BIOGRAPHICAL SKETCH
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NAME: Md Sazzad Hassan

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

POSITION TITLE: Assistant Research 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
Dhaka Medical College, Dhaka, Bangladesh	M.D.	1982-1988	Medicine & Surgery
Kobe University School of Medicine, Kobe, Japan	Ph.D.	1994-1998	Medical Science/Cell Biology
University of Massachusetts Medical School, Worcester, MA	Postdoc	2001-2006	Physiology

A. Personal Statement

I have over 20 years of experience in medical research and my research has focused on human cancers and utilized mouse model systems as well as *in vitro* cellular and molecular studies. Our laboratory investigates signaling pathways that control apoptosis in esophageal cancer cells. In collaboration with clinical gastroenterologist and oncologist I have been working to find a novel and more effective therapeutic strategy for esophageal cancer. We are interested to define novel mechanisms regarding the transition to esophageal adenocarcinoma that could provide valuable insights for molecular diagnosis and to identify new targets for drug intervention. We develop and validate novel *in vitro and in-vivo* model which lead us to its use in future studies on esophageal adenocarcinoma pathogenesis, progression and for the screening of therapeutic drugs. Our goal is to establish and characterize novel *in vitro and in-vivo* models for screening of anticancer drugs of esophageal adenocarcinoma therapy. My extensive experience in cell culture, cancer biology and regenerative medicine is valuable asset for the project. Over the recent years we have described a network of signaling pathways that regulate survival of cancer cells and identified BAD (a BH3-only member of Bcl2 family) as a convergence node of multiple anti-apoptotic signaling pathways. We were first to demonstrate that stress hormone epinephrine protects prostate cancer cells from apoptosis via PKA/BAD signaling pathway and described the role of this signaling pathway in therapy resistance and progression of prostate tumors *in vivo*.

B. Positions and Honors

Positions and Employment

1988-1989 Dhaka Medical College Hospital, Department of Internal Medicine, Dhaka Bangladesh, Internship

1993-1994 Kobe University School of Medicine, Department of Medicine, Kobe, Japan, Research Fellow

1994-1998 Kobe University School of Medicine, Department of Medicine, Kobe, Japan, Ph.D. Student

1998-2001	Laboratory Sciences Division, International Center for Diarrhoeal Disease Research, Dhaka, Bangladesh, Research Associate
2001-2006	Univ. of Mass. Med. Sch., Department of Physiology, Postdoctoral Research Associate
2006-2008	Univ. of Mass. Med. Sch., Department of Physiology, Instructor
2008-2009	Univ. of Mass. Med. Sch., Department of Surgery, Instructor
2009-2011	Wake Forest Univ. Sch. of Med., Department of Cancer Biology, Research Fellow
2012-2015	Wake Forest Univ. Sch. of Med., Department of Cancer Biology & WFIRM, Instructor
2015-present	Indiana University School of Medicine - South Bend, Assistant Research Professor

Awards and Services

2011	Research Day Judge, Wake Forest University 11th Annual Graduate Student and Postdoc Research Day
2010	Best Poster Award, Wake Forest University Cancer Biology 2010 Retreat
2008	Society for Basic Urological Research (SBUR) Travel Award
2003	Young Investigator Award from International Neuropeptide Society for 2003 Neuropeptide Conference
2000	Recipient of monetary award for research from French Science Foundation
1993 – 1998	Recipient of the prestigious and highly selected candidate of Monbusho (Japanese Government) Research Scholarship and award

C. Contribution to Science

1. Role of prostaglandin (PGE2) and its receptor subtypes in the regulation of gastrointestinal function. We established a primary culture of rat gastric mucosal cell by isolating proliferating cells from rat gastric mucosal epithelium using counterflow elutriation. We then characterize this primary culture and found that it differentiate into mucous producing cells expressing prostaglandin EP4 receptor. This primary culture has immense importance in studying the role of different drugs on gastric mucosal biology. We then established an epithelial cell line from gastric mucosa of adult Wistar rats named RGM-1. This was the first gastric mucosal cell line ever established. In this study, we characterized this newly established cell line and found that it expressed prostaglandin EP4 receptor but not EP1 and EP3 receptor. The results in this study suggested that RGM-1 may be a useful model of gastric mucosal cells and that PGE2 plays a role on mucin synthesis in RGM-1 cells via EP4 receptors. We then further studied the role of prostaglandin in the regulation of the gastrointestinal functions. Gene expression of prostaglandin receptors along the rat gastrointestinal tracts were investigated and suggested that prostaglandin E2 (PGE2) modulates gastrointestinal functions through at least three different prostaglandin receptors (EP1, EP3, and EP4), each of which has a distinct contribution in the gastrointestinal tract.

a. **Hassan S**, Nakata H, Asahara M, Matsushima Y, Kawanami C, Ping CY, Min D, Nakamura A and Chiba T. “Establishment of primary cell culture from elutriated rat gastric mucosal cells” J Gastroenterol 1995; 30: 135-141.
b. **Hassan S**, Kinoshita Y, Min D, Nakata H, Kishi K, Matsushima Y, Asahara M, Wang, HY, Okada A, Maekawa T, Matsui H and Chiba T. “Presence of prostaglandin EP4 receptor gene expression in a rat gastric mucosal cell line” Digestion 1996; 57: 196-200.
c. Min D, Kinoshita Y, Kishi K, Nakata H, **Hassan S**, Kawanami C, Sugimoto Y, Katsuyama M, Negishi M, Narumiya S, Ichikawa A and Chiba T. “Distribution of prostaglandin E receptors in the rat gastrointestinal tract” Prostaglandins 1997; 53: 199-216.

