BIOGRAPHICAL SKETCH

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NAME: Umar, Shahid

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

POSITION TITLE: Professor, Vice Chair of Research

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)	END DATE MM/YYYY	FIELD OF STUDY
Aligarh Muslim University, Aligarh, UP	BS	05/1984	Chemistry
Aligarh Muslim University, Aligarh, UP	MS	05/1986	Biochemistry
Aligarh Muslim University, Aligarh, UP	PHD	06/1993	Biochemistry

A. Personal Statement

My research interest for the last 20 years has been the epithelial biology of the colon. My laboratory employs a bacterial infection-induced murine model that involves the earliest molecular and functional changes associated with colon carcinogenesis. We are also engaged in exploring the role of bacterial infection in promoting colitis-associated colon cancer and have developed novel disease models wherein to study the prevention of colon cancer through anti-inflammatory strategies. In addition, my laboratory is also investigating the role of bacterial infection in expediting cancer progression and metastasis. As new links are constantly unveiled between microorganisms and human cancers, it is important to appreciate recent contributions that enabled a topic viewed with skepticism to evolve into a vibrant and dynamic field. More than ever, it is imperative to focus on understanding the mechanistic details of malignant transformation initiated by pathogens, an area that promises exciting prophylactic, diagnostic, and therapeutic applications.

Ongoing and recently completed projects that I would like to highlight include:

R01 DK117296
Sampath & Umar (mPI)
09/18/2018 - 07/31/2024
Single Immunoglobulin Interleukin-1 Related Receptor and Necrotizing Enterocolitis in Premature Infants

Craig H. Neilsen Foundation
Young (PI) & Umar (Co-I)
07/01/2023 – 06/30/2025
A role for CGRP in the development and chronicity of neurogenic bowel after SCI

Lied Pre-Clinical Basic Science Grant
KUMC Research Institute
Selby (PI) and Umar (Co-I)
07/01/22 – 06/30/2023
"VIVA: Volatile or IV Anesthesia for Cancer Surgery"

R01 CA185322
Umar (PI)
01/05/2015 - 12/31/2021
Epigenetics and Infection-induced EMT of Colonic Crypts - Target for Chemoprevention

Highlighted Publications:

1. Attard TM, Septer S, Lawson CE, Attard MI, Lee STM, **Umar S**. Microbiome insights into pediatric familial adenomatous polyposis. Orphanet J Rare Dis. 2022 Nov 14;17(1):416. PubMed Central PMCID: PMC9664625.
2. Martin A, Woolbright BL, **Umar S**, Ingersoll MA, Taylor JA 3rd. Bladder cancer, inflammageing and microbiomes. Nat Rev Urol. 2022 Aug;19(8):495-509. PubMed PMID: 35798831.
3. Ahmed I, Roy BC, Rao Jakkula LUM, Subramaniam D, Dandawate P, Anant S, Sampath V, **Umar S**. Infection-induced signals generated at the plasma membrane epigenetically regulate Wnt signaling *in vitro* and *in vivo*. J Biol Chem. 2020 Jan 24;295(4):1021-1035. PubMed Central PMCID: PMC6983838.
4. Ramamoorthy P, Thomas SM, Kaushik G, Subramaniam D, Chastain KM, Dhar A, Tawfik O, Kasi A, Sun W, Ramalingam S, Gunewardena S, **Umar S**, Mammen JM, Padhye SB, Weir SJ, Jensen RA, Sittampalam GS, Anant S. Metastatic Tumor-in-a-Dish, a Novel Multicellular Organoid to Study Lung Colonization and Predict Therapeutic Response. Cancer Res. 2019 Apr 1;79(7):1681-1695. PubMed Central PMCID: PMC6445669.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2017 -	Professor, University of Kansas Medical Center, Kansas City, KS
2011 - 2017	Associate Professor, University of Kansas Medical Center, Kansas City, KS
2008 - 2011	Associate Professor, University of Oklahoma Health Sciences Center, Oklahoma City, OK
2003 - 2008	Assistant Professor, University of Texas Medical Branch, Galveston, TX
2001 - 2003	Research Assistant Professor, University of Texas Health Sciences Center, Houston, TX
2000 - 2001	Research Instructor, University of Texas Health Sciences Center, Houston, TX
1996 - 2000	Research Associate, University of Texas Health Sciences Center, Houston, TX
1994 - 1996	Post-Doctoral Fellow, MD Anderson Cancer Center, Houston, TX
1993 - 1994	Research Scientist, Wockhardt Biotech, Aurangabad
1990 - 1993	Senior Research Fellow, Central Drug Research Institute, Lucknow
1987 - 1990	Junior Research Fellow, Central Drug Research Institute, Lucknow, Lucknow

Honors

2016	AGA Fellow, American Gastroenterology Association
2016	Research Awards Panelist, American Gastroenterology Association
2006	Committee Chair - GI Infection, American Gastroenterology Association
2003	Researcher of the Year, Crohn's and Colitis Foundation of America
1990	Fellowship, Bhabha Atomic Research Center
1988	Fellowship, Indian Council of Medical Reserach

C. Contribution to Science

1. The functional expression of the cystic fibrosis (CF) gene product, cystic fibrosis transmembrane conductance regulator (CFTR), is pivotal for intestinal Cl- secretion elicited by neurohormonal agonists acting both through cAMP and Ca2+. Homozygous mutations in the CFTR genome have been found to either eliminate or severely curtail the apical membrane cAMP-regulated Cl- permeability pathway in CF epithelia. The localization of CFTR mRNA and protein in the digestive tract of normal and transgenic CF mice correlates with the ability of individual epithelial cells/glands to secrete Cl- in response to cAMP agonists and identifies the intestinal crypt as the primary site of fluid secretion. However, given the proposed importance of the immature intestinal crypt cells to tissue generated cAMP-dependent Cl- transport, little is known about how CFTR expression is regulated in vivo. I was the first one to demonstrate, in a murine model, that (8-fold) colonocyte proliferation was accompanied by increased cellular CFTR mRNA and protein expression and enhanced mucosal cAMP-dependent Cl- secretion. We further showed that CFTR function in vivo can be regulated by changes in PKC isoforms expression.

