BIOGRAPHICAL SKETCH

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NAME: Singh, Amar B

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

POSITION TITLE: Professor, Department of Medicine, KUMC, and Research Career Scientist, KC VA Medical Center, Kansas City, MO.

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
Gorakhpur University, Gorakhpur, India	M.S.	1989	Zoology
Banaras Hindu University, Varanasi, India	Ph. D	1994	Physiology
Department of Physiology, University of Arkansas Medical Center, Little Rock, AR	Visiting Fellow	1995	Physiology
Department of Medicine, University of Arkansas Medical Center, Little Rock, AR	Post-Doc	1995-98	Biochemistry

A. Personal Statement

My research program focuses on understanding the molecular mechanisms that govern intestinal inflammation, with a particular emphasis on the regulation of inflammatory bowel disease (IBD) and its progression to colon cancer. My laboratory investigates the dynamic crosstalk among intestinal epithelial cells, immune cells, and the gut microbiota that collectively determine disease susceptibility and severity. My background in epithelial morphogenesis, injury/repair, and carcinogenesis provides me with a unique interdisciplinary perspective to address fundamental questions in mucosal biology. I have a strong record of productivity in gastrointestinal research, with publications in leading journals such as *Gastroenterology*, *Gut*, *The Journal of Clinical Investigation*, *Mucosal Immunology*, *Cancer Research*, and *Oncogene*. Our laboratory has developed novel genetically engineered mouse models, innovative preclinical systems of intestinal inflammation and dysbiosis, and 3D organoid cultures derived from both murine and patient tissues. These models allow mechanistic investigation of intestinal pathobiology and therapeutic responses. We also employ longitudinal endoscopic imaging using the Carl-Storz mouse system to study the progression of colitis in vivo. As a principal investigator and co-investigator on NIH- and VA-funded projects, I have demonstrated scientific leadership and innovation in mucosal immunology and IBD research. I have also mentored numerous postdoctoral fellows, clinician-scientists, and graduate students, many of whom now hold independent positions in academia and industry worldwide. I have a history of highly productive collaboration with Dr. Dhawan. Thus, through my sustained record of scientific accomplishment, innovation, and collaborative history, I have established a strong foundation to effectively serve as a PI on NIH grant proposal.

Ongoing Grant Support:

1. **VA Merit-1BX002761 (Singh, AB: Role-PI)** 4/1/2016-3-30/2030
   Title: Claudin-3, Gut Dysbiosis and Inflammatory Bowel Disease
2. **VA Research Career Scientist (Singh, AB: PI)** 4/1/2024-3/30/2029
3. **VA Collaborative Merit-1BX002761A (Singh, AB: PI)** 4/1/2024-3/30/2029
   Title: Role of PTSD- associated Gut Dysbiosis and Barrier Dysfunctions in Promoting IBD in Veterans

4. ***1R21CA313619-01 (Singh AB; Role-MPI)*** 6/1/2026-5/31/2028)
Title: Establishing Claudin-2 as a Surgical Biomarker of colorectal cancer.
5. ***KUCC Pilot Award (Singh AB; Role-PI)*** 6/1/2025-5/30/2027 (NCE)
Title: Role of Claudin-2 in renal cancer
There is no overlap in the proposed studies in funded grants with the current proposal.

Selected publications relevant to the proposed studies:

a) Rizwan Ahmad, Balawant Kumar, Ishwor Thapa, Geoffrey A. Talmon, Jeffrey Salomon, Amanda Ramer-Tait, Dhundy K. Bastola, Punita Dhawan, **Amar B. Singh** (2023). Loss of Claudin-3 Expression Promotes Colitis by Promoting Gut Dysbiosis. ***Gut Microbes*** 2023 Dec;15(2):2282789. PMID: 38010872
b) Ahmad R, Kumar B, Thapa I, Tamang RT, Yadav SK, Washington MK, Talmon GA, Yu AS, Bastola DK, Dhawan P and Singh AB (2023). Claudin-2 Protects from Colitis-Associated Cancer (CAC) by Promoting Colitis-associated Mucosal Healing. ***JCI*** 2023 Dec 1;133(23):e170771. PMID: 37815870
c) Duryee, MJ, Ahmad, A*, Eichele, DA, Hunter, CD, Mitra, A, Talmon, GA, Singh, S, Smith, LM, Rosen, MJ, Dhawan, D, Thiele, GM and **Singh, AB** (2022): **I**dentification of IgG Autoantibody against Malondialdehyde-Acetaldehyde Adduct (MAA) as Novel Serological Biomarker for Ulcerative Colitis. ***Clin Transl Gastroenterol.*** 2022 Apr 1;13(4):e00469. *equal contribution, PMID: 35287144
d) Ahmad R, Kumar B, Chen Z, Chen Xi, Muller D, Washington MK, Dhawan P and **Singh AB** (2017): Loss of Claudin-3 Expression Promotes Colon Cancer Malignancy by Hyperactivating Wnt-signaling in Stat3-dependent Manner. ***Oncogene,*** 2017 Nov 23;36(47):6592-6604. *PMID:28783170;* PMCID: PMC6512312

B. Positions, Scientific Appointments, and Honors

Positions and Employments:

Oct 2024-	*Professor (with tenure)*, Department of Medicine, Division of Gastroenterology, Hepatology and Motility, The University of Kansas Medical Center, Kansas City, KS
Oct 2024-	*Research Career Scientist*, Kansas City VA Medical Center, Kansas City, MO
2020-Sep, 2024	*Professor (with tenure)*, Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE
2020- Sep, 2024	Member, Graduate Studies Program, Department of Immunology, Pathobiology, and Infectious Diseases, UNMC, Omaha, NE
2015- Sep, 2024	*Research Scientist*, VA Nebraska-Western Iowa Health Care System, Omaha, NE
2014- Sep, 2024	*Member*, Fred and Pamela Buffet Cancer Center, University of Nebraska Medical Center, Omaha, NE
2014-2020	*Associate Professor*, Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE
2011-2014	*Assistant Professor*, Department of Medicine, Division of Nephrology, Vanderbilt University Medical Center, Nashville, TN
2008-2014	*Assistant Professor*, Department of Surgical Oncology, Vanderbilt University Medical Center, Nashville, TN
2002-2008	*Research Assistant Professor*, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN
1998-2000	*Instructor*, Department of Medicine, University of Arkansas for Medical Sciences, Arkansas

Other Experience and Professional Memberships:

Membership and leadership position in professional scientific organizations.

2019-Current	Councilor, *Basic and Clinical Intestinal Disorders section, AGA*
2010-Current	Member, *American Gastrointestinal Association (AGA)*
2022-Current	Member, *American Physiological Society (APS)*

Manuscript review and Editorial board services in scientific journals:

Manuscript review: Since 1998; ~35 journals including Gastroenterology, Cancer Research, Nature Communications, Science Advances, Theranostics, etc.

Editorial Services:
Associate Editor: Gut and Microbes
Editorial Board: American Journal of Physiology (AJP)
Editorial Board: World Journal of Clinical Oncology
Editorial Board: IJERPH

Federal and non-federal grants review services.