2. Mechanisms of gastric mucosal lesions and role of growth factor in its healing.

During my graduate study our lab in Kobe University school of Medicine, Japan had main interest in studying the role of growth factors including gut-brain peptides in gastric mucosal healing as well as cancer cell proliferation. In this regard, we studied the role of keratinocyte/hepatocyte growth factors, erythropoietin, regeneration gene protein, stem cell factor and gastrin in gastric mucosal healing/proliferation in health and diseases. We also studied the role of these growth factors in gastrointestinal cancer cell proliferation which has led to designing novel anticancer therapeutics.

a. Kinoshita Y, Nakata H, **Hassan S**, Asahara M, Kawanami C, Matsushima Y, Naribayashi Y, Ping CY, Min D, Nakamura A and Chiba T. "Gene expression of Keratinocyte and Hepatocyte growth factors during the healing of rat gastric mucosal lesions" Gastroenterology 1995; 1068-1077.
b. Kinoshita Y, **Hassan MS,** Matsushima Y, Okada A, Maekawa T, Fukui H, Waki S, Wang HY, Kishi K and Chiba T. "Increased hepatocyte growth factor content in rat stomach during omeprazole treatment" Digestion 1998; 59(2): 102-109.
c. Fukui H, Kinoshita Y, Maekawa T, Okada A, Waki S, **Hassan S,** Okamoto H and Chiba T. "Regeneration gene protein may mediate gastric mucosal proliferation induced by hypergastrinemia in rats" Gastroenterology 1998; 115:1483-1493.
d. **Hassan S**, Kinoshita Y, Kawanami C, Kishi K, Matsushima Y, Ohashi A, Funasaka Y, Okada A, Maekawa T, Wang HY, and Chiba T. " Expression of the proto-oncogene *c-kit* and its ligand stem cell factor (SCF) in gastric carcinoma cell lines" Digestive Diseases and Science 1998; 43(1): 8-14.

3. Signaling mechanisms of gut-brain peptide neurotensin induced prostate cancer cell growth.
Dietary fats increase the risk of prostate cancer, stimulate release of intestinal neurotensin (NT), a growth-promoting peptide. This led us to study the role of NT in prostate cancer cells growth. We discovered some novel findings like NT can activate PKC, MAP-kinase, PI3-kinse and EGF-receptor pathways in prostate cancer cells and NT receptor expression in prostate cancer cells can be used as a novel bio-marker for diagnostic and therapeutic purposes.

a. **Hassan S**, Dobner PR and Carraway RE. "Involvement of MAP-kinase, PI3-kinse and EGF-receptor in the stimulatory effect of Neurotensin on DNA synthesis in PC3 cells" Regulatory Peptides 2004; 120: 155-166.
b. **Hassan S** and Carraway RE. "Involvement of arachidonic acid metabolism and EGF receptor in neurotensin-induced prostate cancer PC3 cell growth" Regul Pept. 2006 Jan 15; 133(1-3):105-14.
c. Carraway RE, **Hassan S** and David CE. "Regulation of neurotensin receptor function by the arachidonic acid-lipoxygenase pathway in prostate cancer PC3 cells" Prostaglandins Leukot Essent Fatty Acids. 2006 Feb; 74(2):93-107.
d. Carraway RE, **Hassan S**, and Dobner PR. "Protein kinase C inhibitors alter neurotensin receptor binding and function in prostate cancer PC3 cells". Regul Pept. 2008; 147(1-3):96-109.

4. Signaling mechanisms of stress hormone epinephrine-induced prostate cancer cell growth.
We have studied a network of signaling pathways that regulate survival of prostate cancer cells and identified BAD (a BH3-only member of Bcl2 family) as a convergence node of multiple anti-apoptotic signaling pathways. We were the first to demonstrate that stress hormone epinephrine protects prostate cancer cells from apoptosis via PKA/BAD signaling pathway and described the role of this signaling pathway in therapy resistance and progression of prostate tumors *in vivo*.

a. **Hassan S**, Karpova Y, Flores A, Agostino Jr RD, Kulik G. "Surgical Stress Delays Prostate Involution in Mice" PLoS One. November 2013, 8(11):e78175.
b. Baiz D, **Hassan S**, Choi YA, Flores A, Karpova Y, Yancey D, Pullikuth A, Sui G, Sadelain M, Debinski W, Kulik G. "Combination of the PI3K Inhibitor ZSTK474 with a PSMA-Targeted Immunotoxin Accelerates Apoptosis and Regression of Prostate Cancer" Neoplasia. 2013 Oct; 15(10):1172-83.
c. **Hassan S**, Karpova Y, Baiz D, Yancey D, Pullikuth A, Register T, Cline M, Agostino Jr RD, Danial N, Datta SR and Kulik G. "Behavioral Stress Accelerates Prostate Cancer Development in Mice" Journal of Clinical Investigation (JCI). 2013 Feb 1; 123(2):874-86.

d. **Hassan S**, Karpova Y, Flores A, D'Agostino R Jr, Danhauer SC, Hemal A, Kulik G. “A pilot study of blood epinephrine levels and CREB phosphorylation in men undergoing prostate biopsies” Int Urol Nephrol. 2014 Mar; 46(3):505-10.

