BIOGRAPHICAL SKETCH

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NAME: CHAUHAN, NEERAJ

eRA COMMONS USER NAME (credential, e.g., agency login): nchauhan1

POSITION TITLE: Associate 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)	END DATE MM/YYYY	FIELD OF STUDY
Rohilkhand University, Bareilly, UP	BS	1987	Chemistry, Zoology, Botany
AMU, Aligarh, UP	MS	1990	Microbiology
University of Delhi, New Delhi	MPHIL	1994	Biotechnology
Jawaharlal Nehru University, New Delhi	PHD	2000	Molecular Biology
Georgetown University, Washington, DC	Postdoctoral Fellow	2004	Fungal Pathogenesis

A. Personal Statement

The research in my group focuses on the biology and disease mechanisms of fungal pathogens of the *Candida* genus, primarily *Candida albicans* and *Candida auris*, two leading human fungal pathogens that can cause both mucosal and invasive infections. My initial training in Medical Mycology began in the laboratory of Richard Calderone at Georgetown University. Our research interests are focused on unraveling the mechanisms that allow fungal pathogens to exploit the host and cause disease. The long-term objective our research is to is to develop new strategies for the diagnosis and prevention of antifungal drug resistance and new treatment options for these life-threatening infections. We have been delineating the molecular mechanisms of fungal virulence using functional genomic approaches such as ChiP-/RNA- & ATAC-seq to identify Gene Regulatory Networks controlling fungal virulence. We use mouse models to study the genetic adaptations of fungal pathogens during specific host niche colonization. On the host immunity side, we have been dissecting the cellular / molecular mechanisms of antifungal immunity. In summary, my background and experience in fungal pathogenesis has prepared me to lead this work.

1. Jenull S, Shivarathri R, Tsymala I, Peninnger P, Trinh P, Nogueira F, Chauhan M, Singh A, Petryshyn A, Stoiber A, Chowdhary A, **Chauhan N*,** Kuchler K. 2022. Transcriptomics and phenotyping define genetic signatures associated with echinocandin resistance in *Candida auris.* mBio 2022 Aug 30;13(4):e0079922. doi: 10.1128/mbio.00799-22. *Corresponding author

2. Shivarathri R, Jenull S, Chauhan M, Singh A, Mazumdar R, Chowdhary A, Kuchler K, **Chauhan N*.** 2022. Comparative Transcriptomics Reveal Possible Mechanisms of Amphotericin B Resistance in *Candida auris*. Antimicrob Agents Chemother. Jun 2;e0227621. doi: 10.1128/aac.02276-21.*Corresponding author

3. Shivarathri R, Jenull S, Stoiber A, Chauhan M, Mazumdar R, Singh A, Nogueira F, Kuchler K, Chowdhary A, **Chauhan N***. The Two-Component Response Regulator Ssk1 and the Mitogen-Activated Protein Kinase Hog1 Control Antifungal Drug Resistance and Cell Wall Architecture of Candida auris. mSphere. 2020 Oct 14;5(5) PubMed Central PMCID: PMC7565899. *Corresponding author

4. Jenull S, Tscherner M, Kashko N, Shivarathri R, Stoiber A, Chauhan M, Petryshyn A, **Chauhan N***, Kuchler K. Transcriptome Signatures Predict Phenotypic Variations of *Candida auris*. Front Cell Infect Microbiol. 2021;11:662563. PubMed Central PMCID: PMC8079977. *Corresponding author

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022-	Associate Professor, Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ
2017 - 2022	Associate Professor, Rutgers University, Newark, NJ
2013 - 2017	Assistant Professor, Rutgers University, Newark, NJ
2008 - 2013	Assistant Professor, UMDNJ, Newark, NJ
2004 - 2008	Research Assistant Professor, Georgetown University, Washington, DC

