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)*	Completion 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
National Institute of Allergy and Infectious Diseases, Bethesda, MD	Postdoctoral training	10/2019	Immunology

A. Personal Statement

My lab investigates the mucosal complement system, its cell-intrinsic/extrinsic regulation, and its impacts on mucosal, systemic, and antitumor immunity. Specifically, I am exploring the molecular and cellular mechanisms of how the complement-microbial crosstalk at the mucosa regulates sterilizing antifungal immunity and impacts the outcomes of mucosal malignancies. We recently discovered an essential role for phagocyte-intrinsic complement in the functional regulation of macrophages and neutrophils; building upon this, we aim to uncover the role of cell-intrinsic complement in shaping the pulmonary and gastrointestinal immune response during acute infections and cancer.

I have extensive expertise in immunology, myeloid cell biology, microscopy, high-dimensional data analysis, and molecular mycology, exemplified by my published work exploring (1) complement C5a and myeloid antifungal effector regulation (Desai et al., ***Cell***, 2023), (2) an impact of long-term antibiotics use on enhanced mortality after systemic fungal infections via lymphocyte dysfunction (Drummond and Desai et al., ***Cell Host & Microbe,*** 2022) and (3) identification of a common mutation leading to rare fungal infection in humans upon traumatic inoculation (Drummond & Desai et al, ***Journal of Clinical Investigation****,* 2022). The research in my lab is currently supported by the NIAID, the New Jersey Health Foundation, and the Ruesch Center for the Cure of Gastrointestinal Cancers; the ongoing support is highlighted below:

R00 AI141622
Desai (PI)
07/05/2022 - 06/30/2024
Elucidating the roles of systemic and mucosal complement in protection against invasive fungal infections impacting hematopoietic cell transplant.

PC 177-23
Desai (PI)
02/15/2023 - 02/14/2024
Defining fungal genetic network governing phagocytosis and fungal clearance.

G10195
Desai (PI)
05/01/2023 - 04/30/2024
Functional regulation of tumor-associated neutrophils by tumor-dwelling fungi

B. Positions, Scientific Appointments, and Honors (Reverse Chronological)

Positions and Scientific Appointments

2022 - Present	Assistant Member, Center for Discovery and Innovation (CDI), Hackensack Meridian Health (HMH), Nutley NJ
2022 - Present	Assistant Professor, Department of Medical Sciences, Hackensack Meridian School of Medicine, Nutley, NJ
2022 - Present	Full Research Member, Cancer Host Interactions (CHI) Program, Lombardi Comprehensive Cancer Center, Georgetown University, Washington D.C.
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

2023	2023 CIG William E. Paul Award for the Best Paper (3rd place) in Cytokine Research; paper titled "Phaeohyphomycosis and Human Dectin-1-Deficiency."
2021	Orloff Science Award for work on intracellular complement in inflammatory human diseases, Division of Intramural Research, National Heart, Lung, and Blood Institute
2019	Fellows Award in Research Excellence, National Institutes of Health
2019	NIH/NIAID K99 AI141622-01A1
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. Contributions to Science

1. Investigating the complement system and its roles in immunity: We identified that transcriptional induction of a complement module is predictive of human candidemia and the complement C5a-C5aR1 axis drives phagocyte survival and effector functions for antifungal defense. Furthermore, we defined an essential role of extrahepatic, cell-intrinsic complement is phagocyte functional regulation. Consistently, we observed that an impairment in complement activation correlates with poor outcomes in candidemic humans.

    a. **Desai JV**, Kumar D, Freiwald T, Chauss D, Johnson MD, Abers MS, Steinbrink, J, Perfect JR, Alexander B, Matzaraki V, Snarr BD, Zarakas MA, Oikonomou V, Silva LM, Shivarathri R, Beltran E, Demontel LN, Wang L, Lim JK, Launder D, Conti HR, Swamydas M, McClain MT, Moutsopoulos NM, Kazemian M, Netea MG, Kumar V, Kohl J, Kemper C, Afzali B, Lionakis MS. C5a-licensed phagocytes drive sterilizing immunity during systemic fungal infection. ***Cell***. 2023 May 18;S0092-8674(23)00465-8. doi: 10.1016/j.cell.2023.04.031.

