OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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NAME: Radhika Malik

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

POSITION TITLE: Research Assistant 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) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| St. Stephen’s College, University of Delhi, India  St Stephen’s College, University of Delhi, India | BSc  MSc | 05/2001  05/2003 | Chemistry  Organic Chemistry |
| University of Toledo, Toledo, Ohio, US | Ph. D. | 12/2009 | Biochemistry and  Structural Biology |
| Icahn School of Medicine at Mount Sinai, New York, New York, US | Postdoctoral | 06/2016 | Structural Biology |

1. **Personal Statement**

**I have a broad background in the area of structural biology, with specific training in the areas of Electron Microscopy and X-ray crystallography. In addition, I have received tremendous amount of training on the structural studies of multi-subunit protein complexes. I have successfully collaborated with number of researchers on recent and upcoming publications in the fields of DNA repair and replication. In the past, I have demonstrated my ability to work on a variety of projects including structural and biochemical work on proteins involved in brain disease as well as metabolic function.**

1. **Positions and Honors**

**Positions and Employment**

**2016-2018 Instructor, Department of Pharmacological Sciences, Icahn School of Medicine at Mount Sinai,**

**New York, NY**

**2018- Research Assistant Professor, Department of Pharmacological Sciences, Icahn School of Medicine**

**at Mount Sinai, New York, NY**

**Honors and Awards**

**2003** Graduate Aptitude test in Engineering (GATE) certificate, Indian Institute of Technology (IIT)

2009 Graduate and Postdoctoral Travel award, ASBMB

2013 Travel Award, Neutron Science Directorate (ORNL)

2013 New York Academy of Sciences (NYAS) scholarship, Icahn School of Medicine at Mount Sinai

2014 Best Poster award and Travel grant, ASBMB

2014 Travel award for Bio-XFEL workshop on serial crystallography, Lawrence Berkeley National

Laboratory (LBNL)

**2020 Best poster Award, Department of Pharmacological Sciences, ISMMS.**

1. **Contributions to Science**
2. **Metabolic enzymes. My early publications involved first structural characterization of the metabolic enzyme, tartrate dehydrogenase (TDH) through single wavelength anomalous dispersion (SAD) method. TDH is found in a variety of microorgranisms and functions as part of a pathway through which tartrate is converted to D-glycerate, thereby providing entry of these carbon atoms into primary metabolic pathways. TDH is an unusual NAD-dependent enzyme that exhibits multiple catalytic activities at a single active. Through X-ray crystallographic studies, we were able to determine its high-resolution structure and propose a mechanism of its action.**
3. **Malik, R**., Viola, R. E. **“**Structural Characterization of Tartrate Dehydrogenase: a versatile enzyme catalyzing multiple reactions**”** Acta Crystallographica 2010, D66, 673-684.
4. **Neurological Disorders. Canavan Disease (CD) is a genetically transmitted neurodegenerative disorder that leads to paralysis, blindness and epileptic seizures during the first decade of life. A deficiency in Aspartoacylase activity has been implicated as the cause of CD. I have worked on obtaining mechanistic insights into the function of Aspartoacylase. Among other efforts, I have worked on modifying Aspartoacylase through PEGylation to find an effective treatment for Canavan Disease.**

**I am currently pursuing the structural studies of Leucine-rich repeat kinase 2 (LRRK2). Parkinson’s Disease (PD) is the most common chronic neurodegenerative movement disorder affecting 1 % of the world over the age of sixty. Discovered over a decade ago, LRRK2 has now emerged as a major target not only for understanding the molecular basis of PD but also for therapeutic intervention. LRRK2 mutations have been implicated in a significant number of sporadic PD cases. I am using cryoelectron microscopy (cryo-EM) to get high resolution structural information of full length LRRK2 in order to understand the molecular basis of Parkinson’s disease.**

