robarts Research Institute, Ontario, Canada	Postdoctoral	12/2004	Cell Biology

A. Personal Statement

I am an Associate Professor of Medicine (tenure track) at Rutgers-Robert Wood Johnson Medical School. Prior to this appointment (08/2017), I was an Associate Professor of Physiology and Pharmacology (with tenure, 2005-2017) at Western University in Ontario, and I was supported by federal salary awards from the Canadian Institutes of Health Research (CIHR, 2010-2016, equivalent to NIH R01) and Natural Sciences and Engineering Research Council (NSERC, 2005-2010). My past studies have been continuously funded by the Canadian Federal and Provincial Governments (2005-2021).

I am a cell biologist by training with expertise in G protein coupled receptors (GPCRs) signal transduction and my research focuses on understanding the molecular mechanisms by which GPCR such as the kisspeptin receptor (KISS1R) regulates health and disease. Specifically, we are interested in studying the molecular mechanisms by which KISS1R signaling regulates metabolic reprograming in liver disease and in cancer metastasis. These multidisciplinary studies are conducted using cell and 3-D culture models, genetically engineered mouse models as well as clinical samples.

I have successfully collaborated with other researchers and to date, produced over 55 peer-reviewed publications as senior-author or co-author, in highly respected journals. I have been involved in conducting biomedical research and mentoring students and fellows for over 18 years and to date. Additionally, the mentees have received numerous training and career development awards including a NIH F31 award and NSERC, Ontario Graduate Scholarship, and CIHR studentships (in Canada) and have graduated with first-author papers and co-authored papers that have been published in reputable journals.

1. Cvetković D, Babwah AV, **Bhattacharya M**. KISS1R induces invasiveness of estrogen receptor-negative human mammary epithelial and breast cancer cells. *Endocrinology* 154:1999-2014 (2013). PMID: 23525242

2. Noonan M, Bracksone M, Wondisford F, Babwah A, **Bhattacharya** M. The matrix protein Fibulin-3 promotes KISS1R induced triple negative breast cancer cell invasion. *Oncotarget* 9:30034-30052 (2018). PMC: 6059025.

3. Dragan M, Nguyen M-U, Guzman S, Goertzen C, Brackstone M, Dhillo WS, Bech PR, Clarke S, Abbara A, Tuck AB, Hess DA, Pine S, Zong W-X, Wondisford FE, Su X, Babwah AV, **Bhattacharya M**. G protein-coupled kisspeptin receptor induces metabolic reprograming and tumorigenesis in estrogen receptor-negative breast cancer. *Cell Death & Dis.* 11(2):106 (2020). PMCID: PMC7005685

4. Guzman S, Dragan M, Kwon H, de Oliveira V, Rao S, Bhatt V, Kalemba K, Shah A, Rustgi V, Wang H, Bech P, Abbara A, Izzi-Engbeaya C, Manousou P, Guo Y, Guo G, Radovick S, Dhillo W, *Wondisford F, *Babwah A *__Bhattacharya M__. Targeting hepatic kisspeptin receptor ameliorates non-alcoholic fatty liver disease. *Journal of Clinical Investigation*; 132: e145889 (2022) * co-senior authors. PMID: 35349482

Ongoing projects:

NIH R01 DK129870-01 Bhattacharya, M (PI)
Title: Hepatic fat accumulation in nonalcoholic fatty liver disease: critical regulation by kisspeptin
04/01/2022- 03/31/2026

NJHF Bhattacharya, M (PI)
Title: Kisspeptin receptor agonist for the treatment of liver fibrosis
02/15/2023- 02/14/2024

Canadian Institutes of Health Research (Federal Operating Grant)
Bhattacharya (PI) M Brackstone (CoPI)
Targeting triple negative breast cancer: Role of KISS1R (Rutgers Grant Transfer # 42356/CRT-17-401).
10/2017-04/2024

