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Research Interests:
Protein-nucleic acid interactions are key to fundamental life processes such as DNA replication, transcription, recombination, and protein synthesis. Deciphering the mechanism of protein-nucleic acid interactions is invaluable for understanding human disease pathways and infections. The primary focus of my lab is to characterize protein-DNA/RNA interactions structurally, biochemically, and biophysically. The immediate emphasis is the study of the recently discovered bacterial and archaeal immune system, CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). CRISPR is an RNA-based adaptive immune system that inactivates foreign DNA/RNA entering the cell, based on the sequence similarity of small RNAs, called CRISPR RNA (crRNA) to the invading genetic element. The process requires several proteins called CRISPR associated (Cas) proteins. The CRISPR/Cas9 system has revolutionized the genome editing field due to the ease with which targeted double-stranded DNA breaks can be achieved in cells, using a guide RNA and Cas9 protein. The long-term goals of my laboratory are to understand the role of CRISPR/Cas system in pathogenicity and virulence of bacteria, characterize the mechanism of adaptation of bacteria to phage infection, and to determine the signaling mechanisms of the CRISPR/Cas system. We incorporate molecular biology, biochemistry, X-ray crystallography, and additional biophysical tools to characterize these protein-nucleic acid interactions.

Education:
2007-2013: Post-doc, Biochemistry and Structural Biology, Northwestern University
2002-2007: Ph.D., Biophysics, The Ohio State University
1998-2000: M.S., Biotechnology, Tamil Nadu Agricultural University
1994-1998: B.S., Agriculture, Kerala Agricultural University

Academic Appointments:
2002-2007: Graduate student with Dr. Charles Bell, Department of Biologic
al Chemistry and Pharmacology, Ohio State University, Columbus, OH
2007-2013: Postdoctoral fellow with Dr. Alfons Mondragón,
Department of Molecular Biosciences, Northwestern University, Evanston, IL
2013-2014: Research Associate with Dr. Alfonso Mondragón, Department of Molecular Biosciences, Northwestern University, Evanston, IL
2014-Present: Assistant Professor, Department of Chemistry and Biochemistry, University of Oklahoma (OU),
Norman, OK

Awards and Honors:
2004-2007: Member, Biophysical Society
2006-2007 and 2010-2013: Member, American Association for the Advancement of Science
2010-2011: Member, American Crystallographic Association
2012, 2015, and 2017: Member, American Heart Association
2012 to Present: Reviewer for Nucleic Acids Research
2015 to Present:Reviewer for PLOS ONE, Scientific Reports
2015 to Present: BioCAT SAXS Course 2015, Advanced Photon Source, Argonne, IL
2016: Session chair: Undergraduate Research Day, University of Oklahoma; Poster judge: 4Th Annual Symposium on Structural Biology, University of Oklahoma, Norman, OK
2016: Completed Light Scattering University 2016, Wyatt Technology, Santa Barbara, CA
2018 to Present Reviewer for Molecular Therapy, Viruses
2018-2019: Member, American Association for the Advancement of Science; Member, American Chemical Society
2018 to Present: Associate Editor: Frontiers in Cellular and Infection Microbiology, Specialty section: Molecular Bacterial Pathogenesis
1996-1997: Chinnamma Thomas Memorial Endowment for highest GPA (B.S. 3rdyr., KAU, India)
1998-2000: Jawaharlal Nehru University (M.S.) Scholarship from the Department of Biotechnology (TNAU, India)
2000-2002: University Grants Commission Junior Research Fellow National Eligibility Test Scholarship for pursuing a Ph.D. degree in India
2004: Best poster award, Ohio State University Molecular and Cellular Biochemistry annual retreat
2006: Outstanding Student Research Achievement Award, Ohio State University Biophysics program
2010-2013: American Heart Association Postdoctoral Fellowship, Northwestern University
2012: Best poster award, Northwestern University Biophysics Symposium
2016: Poster abstract selected for the late-breaker poster at the American Society for Microbiology
Microbe 2016 meeting

Research Support:
Current:

- MCB-1716423/MCB-1716744, USC (Co-PI) 09/15/2017-08/31/2021 "Collaborative Research: Mechanisms of RNA-directed activation of a Cas9 nuclease competent for Rajan, Rakhi, OCRID-Pilot Grant 17 DNA interrogation", Role: PI, 09/15/2017-08/31/2021.
- HR17-124 Rajan, R. Oklahoma Center for the Advancement of Science and Technology (OCAST), Health Research Program, "Characterizing the protein-DNA interactions essential for type II-A CRISPR-Cas adaptation", Role: PI, 07/01/2017-06/30/2020.
- Faculty Investment Program, Vice President for Research and Partnerships, University of Oklahoma, Norman, OK, "Evaluation of Cas12a protein variants for cell-based gene editing accuracy", Role: PI, 1/01/2020-12/31/2020.