1. Coq, J. L., Pavlovsky, A., **Malik, R**., Sanishvili, R., Xu, C., Viola, R. E. **“**Examination of the mechanism of the human brain aspartoacylase through the binding of an intermediate analogue**”** Biochemistry 2008, 47(11), 3484-3492.
2. Zano, S., **Malik, R.**, Szucs, S., Matalon, R., Viola, R. E. **“**Modification of aspartoacylase for the potential use in enzyme replacement therapy for the treatment of Canavan Disease**”** Molecular genetics and Metabolism 2011, 102(2), 176-180.
3. Arachea, B. T., Sun, Z., Potente, N., **Malik, R**., Isailovic, D., Viola, R. E. **“**Detergent selection for enhanced extraction of membrane proteins**”** Protein expression and purification 2012, 86(2), 12-20
4. Zano, S., Wijayasinghe, Y. S., **Malik, R.**, Smith, J., Viola, R. E. **“**Relationship between enzyme properties and disease progression in Canavan Disease**”** Journal of inherited metabolic disease 2013, 36(1), 1-6.
5. **Translesion DNA synthesis and repair**. The discovery of translesion synthesis (TLS) DNA polymerases about 15 years ago has changed our view on how cells cope with unrepaired DNA damage during replication. I have used the technique of electron microscopy to solve the challenging structure of an important multi-subunit DNA polymerase, Zeta (Pol ζ). Pol ζ has emerged as the central DNA polymerase for the bypass of the vast majority of DNA lesions formed in eukaryotic cells from genotoxic agents such as sunlight and environmental pollutants. Despite its discovery >20 years ago, there is still no structural understanding of how Pol ζ is organized and the mechanism by which it can bypass the diverse array of DNA lesions in cells. Through our high resolution structural work, we seek to decipher the mechanism of action of this critical enzyme.

In addition, I was involved in solving the structure of a unique DNA polymerase, PrimPol through X-ray crystallographic approaches. This structure of the DNA-bound form of PrimPol addresses how DNA primases actually initiate synthesis and how primase and polymerase activities combine in a single enzyme to carry out DNA synthesis.

1. **Malik, R.**, Kopylov, M., Gomez, Y., Jain, R., Johnson, R. E., Prakash, L. Prakash, S. Ubarretxena, I. B., Aggarwal, A. K. “Structure and mechanism of B-family DNA polymerase Zeta specialized for translesion DNA synthesis” Nature Structural and Molecular Biology 2020, 27, 913-924.
2. Gomez, Y.\*, **Malik, R**.\*, Jain, R., Choudhary, J., Johnson, R. E., Prakash, L., Prakash, S., Ubarretxena, I.B., Aggarwal, A. K. “The architecture of yeast polymerase Zeta” Cell reports 2013, 5(1), 79-86.
3. Rechkoblit, O.\*, Gupta, Y.\*, **Malik, R**.\*, Rajashankar, K., Johnson, R., Prakash, L.,  Prakash, S., Aggarwal, A. K. “Structure and mechanism of human PrimPol, a DNA polymerase with primase activity” Science Advances 2016, 2(10), 1-7.
4. **Other scientific contributions.** I was part of the cryo-EM team to solve the following structures.
5. **Jain, R. William, R. Malik, R., Johnson, R. E., Prakash, L., Prakash, S. Ubarretxena, I. B., Aggarwal, A. K. Cryo-EM structure and dynamics of eukaryotic DNA polymerase δ holoeenzyme Nature Structural and Molecular Biology 2019, 26, 955-962.**
6. **Gomez, Y.\*, Jebara, F.\*, Patra, M.\*, Malik, R., Nisemblat, S., Hecht, O., Parnas, A., Azem, A., Hirsch, J., Ubarretxena, I. B. Structural basis for coexisting active single and double ring complexes in the reaction cycle of the human mitochondrial Hsp60-Hsp10 chaperonin. Nature communications 2020, 11, 1-14.**

\*The authors have contributed equally to this work

1. **Recent teaching contributions. I have been teaching the cryo-EM lecture at ISMMS for the past three years.**

**2019-2021 - Cryo-EM section entitled “High-resolution cryo-EM in drug discovery” in the course “Structural and Chemical approaches to Pharmacology and Drug Discovery (BSR2108).**