B. Positions and Honors

Positions and Employment

08/2017-present	Associate Professor (tenure-track), Department of Medicine, Robert Wood Johnson Medical School, Rutgers Biomedical and Health Sciences, New Brunswick, NJ
08/2017-present	Adjunct Professor, Department of Oncology, Schulich School of Medicine & Dentistry, University of Western Ontario, London, Ontario, Canada
07/2011-07/17	Associate Professor (tenured), Department of Physiology and Pharmacology, Department of Oncology (cross-appointment), Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada
05/2005-06/11	Assistant Professor (tenure track), Department of Physiology and Pharmacology, Schulich School of Medicine & Dentistry, University of Western Ontario, Canada Adjunct Professor, Department of Oncology, University of Western Ontario, Canada

Other Experiences and Professional Memberships (Selected)

2023	Grant Reviewer, NIH NIDDK (CSME), Ad-Hoc
2022	Grant Reviewer, NIH NIDDK (EMNR), Ad-Hoc
2020-	American Association for the Study of Liver Disease (AASLD)
2017-present	Cancer Institute of New Jersey, Associate Member I: Cancer Metabolism & Growth
2017-2018	Grant Reviewer (Ad-Hoc), Breast Cancer Now, United Kingdom,
2015-2017	Grant Reviewer, Canadian Institutes of Health Research, Project scheme
2014-2019	Editorial Board, Oncology Reports
2012-2015	Grant Reviewer, Canadian Breast Cancer Foundation, Review Panel A
2011-2012	Grant Reviewer, Canadian Institutes of Health Research: Pharmaceutical Sciences
2007-2016	Grant Reviewer, Natural Sciences and Engineering Research Council (NSERC)
2008-present	Metastasis Research Society
2007-present	American Association for Cancer Research

Honors (Selected)

2010-2015	Early Researcher Award, Ministry of Research and Innovation, Government of Ontario
2010-2016	Canadian Institutes of Health Research (CIHR) New Investigator Salary Award
2014-2015	Excellence in Undergraduate Teaching, University of Western Ontario, Canada
2005-2010	Natural Sciences and Engineering Research Council University Faculty Salary Award *(Ranked #1 nationally)*
2003	Postdoctoral Scientist Award, 1st Prize Winner, American Society for Pharmacological and Experimental Therapeutics (ASPET), Experimental Biology, San Diego, CA
1999-2003	Canadian Institutes of Health Research Postdoctoral Fellowship
1997-1999	Claude J.P. Giroud Bursary, Faculty of Medicine, McGill University, Montreal, Canada

1998-2001	Canadian Institutes of Health Research, Doctoral Research Award
1998	Melville Prize in Pharmacology, Dept of Pharmacology & Therapeutics, McGill University
1996-1997	Telethon of Stars Research Centre, St. Justine Hospital, Montreal, QC, Canada

C. Contribution to Science (59 publications, H-index: 32)
The focus of my research over the last decade has been understanding the physiological role of KISS1R on the neuroendocrine control of reproduction (collaborative studies with Andy Babwah), the pathophysiological roles of KISS1R in cancer metabolism and metastasis and more recently, the association of KISS1R with metabolic function in the liver.

1. **Nuclear GPCRs**. My earliest contributions to science as a Canadian Institutes of Health Research (MRC), Doctoral Research Award trainee were during my thesis studies in the Department of Pharmacology and Therapeutics, at McGill University, Montreal, in the laboratory of Neonatologist, Dr. Sylvain Chemtob. The goal of my studies was to understand the signaling of prostaglandin E_2 (PGE_2) receptors in neonatal endothelial cells. PGE_2 is known to signal via plasma membrane bound G protein-coupled EP receptors. However, we found that PGE_2 produced endogenously in cells, rapidly stimulated gene transcription. This led to our discovery that functional PGE_2 receptors were localized not only at the cell surface, but also on nuclear membranes *in vivo*. At that time, this discovery challenged researchers to reassess GPCR signaling based solely on the existence of a plasma membrane-bound receptor. These two publications (combined citation of 613) led the way to the now established field of nuclear GPCRs. This resulted in a paradigm shift in our understanding of how GPCRs signals and proposed new avenues for the intracellular actions of prostanoids.

