MADHUSUDAN DEY
Assistant Professor

PRESENT ADDRESS

Department of Biological Sciences
University of Wisconsin-Milwaukee
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EDUCATIONS

Post-doc (Protein synthesis and protein kinases), 2001-2005
National Institutes of Health, Bethesda, USA

Ph. D. (Life Science), June 2000
School of Life Sciences, Jawaharlal Nehru University, New Delhi, India

M. Sc. (Biotechnology), 1992-1994
School of Biotechnology, Madurai Kamaraj University, India

POSITIONS

Aug 2009 – present:	Assistant Professor, Department of Biological Sciences, UW-Milwaukee, Milwaukee, WI-53211
Dec 2005 – Aug 2009:	Research Fellow, NICHD, National Institutes of Health, Bethesda, MD -20892

RESEARCH INTERESTS

The major research focus of my lab is to understand fully the signaling networks that maintain the protein homeostasis within the endoplasmic reticulum, a new therapeutic target of many human diseases, including certain cancers. Three major sensors of these networks are Ire1 (inositol requiring kinase 1), PERK (ER-stress activated protein kinase) and ATF6 (activating transcription factor 6). The Ire1 pathway is a conserved pathway from yeast to human. This pathway processes *HAC1* mRNA in yeast or the homologous *XBP1* mRNA in mammalian cells. Presently, I have focused on two specific research projects: (1) mechanisms of activation of Ire1 and PERK and (2) mechanisms of translational repression and translocation of *HAC1* mRNA.

TEACHING INTERESTS

Over the past three decades, major advances have been made in ribonucleic acid (RNA) research, which discovered that the functional repertoire of RNA is incredibly vast. RNA can carry genetic information (e.g., RNA genomes of viruses), serve as the chemical blueprint for protein synthesis (e.g., messenger RNA), regulate gene expressions (e.g. micro RNA), and act as enzymes (e.g., ribozyme). My lab is actively engaged in multidisciplinary research, including on various aspects of RNA biology. To translate my research experiences, I offer a course (Bio-597), which covers

various topics of RNA biology, including structural and functional complexity in RNA, splicing and cleavage of RNA, and therapeutic potential of RNA interference.

EDUCATIONAL FELLOWSHIPS

1. **Post-doctoral Fellowship:** National Institutes of Health, 2001-2005 (http://www.nih.gov).
2. **Graduate Fellowship**: Council of Scientific and Industrial Research, Govt. of India, 1994**.** (http://www.csir.res.in**):** *A scholarship supporting the graduate studies.*
3. **Junior Fellowship** in Genetics and Plant Breeding, Indian Council of Agricultural Research, Govt. of India, 1992. (http://www.icar.org.in)**:** *A scholarship supporting MS degree.*
4. **National Scholarship**, 1987, Ministry of Human Resource Development, Govt. of India. (http://education.nic.in): *A scholarship supporting BS degree.*

RESEARCH SUPPORTS

1. UW-Milwaukee (start-up) grant
   Title: Mechanisms of activation of Stress Responsive Kinases PKR and Ire1
   Duration: 2009 -

2. RGI (Research Growth Initiative), UW-Milwaukee
   Title: The Novel Kinase Kin2 Signaling in Endoplasmic Stress
   Duration: 2011-2012

3. R15, National Institutes of Health, USA
   Title: Molecular Insights into Activation and Substrate Recognition of Protein Kinase R
   Duration: 2012 -2015

4. RGI (Research Growth Initiative), UW-Milwaukee:
   Title: Mechanistic Insights into Ire1-HAC1/Xbp1 Signaling Pathway
   Duration: 2013-2014

PUBLISHED PAPERS

1. Mannan, M. A., Shadrick, W. R., Biener, G., Shin B-S, Anshu, A., Raicu, V., Frick, D. N., **Dey, M.** An Ire1-Phk1 Chimera Reveals a Dispensable Role of Auto-kinase Activity in Endoplasmic Reticulum Stress Response (2013). *Journal of Molecular Biology,* **425**, 2083-2099. A **featured article** with cover page.