Past:

- P20GM103640, NIH Centers of Biomedical Research Excellence (COBRE) in Structural Biology, "Mechanistic characterization of CRISPR-Cas complexes that mediate pathogenicity in the bacterium Francisella tularensis novicida (Phase II)", Role: Project Leader, 09/06/2017-12/31/2019.
- P20GM103447, Oklahoma IDeA Network of Biomedical Research Excellence (OK-INBRE), "Role of "bridge-helix" in imparting target DNA cleavage specificity by Cas9 and Cas12a", Role: Mentor for Summer Student, 05/22/2019-07/13/2019.
- P20GM103447, Oklahoma IDeA Network of Biomedical Research Excellence (OK-INBRE), "RNA-mediated conformational activation of Cas9", Role: Mentor for Summer Student, 05/21/2018-07/13/2018.
- P20GM103640, NIH Centers of Biomedical Research Excellence (COBRE) in Structural Biology, "Mechanistic studies of CRISPR-mediated bacterial immunity (Phase I)", Role: Project Leader, 01/01/2015-05/31/2017.
- Junior Faculty Fellowship Program, University of Oklahoma, "Identifying the role of Csn2 protein in CRISPR-based bacterial immunity", Role: PI, 06/01/2016 -07/31/2016.
- Junior Faculty Fellowship Program, University of Oklahoma, "Characterization of protein-nucleic acid interactions essential for Cas9 activity", Role: PI, 06/01/2015-07/31/2015.

Selected Publications:

1. Van Orden, M., J. # , Klein, P. # , Babu, K., Najar, F.Z., Rajan, R.* (2017). Conserved DNA motifs in the type II-A CRISPR leader region. PeerJ, 5:e3161. https://peerj.com/articles/3161/. PMCID: PMC5382924. (# equal contributors).
2. Sundaresan, R# , Parameshwaran, H.P.# , Yogesha, S.D., Keilbarth, M.W., and Rajan, R.* (2017). RNAindependent DNA cleavage activities of Cas9 and Cas12a. Cell Rep, 21: 3728-3739. PMCID: PMC5760271. (# equal contributors).
3. Babu, K., Amrani, N., Jiang, W., Yogesha, S.D., Nguyen, R., Qin, P.Z., Rajan, R.* (2019) Bridge helix of Cas9 modulates target DNA cleavage and mismatch tolerance. Biochemistry, 58(24): 1905-1917. PMCID: PMC6496953.
4. Zuo, Z., Zolekar, A., Babu, K., Lin, V.J.T., Hayatshahi, H.S., Rajan, R., Wang, Y.C.,* Liu, J.* (2019). Structural and functional insights into the bona fide catalytic state of Streptococcus pyogenes Cas9 HNH nuclease domain. Elife, 8:e465000. PMCID: PMC6706240.
5. Rajan, R., Taneja, B., and Mondragón, A.* (2010). Structures of minimal catalytic fragments of topoisomerase V reveals conformational changes relevant for DNA binding. Structure, 18 (7): 829-838. PMCID: PMC2907367.
6. Rajan, R., Osterman, A.K., Gast, A.T., Mondragón, A.* (2014). Biochemical characterization of the topoisomerase domain of Methanopyrus kandleri topoisomerase V. J Biol Chem, 289 (42): 28898-28909. PMCID: PMC4200249.
7. Rajan, R., Prasad, R., Taneja, B., Wilson, S.H., and Mondragón, A.* (2013). Identification of one of the apurinic/apyrimidinic lyase active

sites of topoisomerase V by structural and functional studies. Nucleic Acids Res, 41 (1): 657-666. PMCID: PMC3592480.
8. Rajan, R., Osterman, A., Mondragón, A.* (2016). Methanopyrus kandleri topoisomerase V contains three distinct AP lyase active sites in addition to the topoisomerase active site. Nucleic Acids Res, 44 (7): 3464-3474. PMCID: PMC4838376
9. Rajan, R., and Bell, C.E.* (2004). Crystal structure of RecA from Deinococcus radiodurans: insights into the structural basis of extreme radioresistance. J Mol Biol, 344 (4): 951-963. PMID: 15544805.
10. Rajan, R., Wisler, J.W., and Bell, C.E.* (2006). Probing the DNA sequence specificity of Escherichia coli RECA protein. Nucleic Acids Res, 34 (8): 2463-2471. PMCID: PMC1459065.
11. Rajan, R., Zhu, J., Hu, X., Pei, D., and Bell, C.E.* (2005). Crystal structure of S-ribosylhomocyteinase (LuxS) in complex with a catalytic 2-ketone intermediate. Biochemistry, 44 (10): 3745-3753. PMID: 15751951.
12. Shen, G., Rajan, R., Zhu, J., Bell, C.E., and Pei, D.* (2006). Design and synthesis of substrate and intermediate analogue inhibitors of S-ribosylhomocysteinase. J Med Chem, 49 (10): 3003-3011. PMID: 16686542.
13. Gopishetty, B., Zhu, J., Rajan, R., Sobczak, A.J., Wnuk, S.F., Bell, C.E., Pei, D.* (2009). Probing the catalytic mechanism of S-Ribosylhomocysteinase (LuxS) with catalytic intermediates and substrate analogues. J Am Chem Soc, 131 (3): 1243-1250. PMCID: PMC2654206.