2. Microscopy method development and its use towards investigating the immune response: We developed protocols for assessing immune response *in vivo*. Specifically, intravital confocal microscopy and flow cytometry-based assays for phagocytic functions were implemented.

    a. Desai JV*, Lionakis MS*. Evaluation of murine renal phagocyte-fungal interactions using intravital confocal microscopy and flow cytometry. ***STAR Protoc.*** 2023 Dec 18;5(1):102781. doi: 10.1016/j.xpro.2023.102781. Epub ahead of print. PMID: 38113143; PMCID: PMC10770751.

* co-corresponding authors

3. Investigating mucosal and systemic immune response against commensal and environmental fungi: We have identified that a mutation in the fungal-sensing immune receptor DECTIN-1 leads to a deficiency in signaling and macrophage-dependent fungal clearance; this leads to an enhanced susceptibility to a rare fungal infection called phaeohyphomycosis following traumatic fungal inoculation. These findings were recently published in the ***Journal of Clinical Investigation***. Furthermore, we recently described how long-term antibiotic usage leads to dysfunctional IL-17A/GM-CSF-dependent responses within the gastrointestinal tract, promoting systemic bacterial escape and enhancing mortality following systemic candidiasis. I am a co-first author on the manuscript detailing these findings, recently published at the ***Cell Host and Microbe***.

   Besides the above, we have identified why the patients with lymphoma who were treated with Bruton tyrosine kinase (BTK) inhibitors (ibrutinib/acalabrutinib) develop life-threatening aspergillosis. Our work, to be submitted to *Nature Medicine,* revealed a novel role for neutrophil-specific BTK in regulating Rac2 and p40phox-dependent ROS production, degranulation, and fungal killing.

   a. **Drummond RA*, Desai JV***, Ricotta E, Swamydas M, Deming C, Lee C, Green N, Zelazny A, Segre JA, Lionakis MS. Long-term antibiotic exposure promotes mortality after systemic fungal infection by driving lymphocyte dysfunction and systemic escape of commensal bacteria. ***Cell Host and Microbe*** 2022 Jul 13; 30(7): 1020-1033.e6. doi: 10.1016/j.chom.2022.04.013. Epub 2022

      **Equal Contributions*

   b. **Drummond RA*, Desai JV***, Hsu AP, Oikonomou V, Vinh DC, Acklin JA, Abers MS, Walkiewicz MA, Anzick SL, Swamydas M, Vautier S, Natarajan M, Oler AJ, Yamanaka D, Mayer-Barber KD, Iwakura Y, Bianchi D, Driscoll B, Hauck K, Kline A, Viall NS, Zerbe CS, Ferré EM, Schmitt MM, DiMaggio T, Pittaluga S, Butman JA, Zelazny AM, Shea YR, Arias CA, Ashbaugh C, Mahmood M, Temesgen Z, Theofiles AG, Nigo M, Moudgal V, Bloch KC, Kelly SG, Whitworth MS, Rao G, Whitener CJ, Mafi N, Gea-Banacloche J, Kenyon LC, Miller WR, Boggian K, Gilbert A, Sincock M, Freeman AF, Bennett JE, Hasbun R, Mikelis CM, Kwon-Chung KJ, Belkaid Y, Brown GD, Lim JK, Kuhns DB, Holland SM, Lionakis MS. Phaeohyphomycosis and Human Dectin-1-Deficiency. ***Journal of Clinical Investigation,*** 2022 Nov 15;132(22):e159348. Doi: 10.1172/JCI159348..

      **Equal Contributions*

   c. Lionakis MS, Dunleavy K, Roschewski M, Widemann BC, Butman JA, Schmitz R, Yang Y, Cole DE, Melani C, Higham CS, **Desai JV**, Ceribelli M, Chen L, Thomas CJ, Little RF, Gea-Banacloche J, Bhaumik S, Stetler-Stevenson M, Pittaluga S, Jaffe ES, Heiss J, Lucas N, Steinberg SM, Staudt LM, Wilson WH. Inhibition of B Cell Receptor Signaling by Ibrutinib in Primary CNS Lymphoma. ***Cancer Cell***. 2017 Jun 12;31(6):833-843.e5. doi: 10.1016/j.ccell.2017.04.012. Epub 2017 May 25. PMID: 28552327; PMCID: PMC5571650.

4. 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.

5. 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*

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/jigarkumar.desai.1/bibliography/public/