Honors

2022	Reviewer, SBIR ZRG1 AIDC-V (13), NIH
2022	Reviewer, Special Emphasis Panel R13, ZAI1 KJK-D (M1) 1, NIH
2021	Reviewer, Small Business: Non- viral Anti-infective Therapeutics Special Emphasis Panel, ZRG1 AIDC-C (14), NIH
2020	Adhoc Reviewer, Oral, Dental and Craniofacial Sciences (ODCS) study section, NIH
2020	Associate Editor, Frontiers in Microbiology
2020	Associate Editor, BMC Microbiology
2019	Adhoc Reviewer, HIV Confections and HIV Associated Cancers (HCAC) study section, NIH
2019	Adhoc Reviewer, Clinical Research and Field Studies of Infectious Diseases (CRFS) study section, NIH
2018	Reviewer, NIAID support for conferences and scientific meetings (R13), ZAI1TS-D(S2), NIH
2018	Editorial board, Journal of Fungi
2017	Adhoc reviewer, Topics in Non-HIV Microbial Diagnostic and Detection Research, ZRG1 IDM–V (12/81), NIH
2017	Adhoc reviewer, Small buisness: Non-HIV Diagnostics, Food Safety, Sterilization/Disinfection, and Bioremediation, ZRG1-IDM-V-12, NIH
2017	Adhoc Reviewer, Support of Competitive Research (SCORE) Award Applications, ZGM1 RCB-9 (SC), NIH
2016	Adhoc reviewer, Pathogenic Eukaryotes (PTHE) study section, NIH
2016	Adhoc Reviewer, Special Emphasis Panel, ZRG1 PTHEM 07, NIH
2013	Early career reviewer (ECR) program, NIH
2007	Travel grant, ASM/MMSA
1995	Senior Research Fellowship, PhD, Council of Scientific and Industrial Research (CSIR), New Delhi, India
1990	University PG Merit Scholarship, M.Sc., AMU Aligarh, India

C. Contributions to Science

1. My initial training in medical mycology began in the lab of Richard Calderone at Georgetown University. My postdoctoral research was focused on the role of two-component signal transduction pathways in fungal pathogenesis, which was at the time very poorly understood. My early studies showed that Ssk1 response regulator protein regulates a number of important events for the cell, including expression of host recognition proteins, adaptation to oxidative stress and resistance to triazoles. These studies also identified the association of Ssk1 with downstream phosphorylation of the MAPK protein Hog1, but only when cells were under oxidative stress. For each of these studies I used state-of-the-art approaches available at the time, including microarray analysis. These studies demonstrated for the first time that in C. albicans the Ssk1 pathway was functionally highly distinct from the paradigmatic fungal two-component Ssk1 pathway in the non-pathogenic model fungus Saccharomyces cerevisiae.

    a. Chauhan N, Inglis D, Roman E, Pla J, Li D, Calera JA, Calderone R. Candida albicans response regulator gene SSK1 regulates a subset of genes whose functions are associated with cell wall biosynthesis and adaptation to oxidative stress. Eukaryot Cell. 2003 Oct;2(5):1018-24. PubMed Central PMCID: PMC219380.

b. Menon V, Li D, Chauhan N, Rajnarayanan R, Dubrovska A, West AH, Calderone R. Functional studies of the Ssk1p response regulator protein of Candida albicans as determined by phenotypic analysis of receiver domain point mutants. Mol Microbiol. 2006 Nov;62(4):997-1013. PubMed PMID: 17038117.

c. Chauhan N, Kruppa M, Calderone R. The Ssk1p response regulator and Chk1p histidine kinase mutants of Candida albicans are hypersensitive to fluconazole and voriconazole. Antimicrob Agents Chemother. 2007 Oct;51(10):3747-51. PubMed Central PMCID: PMC2043284.

d. Menon V, De Bernardis F, Calderone R, Chauhan N. Transcriptional profiling of the Candida albicans Ssk1p receiver domain point mutants and their virulence. FEMS Yeast Res. 2008 Aug;8(5):756-63. PubMed Central PMCID: PMC2576740.

2. After obtaining my faculty appointment at UMDNJ (now Rutgers University), my research group continued to build on my initial studies of two-component signaling systems in C. albicans. The primary motivation behind our research on two-component signaling systems in fungal pathogens is that these signaling cascades are important for virulence and are absent in the human genome, therefore representing potential drug targets. In my lab, we identified a new putative two-component response regulator Srr1 in C. albicans. Our initial studies showed that Srr1 is important for stress response and virulence of C. albicans. Subsequently, we discovered that Srr1 is located in the mitochondria and regulates a subset of genes whose functions are associated with the oxidative stress response and programmed cell death (apoptosis). To the best of our knowledge, thus far, this remains the only study where a fungal nuclear genome is shown to contain elements of a two-component signaling pathway that are targeted to the mitochondria. Furthermore, we also reported that Ypd1, a histidine phosphotransfer protein, is not essential for viability in C. albicans. Ypd1 is reported to be essential for viability in the model yeast Saccharomyces cerevisiae and prior to our work was widely believed to be essential in C. albicans as well. Our studies also revealed that Ypd1 is localized to both the nucleus and the cytoplasm. The subcellular segregation of Ypd1 hints at an important role(s) of Ypd1 in regulation of Ssk1 (cytosolic) and Skn7 (nuclear) response regulator proteins via phosphorylation in C. albicans. This discovery has profound implications for a mechanistic understanding of two-component signaling pathways in C. albicans, and perhaps in other pathogenic fungi.