2024	Reviewer, NIH/NHI Study section
2023	Reviewer, NIH/Special Emphasis and DOD Study sections
2022	Reviewer, Center of Disease Control (CDC) Study section
2021 and 2022	Reviewer, NIH/DHMI Study section
2020	Reviewer, DOD, Discovery award, CTA, and Colon cancer review panels
2019 and 2020	Reviewer, NIH/GMPB Study section
2016 and 2020	Reviewer, NIH/TME Study Section
2019	Reviewer, NIH Special Emphasis Panel ZRG1-DKUS-J (82)
2019	Reviewer, *NIH Special Emphasis Panel ZCA1-TCRB-V-O2*
2019	Reviewer, *NIH Special Emphasis Panel ZRG1-OTC-K-03*
2019	Chairperson, *Department of Defense (DOD)* Colorectal (Horizon Award) Panel
2018	Reviewer, *CSR Anonymization Study (OBT), NIH*
2018-Current	Reviewer, *ORAU/Pennsylvania Department of Health*
2018	Reviewer, *NIH Special Emphasis Panel ZRG1-DKUS-N-05*
2018	Reviewer, *NIH Special Emphasis Panel ZRG1-OTC-R-04*
2018	Reviewer, *Department of Defense (DOD)* Pancreatic Cancer (CC1) Panel
2013 and 2018	Reviewer, *NIH/* CIMG Study section
2017	Reviewer, *Department of Defense (DOD)* Colorectal Cancer (CC1) Panel
2017-current	Reviewer, *ORAU/Florida Department of Health*
2017-current	Reviewer, Oak Ridge Associated Universities (ORAU)/Nazarbazon University
2016	Reviewer, *NIH Special Emphasis Panel (DKUS C)*
2016	Reviewer, *Department of Defense (DOD)* Colorectal Cancer (CC2) Panel
2015	Reviewer, *NIH Special Emphasis Panel (ZRG1)*
2007-2011	Reviewer, *American Heart Association (AHA)*

International grant and academic review services.
Reviewer, *Ph. D Thesis; Jawaharlal Nehru Institute (JNU), New Delhi India*; *Qatar National Research Fund* (QNRF); *Dutch Kidney Foundation (DKF); Mohammed $_{Bin}$ Rashid Al Maktoum Global Initiative; Austrian Science Fund; France National Cancer Institute; NC3Rs, United Kingdom; MOH/NMRC Grants, Singapore.*

Awards & Honors

2024	Research Career Scientist (RCS) Award, Veterans Administration
2022	Frances E. Lageschulte and Evelyn B. Weese New Frontiers in Medical Research Fund, UNMC
2019	*Nebraska Collaborative Initiative Award*, University of Nebraska, Omaha, NE
2018-current	*Councilor*, American Gastrointestinal Association (AGA), Basic and Clinical Intestinal Disorders (BCID), USA
2017	*Distinguished Scientist Award*, University of Nebraska, Omaha, NE
2016	*Nebraska Collaborative Initiative Award*, University of Nebraska, Omaha, NE
2004	*Scientist Development Grant Award*, American Heart Association (AHA), USA
2002	*Beginning Grant-in-Aid (BIG) Award*, American Heart Association (AHA), USA
1994	*International Post-doctoral Fellowship*, *Human Frontier Science Program Organization (HFSPO)*, Nice, France
1991	Senior Research Fellowship, *Government of India*, New Delhi, India
1988	Junior Research Fellowship, *Government of India*, New Delhi, India
1988	University Grant Commission (UGC) Research Fellowship, India
1977	Ekikrit Scholarship, Government of Uttar Preadesh, India

C. Contributions to Science

1. **Mechanisms regulating Inflammatory Bowel Disease and oncogenesis:** A single layer of epithelium regulates the normal immune-antigen interaction in the intestinal tissues by serving as a physical (however regulated) barrier. Tight junctions, the most apical cell-cell adhesions, help create the gut epithelial barrier by regulating paracellular transport. Tight junctions also help maintain epithelial cell polarity. Inflammatory pathological conditions, like IBD are associated with dysregulated gut barrier functions and postulated to play critical role in the pathobiology of the disease. A loss of barrier function also associates with the oncogenic processes including the loss of cell polarity. Here it is worthy of noting that while, a breach in the barrier is considered promotive of the immune activation and inflammation, some antigen immune interaction is essential to maintain normal immune homeostasis and to maintain adaptive immunity. We have investigated this complexity for the role of the gut barrier deregulations in promoting IBD and colorectal cancer using mouse modeling of the disease, using mice genetically modified for specific claudin proteins in gut epithelial specific manner and 3D-organ culture. Our studies while attest key role of gut barrier proteins in intestinal homeostasis including the gut microbiota colonization, have also revealed that the effects are context oriented and dynamic. Some of the key publications in this line of investigations include:

   a. Ahmad R, Kumar B, Thapa I, Tamang RT, Yadav SK, Washington MK, Talmon GA, Yu AS, Bastola DK, Dhawan P and **Singh AB** (2023). Claudin-2 Protects from Colitis-Associated Cancer (CAC) by Promoting Colitis-associated Mucosal Healing. ***JCI*** 2023 Dec 1;133(23):e170771. PMID: 37815870

   b. Ahmad R, Kumar B, Chen Z, Chen Xi, Muller D, Washington MK, Dhawan P and **Singh AB** (2017): Loss of Claudin-3 Expression Promotes Colon Cancer Malignancy by Hyperactivating Wnt-signaling in Stat3-dependent Manner. ***Oncogene.*** 2017 Nov 23;36(47):6592-6604.