a. **Bhattacharya M**, Peri KG, Almazan G, Ribeiro-da-Silva A, Shichi H, Durocher Y, Abramovitz M, Hou X, Varma DR, Chemtob S. Nuclear localization of prostaglandin E2 receptors. *Proc Natl Acad Sci U S A*. 95(26):15792-7 (1998) PMCID: PMC28123

b. **Bhattacharya M**, Peri K, Ribeiro-da-Silva A, Almazan G, Shichi H, Hou X, Varma DR, Chemtob S Localization of functional prostaglandin E2 receptors EP3 and EP4 in the nuclear envelope. *J Biol Chem.* 274(22):15719-24 (1999). PMID: 10336471

c. Gobeil F Jr, Marrache AM, **Bhattacharya M**, Checchin D, Bkaily G, Lachapelle P, Ribeiro-Da-Silva A, Chemtob S. Nuclear prostaglandin signaling system: biogenesis and actions via heptahelical receptors. *Can J Physiol Pharmacol*. 81(2):196-204 (2003). PMID: 12710534

2. **Discovering that GPCRs regulates the cytoskeleton via β-arrestin.** As a Canadian Institutes of Health Research postdoctoral fellow in Cell Biology at the Robarts Research Institute, in Ontario Canada, I continued developing my interest in GPCR signal transduction. I initiated studies on deciphering the molecular mechanisms by which GPCRs stimulate cell motility. My studies led to the novel discovery that upon activation by certain GPCRs, the GPCR adaptor protein, β-arrestin regulates cytoskeletal reorganization of motile cells such as neutrophils. Specifically, I found β-arrestin regulates the activity of small GTPases such a Ral. Our pioneering work has discussed in many top-review articles. I was invited by the American Society for Pharmacology and Experimental Therapeutics to present these findings at Experimental Biology 2003, San Diego, CA, and was subsequently awarded the top prize in the Research Fellow Category. This study formed the basis for ongoing research in my independent lab.

a. **Bhattacharya M**, Anborgh PH, Babwah AV, Dale LB, Dobransky T, Benovic JL, Feldman RD, Verdi JM, Ferguson SS. Beta-arrestins regulate a Ral-GDS Ral effector pathway that mediates cytoskeletal reorganization. *Nat. Cell Biol.* 4(8):547-55 (2002). PMID: 12105416

b. **Bhattacharya M**, Babwah AV, Godin C, Anborgh PH, Dale LB, Ferguson SS. Ral and phospholipase D2-dependent pathway for constitutive metabotropic glutamate receptor endocytosis. *J Neurosci.* 24(40):8752-61 (2004). PMCID: PMC6729950

c. **Bhattacharya M**, Babwah AV, Ferguson SS. Small GTP-binding protein-coupled receptors. *Biochem Soc Trans*. 32(Pt 6):1040-4 (2004). PMID: 15506958

3. **Discovering that KISS1R stimulates malignant transformation of ERα-negative mammary cells, reprograms metabolism of primary TNBC tumors and promotes metastasis *in vivo***. As an independent investigator, I developed a research program with the goal of understanding how GPCRs such as the kisspeptin receptor (KISS1R) regulate the cytoskeleton, to thereby promote cell migration and invasion. Kisspeptins are peptide products of *KISS1*, classified as a metastasis suppressor gene and thus activation of KISS1R receptor signaling typically has *anti-cancer* roles. We found that KISS1R signaling is altered in breast cancer cells, compared to normal breast cells. Specifically, we found that estrogen receptor (ERα) critically regulates KISS1R expression and activity, and when ERα is lost from mammary cells, as in triple negative breast cancer (TNBC), KISS1R promotes tumor cell migration, and invasion. Mechanistically, we found KISS1R stimulates epithelial-to-mesenchymal transition and promotes cell invasion by promoting invadopodia formation and activating EGFR. In contrast, KISS1R failed to promote cell migration and invasion of ER-positive breast cancer cells. This work received attention in the lay and scientific communities, including a feature story entitled "Kisspeptins and breast cancer" *on Canadian National TV-CTV2 News, Science Daily* "When a KISS goes bad" (April 16, 2013) in addition to receiving an Editorial feature. Furthermore, we demonstrated KISS1R signaling induced 'glutamine addiction' phenotype of primary tumors by increasing c-Myc and glutaminase levels and that KISS1R promotes metastasis *in vivo,* using pre-clinial xenograft mouse models.