5. Novel combination therapies for esophageal adenocarcinoma.
We are currently investigating esophageal adenocarcinoma (EAC) focusing on evaluating combination treatment benefits of cytotoxic agents with targeted agents for the development of more effective therapeutic approaches. We have recently shown that aggressive EAC cells with elevated c-Myc expression are preferentially more sensitive to specific cyclin-dependent kinase (CDK) inhibitor induced cell-death. Thus CDK inhibitor alone or in combination with other cytotoxic or targeted agents can be a potential therapy for c-Myc overexpressing EAC. In addition, we have shown novel role IGF and HGF/Met signaling in esophageal adenocarcinoma progression. Recently in our laboratory peritoneal metastatic EAC xenograft model was successfully established after intraperitoneal injection of EAC cells and this mouse survival model of peritoneal dissemination will provide useful survival outcome assessment for evaluation of cancer therapeutics in experimental EAC.

a. **Hassan MS**, Awasthi N, Li J, Schwarz MA, Schwarz RE, von Holzen U. “A novel intraperitoneal metastatic xenograft mouse model for survival outcome assessment of esophageal adenocarcinoma” PLoS One. 2017 Feb 22; 12(2):e0171824.
b. **Hassan MS**, Awasthi N, Li J, Williams F, Schwarz MA, Schwarz RE, von Holzen U. “Superior Therapeutic Efficacy of Nanoparticle Albumin Bound Paclitaxel Over Cremophor-Bound Paclitaxel in Experimental Esophageal Adenocarcinoma” Transl Oncol. 2018 Apr; 11(2):426-435.
c. **Sazzad Hassan**, Niranjan Awasthi, Margaret A. Schwarz, Roderich E. Schwarz and Urs Von Holzen. “Therapeutic potential of the cyclin- dependent kinase inhibitor on c-Myc overexpressing esophageal adenocarcinoma” AACR 2016; Abstract #1258.
d. **Md Sazzad Hassan**, Fiona Williams, Niranjan Awasthi, Margaret A. Schwarz, Roderich E. Schwarz and Urs Von Holzen. “Enhancement of nab-paclitaxel response by inhibition of insulin-like growth factor (IGF) signaling in experimental esophageal adenocarcinoma” AACR 2018; Abstract #4813.
e. **Md Sazzad Hassan**, Fiona Williams, Niranjan Awasthi, Margaret A. Schwarz, Roderich E. Schwarz and Urs Von Holzen. “Synergistic effects of foretinib with lapatinib in MET and HER2 co-activated experimental esophageal adenocarcinoma” AACR 2018; Abstract #4826.

Complete List of Published Work in My Bibliography:
https://scholar.google.com/citations?user=0QaYqOoAAAAJ&hl=en&citsig=AMstHGS9rPiGKfTr4Up63ohrELh1bhN9cg

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Indiana University School of Medicine – South Bend
Urs von Holzen (PI) 7/1/15 – continuing
“Investigation of a novel and more effective therapeutic strategy for esophageal cancer”.
Role: **Co-Investigator**

American Cancer Society
INSTITUTIONAL RESEARCH GRANT #IRG-14-195-01
Md Sazzad Hassan (PI) 1/1/17 – 12/31/18
“Identification of genes involved in pathogenesis of esophageal adenocarcinoma using RNA sequencing from laser capture micro-dissected formalin-fixed paraffin-embedded tissue specimens”
Role: **Principal-Investigator**

Completed Research Support

1R01CA118329 George Kulik (PI) 7/1/08 - 4/30/13
NCI
“Stress-activated signaling in prostate cancer”
Grant examines mechanisms by which stress hormones influence prostate tumor growth.
Role: **Co-investigator**

PC991068 Robert Carraway (PI) 10/1/00 - 10/10/04
Department of Defense
"Prostate Cancer Cell Growth: Role of Neurotensin in Mediating Effect of Dietary Fat and Mechanism of Action"
The goal of this work is to assess the role of neurotensin in prostate cancer cell growth.
Role: **Co-investigator**

PC051202 Robert Carraway (PI) 1/1/06 – 12/31/08
US Army Medical Research and Materiel Command
“Prostate Cancer Cell Growth: Stimulatory Role of Neurotensin and Mechanism of Inhibition by Flavonoids as Related to Protein Kinase C”
The goal of this work is to define the relationship between PKC isotypes and NT signaling and also effects of flavonoids on this.
Role: **Co-Investigator**