BIOGRAPHICAL SKETCH

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NAME: Desai, Jigarkumar V.

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

POSITION TITLE: Assistant Member

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
The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat	B.Pharm.	07/2008	Pharmacy
Virginia Commonwealth University, Richmond, VA	M.S.	08/2010	Pharmaceutical Sciences
Carnegie Mellon University, Pittsburgh, PA	Ph.D.	08/2014	Biological Sciences

A. Personal Statement

My long-term objective is to characterize the tissue-specific interplay between the complement system and fungi and its impact on local and systemic immunity. Specifically, I aim to characterize how the bioactive complement proteins are regulated in a fungal-responsive manner and how these interactions, in turn, condition the local and systemic immune system. To this end, I will utilize clinically relevant mouse models, intravital microscopy, cell-type-specific conditional knockout mice, genetically modified fungal strains, primary murine/human cell cultures, and transcriptomics approaches. My multi-disciplinary training spanning immunology, molecular mycology, biochemistry, and microscopy provides me a strong foundation to carry out these investigations. As a graduate student pursuing M.S. in Dr. Martin K. Safo's lab, I worked on characterizing the enzymes involved in vitamin B6 metabolism; I got extensive training in enzyme biochemistry, protein purification, and X-ray crystallography during this period. During my Ph. D. with Drs. Aaron P. Mitchell and Frederick Lanni, my research focused on understanding the genetic control of *Candida albicans* (Ca) biofilm formation and hyphal invasion. During this time, I got extensive training in the genetic manipulation of Ca and optical microscopy. My work during graduate school was awarded, and I was also nominated for a university-wide award for my interdisciplinary work. After my doctoral training, I wanted to acquire the skills necessary to investigate how the host immune system controls fungal challenge, which led me to Dr. Michail S. Lionakis at the NIH for my postdoctoral fellowship; I uncovered an essential role for the complement C5a in protective anti-fungal immunity during my fellowship. These findings underscored the importance of cell-intrinsic and hepatic complement in promoting early fungal clearance and prevention of renal pathology during systemic candidiasis. This work has been consistently recognized and awarded as it adds to a growing recognition of the critical roles played by the complement system and fungi in human health. In my lab, I will build up on these findings and will pursue the central hypothesis that fungal-dependent complement pathway regulation is crucial for local and systemic fungal control. I expect that this work will unveil novel aspects of complement biology and anti-fungal immune response. Furthermore, the insights gained into complement biology will have implications beyond anti-fungal immunity due to the critical role of complement proteins in the pathology of diverse human diseases.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022	Assistant Member, Center for Discovery and Innovation, Hackensack Meridian Health, Nutley NJ
2019 - 2022	Research Fellow, Fungal Pathogenesis Section, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD

2014 - 2019	Visiting Fellow, Fungal Pathogenesis Section, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
2010 - 2014	Graduate Research Assistant, Carnegie Mellon University, Pittsburgh, PA
2009 - 2010	Graduate Research Assistant, Virginia Commonwealth University, Richmond, VA

Honors

2021	Orloff Science Award for work on intracellular complement in inflammatory human diseases, Division of Intramural Research, National Heart, Lung, and Blood Institute
2019	NIAID Pathway to Independence Award (K99/R00)
2019	Fellows Award in Research Excellence, National Institutes of Health
2019	Outstanding Oral Presentation, Gordon Research Seminar for Immunology of Fungal Infections
2017	Fellows Award in Research Excellence, National Institutes of Health
2013	Stupakoff Fellowship for Excellence in Graduate Research, Carnegie Mellon University
2012	Dr. Margaret Carver Graduate Student Travel Award, Carnegie Mellon University

C. Contribution to Science

Complete list of my published work:
https://www.ncbi.nlm.nih.gov/myncbi/jigarkumar.desai.1/bibliography/public/

1. Structural biochemical characterization of enzymes involved in vitamin B6 metabolism: I identified that therapeutic compounds structurally similar to pyridoxal phosphate (active form of vitamin B6) inhibit the enzyme pyridoxal kinase and cause the associated neurotoxic side-effects. Furthermore, I defined small-molecule (enzymes' substrate) channeling between enzyme pairs; such a mechanism prevents the release of reactive substrate molecule to cytoplasm via direct channeling between the macromolecular enzyme pairs.

    a. Ghatge MS, Contestabile R, di Salvo ML, **Desai JV**, Gandhi AK, Camara CM, Florio R, González IN, Parroni A, Schirch V, Safo MK. Pyridoxal 5'-phosphate is a slow tight binding inhibitor of E. coli pyridoxal kinase. *PLoS One*. 2012;7(7):e41680. PubMed Central PMCID: PMC3404986.

    b. Gandhi AK*, **Desai JV***, Ghatge MS, di Salvo ML, Di Biase S, Danso-Danquah R, Musayev FN, Contestabile R, Schirch V, Safo MK. Crystal structures of human pyridoxal kinase in complex with the neurotoxins, ginkgotoxin and theophylline: insights into pyridoxal kinase inhibition. *PLoS One*. 2012;7(7):e40954. PubMed Central PMCID: PMC3412620. **Equal Contributions*