   c. Ahmad R, Chaturvedi R, Habib T, Asim M, Shivesh P, Olivares-Villagómez D, Polk BD, Kaer LV, Washington KM, Wilson KT, Dhawan P and **Singh AB** (2014): Claudin-2 Expression Induces Immune Tolerance and Protects from Colitis Despite Increased Mucosal Permeability. ***Mucosal Immunology,*** 2014 Nov;7(6):1340-53. PMID: 24670427

   d. **Singh AB**, Sharma A, Smith JJ, Krishnan M, Chen X, Eschrich S, Washington KM, Yeatman TJ, Beauchamp RD and Dhawan P (2011): Claudin-1 Upregulates the Repressor ZEB-1 to Inhibit E-Cadherin Expression in Colon Cancer Cells. ***Gastroenterology***;141(6):2140-53. PMID: 21878201

2. **Translational studies focused on IBD and Gastrointestinal Oncogenesis:** Receptor and cytoplasmic protein tyrosine kinases play prominent roles in the control of a range of cellular processes during embryonic development and in the regulation of metabolic and physiological processes in a variety of tissues and organs. Such receptor kinases function in a wide range of cellular processes, including cell fate determination, proliferation, cell migration and apoptosis. Considering the key role of these cellular processes, there is growing interest in targeting such molecules and associated signaling processes in the regulation of epithelial and immune homeostasis, and oncogenic processes. Our research has focused on modes of activation of the inflammatory and oncogenic processes, and associated signaling processes in regulating IBD and colorectal cancer. In addition, we have focused upon the role of such proteins in regulating the cell cycle and thus mucosal healing, and oncogenic growth. Some of the key publications in this line of investigations include:

   a. Kesharwani SS, Ahmad R, Bakkari MA, Rajput MKS, Dachineni R, Kapur S, Bhat GJ, Tumala H* and **Singh AB*** (2018): Site-Directed Polymer-Drug Complexing Increases Colon Specific Bioavailability of Curcumin and Inhibits Colitis by Modulating Gut Innate Immune System. ***Journal of Controlled Release***. 2018 Nov 28;290:165-179. *co-corresponding Authors). *PMID:* 30142410

   b. Kanvinde S, Chhonker YS, Ahamd R, Jaramillo L, Sheinin Y, Sleightholm R, Murry DJ, **Singh AB** and Oupicky (2018): Therapeutic potential of orally administered polymeric chloroquine in Citrobacter rodentium-induced colitis in mice. ***Acta Biomater.*** 2018 Dec;82:158-170. doi: 10.1016/j.actbio.2018.10.027. PMID: 30342282

   c. Uppada SP, Ahmad R, Gowrikumar S, Smith J, Chen S, **Singh AB** and Dhawan P (2018): A Novel Role for MASTL in the regulation of Wnt/beta-catenin Signaling Pathway in Colorectal cancer. ***Mol. Cancer*** 2018 Aug 1;17(1):111. PMID: 30068336

   d. Dhawan P, Ahmad R, Chaturvedi R, Smith JJ, Midha R, Mittal M, Krishnan, M, Chen X, Eschrich S, Yeatman TJ, Harris RC, Washington KM, Wilson KT, Beauchamp RD and **Singh AB** (2011): Claudin-2 Expression Increases Tumorigenicity of Colon Cancer Cells: Role of Epidermal Growth Factor Receptor Activation. ***Oncogene***;30(29):3234-47.2. PMID: 21383692