a. Cvetković D, Dragan M, Pape C, Leong HS, Pampillo M, **Bhattacharya M**. KISS1R induces invasiveness of estrogen receptor-negative human mammary epithelial and breast cancer cells. *Endocrinology* 154:1999-2014 (2013). PMID: 23525242
[*Journal Cover Feature* and editorial review in Endocrinology; González C. 'Deepening on breast cancer metastasis: the ERα-mediated modulation of KISS/KISS1R system']. PMID: 23687110

b. Noonan M, Dragan D, Dragan, M, Mehta M, Hess, DA, Bracksone M, Tuck A, Wondisford F, Babwah AVB, **Bhattacharya** M. The matrix protein Fibulin-3 promotes KISS1R induced triple negative breast cancer cell invasion. *Oncotarget* 9:30034-30052 (2018). PMCID: PMC6059025

c. Guzman S, Brackstone M, Radovick S, Babwah AV, **Bhattacharya M**. KISS1/KISS1R in Cancer: Friend or Foe*? Front. Endocrinol. (Lausanne)* 9: 437 (2018). Invited Review. PMCID: PMC6085450

d. Dragan M, Nguyen M-U, Guzman S, Goertzen C, Brackstone M, Dhillo WS, Abbara A, Tuck AB, Hess DA, Pine S, Wondisford FE, Su X, Babwah AV, **Bhattacharya M**. G protein-coupled kisspeptin receptor induces metabolic reprograming and tumorigenesis in estrogen receptor-negative breast cancer. *Cell Death & Dis.*11(2):106 (2020). PMCID: PMC7005685

4. **Uncovering that KISS1R signaling regulates hepatic lipogenesis**. The role of peripheral kisspeptin signaling is poorly understood and the function of KISS1R in the liver cells (hepatocytes) was not known. In recent collaborative studies, we were the first to demonstrate that activation of KISS1R signaling inhibits fat metabolism in hepatocytes, and thus protect against the development of fatty liver (steatosis) and disease progression. These studies lay the groundwork of the proposed work in this NJHF application.

a. Guzman S, Dragan M, Kwon H, de Oliveira V, Rao S, Bhatt V, Kalemba K, Shah A, Rustgi V, Wang H, Bech P, Abbara A, Izzi-Engbeaya C, Manousou P, Guo Y, Guo G, Radovick S, Dhillo W, *Wondisford F, *Babwah A *Bhattacharya M. Targeting hepatic kisspeptin receptor ameliorates non-alcoholic fatty liver disease. *Journal of Clinical Investigation*; 132: e145889 (2022) * co-senior authors. PMID: 35349482

b. **Bhattacharya M**, Babwah AV. Kisspeptin: Beyond the brain*. Endocrinology*, 156:1218-27 (2015). PMID: 25590245

5. **PCT Patent Application** PCT/US21/70363 (RU Docket #2020-071); "Modified Kisspeptin Receptor Agonists for Fatty Liver Disease' (Principal Inventor: M. Bhattacharya; Co-Inventors: A. Babwah, F. Wondisford, S. Radovick): details described in grant Research proposal

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/moshmi.bhattacharya.1/bibliography/public/