2. **Dey, M.**, Velyvis, A., Li, J., Chiu, E., Chiovitti, D., Kay, L., Sicheri, F., Dever, T. E. Requirement for kinase-induced conformational change in eIF2α restricts phosphorylation of Ser-51 (2011). *Proceedings of the National Academy of Sciences, USA,* **108** (11), 4316-21.

3. Dev, K., Santangelo T. J., Rothenburg, S., Neculai, D., **Dey, M.**, Sicheri, F., Dever, T. E., Reeve, J. N., Hinnebusch, A. G. Archaeal aIF2B interacts with eukaryotic translation initiation factors eIF2alpha and eIF2Balpha: Implications for aIF2B function and aIF2B regulation (2009). *Journal of Molecular Biol*ogy, **392**, 701-22.

4. Garriz, A., Qiu, H., Dey, M., Seo, E. J., Dever, T. E. Hinnebusch, A. G. A network of hydrophobic residues impeding helix alphaC rotation maintains latency of kinase Gcn2, which phosphorylates the alpha subunit of translation initiation factor 2 (2009). *Molecular and Cellular Biology,* **29**, 1592-607.

5. Rothenburg, S., Deigendesch, N., **Dey, M.**, Dever, T. E., Tazi, L. Double-stranded RNA-activated protein kinase PKR of fishes and amphibians: varying number of double-stranded RNA binding domains and lineage specific duplications (2008). *BMC Biology,* **6**, 12.

6. Lee, K. P. K., **Dey, M**, Dante, N., Cao, C., Dever, T. E., Sicheri, F. Structure of the dual enzyme Ire1 reveals the basis for catalysis and regulation in nonconventional RNA splicing (2008). *Cell,* **132**, 89-100.

   Preview: Ron, D. and Hubbard, S. R. How IRE1 Reacts to ER Stress (2008). *Cell,* **132**, 24-26.

7. Moraes, M. C. S., Jesus, T. C. L., Hashimoto, N. N., Alves, A. S., Avila, C. C., **Dey, M.**, Dever, T. E., Schenkman, S., Castilho, B. A. A novel transmembrane kinase phosphorylates the unusual form of the translation initiation factor 2α of *Trypanosoma brucei* (2007). *Eukaryotic Cell,* **6**, 1979-91.

8. **Dey, M.**, Cao, C., Sicheri, F., and Dever, T. E. Conserved salt-bridge interactions required for activation of protein kinases PKR, GCN2 and PERK (2007). *Journal Biological Chemistry,* **282**, 6653-6660.
9. **Dey, M.**, Cao, C., Dar, A., Tamura, T., Ozato, K., Sicheri, F., and Dever, T. E. Mechanistic link between protein kinase PKR catalytic domain dimerization, autophosphorylation and eIF2α phosphorylation (2005). *Cell,* **122**, 901-913.

   Preview I: Taylor, S. S., Haste, N. M., Ghosh, G. PKR and eIF2alpha: integration of kinase dimerization, activation, and substrate docking (2005). *Cell,* **122**, 823-825.

   Preview II: Hinnebusch A. G. eIF2alpha kinases provide a new solution to the puzzle of substrate specificity (2005). *Nature Structure and Molecular Biology*, **12**, 835-838.

10. **Dey, M.**, Trieselmann, B., Locke, E. G., Lu, J., Cao, C., Dar, A., Krishnamurthy, T., Dong, J., Sicheri, F., and Dever, T. E. PKR and GCN2 kinases and guanine nucleotide exchange factor eukaryotic translation initiation factor eIF2B recognize overlapping surfaces on translation factor eIF2α (2005). *Molecular and Cellular Biology,* **25**, 3063-75.