2. Genetic control of *Candida albicans* (Ca) biofilm formation and hyphal invasion: I identified that glycerol serves as a regulatory molecule in Ca biofilm formation for its roles in transcription regulation of genes that encode cell-wall proteins involved in adhesion. I also identified that glycerol accumulation in Ca biofilm formation provides the turgor pressure for Ca filamentous hyphal cells for invading an underlying substratum.

    a. **Desai JV**, Cheng S, Ying T, Nguyen MH, Clancy CJ, Lanni F, Mitchell AP. Coordination of Candida albicans Invasion and Infection Functions by Phosphoglycerol Phosphatase Rhr2. *Pathogens*. 2015 Jul 24;4(3):573-89. PubMed Central PMCID: PMC4584273.

    b. **Desai JV**, Mitchell AP. Candida albicans Biofilm Development and Its Genetic Control. *Microbiol Spectr.* 2015 Jun;3(3) PubMed Central PMCID: PMC4507287.

    c. **Desai JV**, Mitchell AP, Andes DR. Fungal biofilms, drug resistance, and recurrent infection. *Cold Spring Harb Perspect Med.* 2014 Oct 1;4(10) PubMed Central PMCID: PMC4200207.

    d. **Desai JV**, Bruno VM, Ganguly S, Stamper RJ, Mitchell KF, Solis N, Hill EM, Xu W, Filler SG, Andes DR, Fanning S, Lanni F, Mitchell AP. Regulatory role of glycerol in Candida albicans biofilm formation. *mBio*. 2013 Apr 9;4(2):e00637-12. PubMed Central PMCID: PMC3622937.

3. Antifungal immunity: I have identified that the complement receptor- C5ar1 regulates anti-*Candida* effector function of the myeloid phagocytes and is required for protection during systemic candidiasis. With the use of clinically relevant mouse models, intravital renal microscopy, cell-type specific conditional knockout mice, genetically modified fungal strains, transcriptome profiling and phagocytes/sera from humans; I have demonstrated cell-type specific roles of C5a signaling in regulation of cellular metabolism, survival and antifungal effector functions.
   Additionally, I have characterized that during phaeohyphomycosis, DECTIN-1/CARD9-dependent signaling in macrophages is critical for protection, and human DECTIN-1 deficiency may underlie an enhanced susceptibility following traumatic fungal inoculation. These findings are currently under revision at the ***Journal of Clinical Investigation***, where I am the co-first author. I have also actively assisted the efforts to unravel how long-term antibiotic usage leads to a dysfunctional IL-17A/GM-CSF-dependent responses within the gastrointestinal tract, which promotes bacterial co-infection with systemic candidiasis. I am a co-first author on the manuscript detailing these findings; a manuscript was recently published at the ***Cell Host and Microbe***.
   In addition to the above, I have developed real-time intravital microscopy protocols for imaging kidneys, liver and spleen in live anesthetized animals. This approach will allow, for the first time, an in-depth real-time investigation of host-fungal interactions. Besides these, I have made significant collaborative contributions and have assisted via my expertise in microscopy, molecular mycology and anti-fungal immunity.

   a. Break TJ, Oikonomou V, Dutzan N, **Desai JV**, Swidergall M, Freiwald T, Chauss D, Harrison OJ, Alejo J, Williams DW, Pittaluga S, Lee CR, Bouladoux N, Swamydas M, Hoffman KW, Greenwell-Wild T, Bruno VM, Rosen LB, Lwin W, Renteria A, Pontejo SM, Shannon JP, Myles IA, Olbrich P, Ferré EMN, Schmitt M, Martin D, Barber DL, Solis NV, Notarangelo LD, Serreze DV, Matsumoto M, Hickman HD, Murphy PM, Anderson MS, Lim JK, Holland SM, Filler SG, Afzali B, Belkaid Y, Moutsopoulos NM, Lionakis MS. Aberrant type 1 immunity drives susceptibility to mucosal fungal infections. *Science*. 2021 Jan 15;371(6526) PubMed Central PMCID: PMC8326743.
   b. Drummond RA*, **Desai JV***, Ricotta E, Swamydas M, Deming C, Lee C, Green N, Zelazny A, Segre JA, Lionakis MS. Vancomycin promotes mortality following systemic fungal infection by driving escape of commensal bacteria and lymphocyte Dysfunction. *Cell Host and Microbe,* 2022 May 7;. doi: 10.1016/j.chom.2022.04.013. [Epub ahead of print] PubMed PMID: 35568028***.*** **Equal Contributions*
   c. Drummond RA*, **Desai JV***, Swamydas M, Vautier S, Hsu A, Lee R, Acklin J, Lim J, Meyer-Barber K, Zelazny A, Kuhns D, Holland S, Lionakis MS. Phaeohyphomycosis and Human Dectin-1-Deficiency. *Journal of Clinical Investigation**,*** In revision after initial peer-review, **Equal Contributions*
   d. **Desai JV**, Zarakas M, Swamydas M, Chauss D, Freiwald T, Johnson MD, Perfect JR, Kabat J, Matzaraki V, Niyonzima N, Kumar V, Stienstra R, Netea MG, Kohl J, Kemper C, Afzali B, Lionakis MS. C5a-licensed phagocytes drive sterilizing immunity during systemic fungal infection. (In Preparation).