3. **Regulation of Epithelial Morphogenesis, Differentiation, and Death:** To maintain the normal functioning of the mammalian body and its organ system, a balance between cell death and cell multiplication must be maintained. However, cell death can be reversible (apoptosis) or irreversible (necrosis). Thus, understanding the processes that regulate cell death during specific disease processes can help device mechanisms to prevent irreversible cell death and thus severe organ damage and/or failure. In this regard, we studied the regulation of renal proximal tubular epithelial cell homeostasis and renal carcinogenesis. In this regard, we have studied the roles of proteins that regulate renal epithelial cell proliferation, apotosis, polarity and oncogenesis. We were also the first to clone Caspse-6 and alternatively spliced DNAS-1, and then demonstrate their role in renal epithelial cell death.

   a. Kumar B, Ahmad R, Giannico GA, Zent R, Talmon GA, Harris RC, Clark PE, Lokeshwar V, Dhawan P, **Singh AB**. (2021): Claudin-2 inhibits renal clear cell carcinoma progression by inhibiting YAP-activation. ***J Exp Clin Cancer Res.*** 2021 Feb 23;40(1):77. *PMID:* 33622361

   b. Jordan AR, Wang J, Yates TJ, Hasanali SL, Lokeshwar SD, Morera DS, Shamaladevi N, Li CS, Klaassen Z, Terris MK, Thangaraju M, **Singh AB**, Soloway MS, Lokeshwar VB. (2020): Molecular Targeting of Renal Cell Carcinoma by an Oral Combination. ***Oncogenesis*.** 2020 May 19;9(5):52. PMID: 32427869

   c. Zhang MZ, Yao B, Yang S, Jiang L, Wang S, Fan X, Yin H, Wong K, Miyazawa T, Chen J, Chang I, **Singh A** and Harris RC (2012): CSF-1 signaling mediates recovery from acute kidney injury. ***J Clin. Inves.*** 2012 Dec 3;122(12):4519-32. PMID:23143303

   d. Basnakian AG, Apostolov EO, Yin X, Abiri SO, Stewart AG, **Singh AB**, Shah SV (2006): Endonuclease G promotes cell death of non-invasive human breast cancer cells. ***Exp Cell Res.*** 10;312(20):4139-49. PMID:17046751

4. **Neurohormonal regulation of mammalian circadian physiology and reproduction:** My Ph. D. dissertation work focused upon understanding the neuroendocrine control of the mammalian circadian cycling with specific focus on the role of the Dopamine and Serotonin circuity in regulating mammalian reproductive cycle. The causal interaction of the hormone HCG with Serotonin and Dopamine, prominent neurotransmitters in the regulation of the development of male gonadal maturity and functioning was investigated. The overall outcome suggested a complex however antagonistic interaction between HCG and the neurotransmitters in determined endpoints. Overall, the cumulative findings suggested regulation of the neurotransmitter axis as potential opportunity for therapeutic intervention to help regulate mammalian reproductive abilities and hence to maintain a healthy population density.

   a. Chaturvedi CM and **Singh AB** (1992): Suppression of annual testicular development in Indian Palm squirrel, Funambulus pennanti by 8 hr temporal relationship of serotonin and dopamine precursor drugs. *J Neural Transm*.; 88(1): 53-60. PMID:1575953.

   b. **Singh AB** and Chaturvedi CM (1993): Effect of altered Thyroid and Adrenal activity on the seasonal reproduction of Indian palm squirrel, Funambulus pennanti. *Can J Zool*., 1558-1561 (72).

   c. **Singh AB** and Chaturvedi CM (1995): Effect of photoperiod in the regulation of the annual testicular cycle of a subtropical mammal, the Indian palm squirrel, Funambulus pennanti. *Biomed Environ Sci*.; 8(1): 65-73. PMID: 7605602

   d. Phillips D, **Singh AB**, Das US, Chaturvedi CM(1997): Effect of gonadotrophin and sex steroid on the scotoresponses of day old chicks of Japanese quail, Coturnix coturnix japonica. *Life Sci*.; 61(15): 1487-1495. PMID: 9328228

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