11. Sharma N, **Dey, M**., and Schaar, S. C. Evidence of two forms of poly (A) polymerase in germinated wheat embryos and their regulation by a novel protein kinase (2002). *Biochemical and Biophysical Research Communications,* **293**, 403-411.

12. **Dey, M.**, and Choudhury, S. Genetically modified organism – A Brave New World! (2001). *Current Science,* **80**, 722-723.

13. **Dey, M.**, and Guha-Mukherjee, S. Aspartate metabolism in *Cicer* immature seeds requires Ca^{2+}, protein phosphorylation and dephosphorylation (2000). *Plant Science,* **150**, 85-91.

14. **Dey, M.**, and Guha-Mukherjee, S. Phytochrome activation of aspartate kinase in etiolated chickpea (*Cicer arietinum*) seedling (1999). *Journal of Plant Physiology,* **154**, 454-458.

15. **Dey, M.**, Kalia, S., Ghosh, S., and Guha-Mukherjee, S. Biochemical and molecular basis of differentiation in plant tissue culture (1998). *Current Science,* **74**, 591-596.

PUBLISHED ABSTRACTS (Selected)

1. Mannan, M. A., Chakraborty, A., Chakrabarti, S. and **Dey, M**. Identification of Residues in the Ire1-RNase Domain Involved in Recognition and Splicing of HAC1 mRNA (2013). FASEB Science Research Conference, From Unfolded Proteins in the ER to Disease, June 16-21Vermont Academy Saxtons River, VT.

2. Mann, B. and **Dey, M.** Unfolding The Regulatory Mechanisms Of Thr-446 Autophosphorylation In The Activation Loop Of PKR (2012). *Cold Spring Harbor Laboratory Meeting on Translational Control*, Cold Spring Harbor, New York

3. Mannan M. A., Shadrick W. R., Shin B-S, Anshu, A., Frick, D. N., **Dey, M.** Activation Loop Phosphorylation is Dispensable for the Regulation of Dual Kinase/Endonuclease Ire1 Function (2012). Gordan Research Conference "Post-Transcriptional Gene Regulation, The Biology of" July 15-20, 2012 at Salve Regina University, Newport, RI.

4. **Dey, M.** Translational Regulation by Phospho-eIF2α Requires Phosphorylation of Specifically Position 51 (2010). *Cold Spring Harbor Laboratory Meeting on Translational Control*, Cold Spring Harbor, New York.

5. Stoneman, M., Patowary, s., Roesch, M., **Dey, M.**, Raicu, V. In vivo monitoring of agonist-induced relative movements between G-protein coupled receptor segments in oligomeric complexes using spectrally resolved FRET (2010). *Biophysical Society Annual Meeting*, Baltimore, Maryland.

6. **Dey, M.** Binding to PKR Induces a Conformational Change in eIF2α to Expose Ser51 for Phosphorylation (2008). *Cold Spring Harbor Laboratory Meeting on Translational Control*, Cold Spring Harbor, New York.

7. **Dey, M.** Cao, C., Sicheri, F., Dever, T.E. Conserved Intermolecular Salt-bridge Required for Activation of Protein Kinases PKR, GCN2 and PERK (2007). *Annual Meeting*, NICHD, Bethesda, Maryland.

8. **Dey, M**. Cao, C., Dar, A., Sicheri, F., Dever, T. E. Mechanistic Link between Catalytic Domain Dimerization, Autophosphorylation and eIF2α Substrate Recognition by the RNA-dependent Protein Kinase PKR (2005). *FASEB Summer Research Conference on Protein Kinases and Protein Phosphorylation*, Snowmas, Colorado.

9. **Dey, M**., Trieselman, B., Locke, E. and Dever, T. E. Analysis of Substrate Recognition by the eIF2α Protein Kinases. (2002) *Cold Spring Harbor Laboratory Meeting, Translational Control*, Cold Spring Harbor, New York.