a. Broughman JR, Sun L, **Umar S**, Sellin JH, Morris AP. Chronic PKC-beta2 activation in HT-29 Cl.19a colonocytes prevents cAMP-mediated ion secretion by inhibiting apical membrane CFTR targeting. Am J Physiol Gastrointest Liver Physiol. 2006 Aug;291(2):G331-44. PubMed PMID: 16574992.

b. Broughman JR, Sun L, **Umar S**, Scott J, Sellin JH, Morris AP. Chronic PKC-beta activation in HT-29 Cl.19a colonocytes prevents cAMP-mediated ion secretion by inhibiting apical membrane current generation. Am J Physiol Gastrointest Liver Physiol. 2006 Aug;291(2):G318-30. PubMed PMID: 16574993.

c. **Umar S**, Sellin JH, Morris AP. Murine colonic mucosa hyperproliferation. II. PKC-beta activation and cPKC-mediated cellular CFTR overexpression. Am J Physiol Gastrointest Liver Physiol. 2000 May;278(5):G765-74. PubMed PMID: 10801269.

d. **Umar S**, Scott J, Sellin JH, Dubinsky WP, Morris AP. Murine colonic mucosa hyperproliferation. I. Elevated CFTR expression and enhanced cAMP-dependent Cl(-) secretion. Am J Physiol Gastrointest Liver Physiol. 2000 May;278(5):G753-64. PubMed PMID: 10801268.

2. β-Catenin performs critical roles in development, cellular adhesion and oncogensis. In colon cancer, decreased E-cadherin/b-catenin association is causally linked to increased β-catenin-regulated gene expression and increased cellular division. We demonstrated for the first time in a murine model that an enteric pathogen can activate the same pathway in native colonic epithelia. Utilizing the same model, we were the first to link dramatic increases in Wnt/β-catenin and NF-kB signaling to the pathogenesis of colonic crypt hyperplasia. More recently, we have discovered that both Notch and Wnt/β-catenin pathways work in-tandem to regulate hyperplasia and/or colitis following bacterial infection.

   a. Ahmed I, Chandrakesan P, Tawfik O, Xia L, Anant S, **Umar S**. Critical roles of Notch and Wnt/β-catenin pathways in the regulation of hyperplasia and/or colitis in response to bacterial infection. Infect Immun. 2012 Sep;80(9):3107-21. PubMed Central PMCID: PMC3418747.

   b. Sellin JH, Wang Y, Singh P, **Umar S**. β-Catenin stabilization imparts crypt progenitor phenotype to hyperproliferating colonic epithelia. Exp Cell Res. 2009 Jan 1;315(1):97-109. PubMed Central PMCID: PMC2868370.

   c. **Umar S**, Wang Y, Morris AP, Sellin JH. Dual alterations in casein kinase I-epsilon and GSK-3β modulate β-catenin stability in hyperproliferating colonic epithelia. Am J Physiol Gastrointest Liver Physiol. 2007 Feb;292(2):G599-607. PubMed PMID: 17053159.

   d. **Umar S**, Wang Y, Sellin JH. Epithelial proliferation induces novel changes in APC expression. Oncogene. 2005 Oct 6;24(44):6709-18. PubMed PMID: 16007167.

3. Epithelial mesenchymal transition (EMT) is a key development program that is often activated during cancer invasion and metastasis, and also imparts a self-renewal capability to disseminating cancer cells. My laboratory focuses on how bacterial infection affects the epigenetic signaling that are implicated in the regulation of colonic stem cells and trans-differentiation of colonic epithelial cells and whether these changes facilitate colon cancer initiation and/or progression.

   a. Iyer SV, Ranjan A, Elias HK, Parrales A, Sasaki H, Roy BC, **Umar S**, Tawfik OW, Iwakuma T. Genome-wide RNAi screening identifies TMIGD3 isoform1 as a suppressor of NF-κB and osteosarcoma progression. Nat Commun. 2016 Nov 25;7:13561. PubMed Central PMCID: PMC5133659.

   b. Roy BC, Subramaniam D, Ahmed I, Jala VR, Hester CM, Greiner KA, Haribabu B, Anant S, **Umar S**. Role of bacterial infection in the epigenetic regulation of Wnt antagonist WIF1 by PRC2 protein EZH2. Oncogene. 2015 Aug 20;34(34):4519-30. PubMed Central PMCID: PMC4459936.

   c. Chandrakesan P, Roy B, Jakkula LU, Ahmed I, Ramamoorthy P, Tawfik O, Papineni R, Houchen C, Anant S, **Umar S**. Utility of a bacterial infection model to study epithelial-mesenchymal transition, mesenchymal-epithelial transition or tumorigenesis. Oncogene. 2014 May 15;33(20):2639-54. PubMed Central PMCID: PMC3883801.

   d. Chandrakesan P, Ahmed I, Chinthalapally A, Singh P, Awasthi S, Anant S, **Umar S**. Distinct compartmentalization of NF-κB activity in crypt and crypt-denuded lamina propria precedes and accompanies hyperplasia and/or colitis following bacterial infection. Infect Immun. 2012 Feb;80(2):753-67. PubMed Central PMCID: PMC3264290.