a. Desai C, Mavrianos J, Chauhan N. Candida albicans SRR1, a putative two-component response regulator gene, is required for stress adaptation, morphogenesis, and virulence. Eukaryot Cell. 2011 Oct;10(10):1370-4. PubMed Central PMCID: PMC3187061.

b. Mavrianos J, Berkow EL, Desai C, Pandey A, Batish M, Rabadi MJ, Barker KS, Pain D, Rogers PD, Eugenin EA, Chauhan N. Mitochondrial two-component signaling systems in Candida albicans. Eukaryot Cell. 2013 Jun;12(6):913-22. PubMed Central PMCID: PMC3675996.

c. Mavrianos J, Desai C, Chauhan N. Two-component histidine phosphotransfer protein Ypd1 is not essential for viability in Candida albicans. Eukaryot Cell. 2014 Apr;13(4):452-60. PubMed Central PMCID: PMC4000104.

d. Shor E, Chauhan N. A case for two-component signaling systems as antifungal drug targets. PLoS Pathog. 2015 Feb;11(2):e1004632. PubMed Central PMCID: PMC4344368.

3. C. albicans is reported to be the most common cause of candidiasis, but over the past two decades there is a steady increase in reported cases of life-threatening systemic infections due to C. glabrata. By performing a genome wide comparison of C. glabrata with its non-pathogenic cousin S. cerevisiae we identified a family of glycosylphosphatidylinositol-anchored cell wall proteins in C. glabrata. These proteins are absent in both S. cerevisiae and C. albicans, suggesting that C. glabrata has evolved different mechanism(s) for interaction with host cells. Our initial efforts were focused on the characterization of Pwp7 and Aed1 of this family in the interaction of C. glabrata with human umbilical vein endothelial cells (HUVECs). The deletion of C. glabrata genes PWP7 and AED1 resulted in a significant reduction in adherence to endothelial cells compared to the wild-type parent. These findings showed that C. glabrata utilizes these proteins for adherence to endothelial cells in vitro.

a. Gómez-Molero E, de Boer AD, Dekker HL, Moreno-Martínez A, Kraneveld EA, Ichsan, Chauhan N, Weig M, de Soet JJ, de Koster CG, Bader O, de Groot PW. Proteomic analysis of hyperadhesive Candida glabrata clinical isolates reveals a core wall proteome and differential incorporation of adhesins. FEMS Yeast Res. 2015 Dec;15(8) PubMed PMID: 26546455.

b. de Groot PW, Bader O, de Boer AD, Weig M, Chauhan N. Adhesins in human fungal pathogens: glue with plenty of stick. Eukaryot Cell. 2013 Apr;12(4):470-81. PubMed Central PMCID: PMC3623432.

c. Desai C, Mavrianos J, Chauhan N. Candida glabrata Pwp7p and Aed1p are required for adherence to human endothelial cells. FEMS Yeast Res. 2011 Nov;11(7):595-601. PubMed Central PMCID: PMC3202042.