INVITED TALKS (Selected)

2013: ASBMB Symposium on The Multitasking ER, Warrenton, Virginia, USA

Title: An Ire1-Phk1 Chimera Reveals a Dispensable Role of Autokinase Activity in Endoplasmic Reticulum Stress Response

2011: Indian Institute of Chemical Biology, Kolkata, India.
Title: Requirement for kinase-induced conformational change in eIF2α restricts phosphorylation of Ser-51.

2010: Milwaukee Microbiology Society Talk, Milwaukee, Wisconsin, USA
Title: Yeast *HAC1* mRNA Processing and Cleavage: Kissing Hairpin Complex Requirement.

2009: School of Medicine, Iowa State University, Iowa, USA
Title: Substrate Recognition by Protein Kinase PKR.

2009: Dept. of Biology, University of Delaware, Delaware, USA
Title: Stress Responsive Kinases PKR and Ire1: Molecular Insights and Mechanistic Paradigm.

2008: Developmental Biology, Cincinnati Children Hospital, Cincinnati, Michigan, USA
Title: Stress Responsive Kinases PKR and Ire1: Molecular Insights and Mechanistic Paradigm.

2008: Dept. of Biology, The Catholic University of America, Washington DC, USA
Title: Mechanistic Link between PKR Dimerization, Autophosphorylation and eIF2α Phosphorylation.

2008: Dept. of Biology, University of Oakland, Rochester, Michigan, USA
Title: PKR Dimerization, Autophosphorylation and eIF2α Phosphorylation.

2006: Cold Spring Harbor Laboratory Meeting on Translational Control, New York, USA
Title: eIF2α Kinases Require a Common Dimer Interface and Induce a Conformational Change to access the Ser-51 Phosphorylation Site in eIF2α.

2005: Washington Yeast Club, Washington DC
Title: Mechanisms of PKR kinase-eIF2α substrate recognition and Specificity.

2004: Cold Spring Harbor Laboratory Meeting on Translational Control, New York, USA.
Title: PKR and GCN2 Kinases and GEF eIF2B Recognize Overlapping Surfaces on Translation Factor eIF2α.

PROFESSIONAL ACTIVITIES:

Reviewer: For the journals: *Journal of Biological Chemistry*, *Trends in Biochemical Sciences (TiBS)*, *Invitro Biology*, *Plant Science*, *Molecular Cell*, *Biochemistry, FEBS letter.*

Member: The American Society for Biochemistry and Molecular Biology, USA

COMMUNITY SERVICES

2012-13: Mentor of SMART (Students Modeling A Research Topic) teams, Milwaukee School of Engineering, Milwaukee, Wisconsin.

1. Team of Brookfield Central High School
2. Team of Wisconsin Virtual Center
3. Team of Brookfield Academy

2011-12: Mentor of undergraduate students from Milwaukee Area Technical College (MATC), Milwaukee, Wisconsin.

PRESENT and PAST STUDENTS

A. Undergraduate

1. Nicholas Kleine, Department of Chem. and Biochemistry, UW-Milwaukee (past)
2. Christopher Beal, Department of Health Sciences, UW-Milwaukee (past)
3. Brian Rick Mann, Department of Chem. and Biochemistry, UW-Milwaukee (past)
4. Douglas Johnson, Department of Chem. and Biochemistry, UW-Milwaukee (past)
5. Sam Thomson, Milwaukee Area Technical College, Milwaukee (past)
6. Anna Koziel, Milwaukee Area Technical College, Milwaukee (past)
7. Timothy Zeidler, Department of Biology, UW-Milwaukee (present)
8. Simar Puri, Brookfield Academy, Brookfield, WI (present)

B. Graduate

1. Ashish Ansu, Department of Biological sciences, UW-Milwaukee (present)
2. Leena Sathe, Department of Biological Sciences, UW-Milwaukee (present)

C. Post-graduate

1. Amin-ul Mannan, Ph.D. (present)
2. Durgesh Singh, Ph.D. (will join on Oct 1st 2013)