4. One of the major research interests of my laboratory is on a principally novel and unexplored area of Candida biology – the role of post-translational modification of proteins via lysine acetylation. Lysine acetylation is a well-established major mechanism of regulating protein function, and lysine acetylases have been shown to play important roles in many cellular processes. However, while C. albicans contains several conserved lysine acetylases, their functions in fungal morphogenesis and virulence have remained unexplored. We have shown that lysine acetylase Hat1 and Gcn5 are required for normal virulence in C. albicans. This work was published in PLoS Pathogens and Nature Scientific Reports. We have also shown that C. albicans chromatin chaperones are critical for fungal response to host immune surveillance. The overall goal of this research is to define the role of protein acetylation in C. albicans pathogenesis, with a long-term objective of identifying new drug targets for antifungal therapies.

   a. Shivarathri R, Tscherner M, Zwolanek F, Singh NK, Chauhan N, Kuchler K. The Fungal Histone Acetyl Transferase Gcn5 Controls Virulence of the Human Pathogen Candida albicans through Multiple Pathways. Sci Rep. 2019 Jul 1;9(1):9445. PubMed Central PMCID: PMC6603162.

   b. Jenull S, Tscherner M, Gulati M, Nobile CJ, Chauhan N, Kuchler K. The Candida albicans HIR histone chaperone regulates the yeast-to-hyphae transition by controlling the sensitivity to morphogenesis signals. Sci Rep. 2017 Aug 16;7(1):8308. PubMed Central PMCID: PMC5559454.

   c. Kuchler K, Jenull S, Shivarathri R, Chauhan N. Fungal KATs/KDACs: A New Highway to Better Antifungal Drugs?. PLoS Pathog. 2016 Nov;12(11):e1005938. PubMed Central PMCID: PMC5104479.

   d. Tscherner M, Zwolanek F, Jenull S, Sedlazeck FJ, Petryshyn A, Frohner IE, Mavrianos J, Chauhan N, von Haeseler A, Kuchler K. The Candida albicans Histone Acetyltransferase Hat1 Regulates Stress Resistance and Virulence via Distinct Chromatin Assembly Pathways. PLoS Pathog. 2015 Oct;11(10):e1005218. PubMed Central PMCID: PMC4608838.

5. Candida auris is an emerging drug-resistant fungal pathogen that presents a serious global threat to human health. Importantly, C. auris is the first fungal pathogen showing pronounced and sometimes untreatable clinical drug resistance to all known antifungal classes, including azoles, amphotericin B (AmB) and echinocandins. However, the molecular basis of multidrug resistance, adhesive traits and virulence of C. auris are not understood at all. One of our primary objective is to understand the molecular mechanisms of antifungal drug resistance, skin adhesion and virulence of C. auris. We have developed a set of fluorescent C. auris strains to facilitate studies on host-pathogen interactions. We recently reported that genetic removal of SSK1 encoding a response regulator and the mitogen-associated protein kinase HOG1 restores the susceptibility to both amphotericin B (AMB) and caspofungin (CAS) in C. auris clinical strains. The C. auris fungal two-component system, a signal transduction pathway conserved in most fungi, holds promise for developing new antifungals, since it controls key pathogenic traits such as virulence and anti-infective drug susceptibilities.

   a. Shivarathri R, Jenull S, Chauhan M, Singh A, Mazumdar R, Chowdhary A, Kuchler K, Chauhan N. 2022. Comparative Transcriptomics Reveal Possible Mechanisms of Amphotericin B Resistance in *Candida auris*. Antimicrob Agents Chemother. Jun 2;e0227621. doi: 10.1128/aac.02276-21.

   b. Jenull S, Shivarathri R, Tsymala I, Peninnger P, Trinh P, Nogueira F, Chauhan M, Singh A, Petryshyn A, Stoiber A, Chowdhary A, Chauhan N**,** Kuchler K. 2022. Transcriptomics and phenotyping define genetic signatures associated with echinocandin resistance in *Candida auris.* mBio 2022 Aug 30;13(4):e0079922. doi: 10.1128/mbio.00799-22.

   c. Jenull S, Tscherner M, Kashko N, Shivarathri R, Stoiber A, Chauhan M, Petryshyn A, Chauhan N, Kuchler K. Transcriptome Signatures Predict Phenotypic Variations of *Candida auris*. Front Cell Infect Microbiol. 2021;11:662563. PubMed Central PMCID: PMC8079977.

d. Shivarathri R, Jenull S, Stoiber A, Chauhan M, Mazumdar R, Singh A, Nogueira F, Kuchler K, Chowdhary A, Chauhan N. The Two-Component Response Regulator Ssk1 and the Mitogen-Activated Protein Kinase Hog1 Control Antifungal Drug Resistance and Cell Wall Architecture of Candida auris. mSphere. 2020 Oct 14;5(5) PubMed Central PMCID: PMC7565899.

Complete List of Published Work in My Bibliography:

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