

## **Dr. Arumugam Madhumalar**

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Pubmed link : <https://www.ncbi.nlm.nih.gov/pubmed/?term=Madhumalar>

### **Expertise**

Computational structural biology

### **Research Experience**

**Assistant professor (UGC-FRP), Multidisciplinary Centre for Advanced Research and Studies (MCARS), Jamia Millia Islamia, New Delhi, 17<sup>th</sup> August 2016-present:**

My research interest is to develop atomistic models using laws of physics, to understand the role of biomolecular structural dynamics in orchestrating functions so as to probe, engineer, and design better therapeutics. My current research focus includes

- **Repurposing antiviral drugs against SARS CoV-2 Main Protease (M<sup>pro</sup>).**
- **Structure-based inhibitor/modulator design for GalNAc transferases.**
- **Modelling permeability of small molecules through lipid bilayer.**

**Research scientist, National Institute of Immunology, INDIA (Apr 2012-Oct 2015)**

- Modelling and Molecular Dynamics on p53 from species *Spalax* and *Urodele* which are known to survive human cancerous mutations, to understand the evolution of dynamics of p53.
- Modelled the evolutionary dynamics of Spindle kinetochore assembly protein (Ska1) from *Human* and *C.elegans*, hence their functional differences.
- *Phylogenetic analysis of p53, p63, p73 from newly sequenced Lamprey genome.*

**SENIOR POSTDOCTORAL RESEARCH FELLOW, BIOINFORMATICS INSTITUTE, A\*STAR, SINGAPORE (2006-DEC, 2010)**

- Applied Modelling and Molecular Dynamics techniques to understand the structural and functional differences of tumour suppressor p53 family of proteins and its regulators MDM2/MDMX.
- Designed a peptide inhibitor, which has a potential to rescue p53 function in tumours with over expression of MDM2/MDMX. Patent has been filed and published.
- Applied Modelling and MD to underpin the molecular basis for the differential binding of p53 and nutlin to MDM2 and MDMX
- Abinitio folding of p53 family of peptides to understand its differential binding with regulators MDM2/MDMX.
- Proposed a new mechanism for the oligomerisation of p53, based on modelling studies.

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- Evolutionary analysis on p53 and MDM2 from ancient invertebrate *Trichoplax*, *Deer tick* and early vertebrates *lamprey*, *Eshark*.
  - Modelled various cancerous mutants and posttranslational modifications of p53 to probe the mechanism of its functional and diseased states.
  - Actively collaborated with researchers from UK, Singapore and provided insights into the mechanisms behind their experimental findings using modelling and further designing experiments.
  - Mentored interns, students, postdocs across the institutes and actively participated in discussions.

**Ph.D., STRUCTURAL BIOLOGY, INDIAN INSTITUTE OF SCIENCE, BANGALORE, INDIA**  
**Doctoral thesis on:**

**“Effect of sequence on DNA structure: Insights form Molecular Dynamics studies”.**

- Modelling and Molecular Dynamics studies on variety of DNA sequences to understand the effect of sequence, hydration and ions on the topology of DNA structure.

**Patent**

**Novel MDM2 binding peptides and uses thereof (WO 2011/005219 A1; International Patent Publication Number)**

Designed a peptide that has a higher affinity for MDM2 and MDMX, which may potentially rescue p53 function in tumours with over expression of MDM2/MDMX.

p53 is a major tumour suppressor protein, which is negatively regulated by the oncoprotein MDM2. In tumours with over-expression of MDM2, the activity of p53 can be rescued by disrupting this MDM2-p53 interaction using peptides or small molecules. The factors necessary for the binding interaction between MDM2 and p53 family members have been identified which enabled to design the peptide that has a higher affinity for MDM2 and MDMX and may be able to rescue p53 function in apoptosis by disruption of the MDM2/MDMX-p53 interaction.

**Academic background**

- Ph.D., Structural Biology, Indian Institute of Science, Bangalore, India (1998-2005)
- Master of Science (M.Sc.), Physics, The American College, Madurai, India (1996-1998)
- Bachelor of Science (B.Sc.), Physics, VVV College for Women, Virudhunagar, India (1993-1996)

**Teaching Experience**

1. Research Methodology (4 credit) 2018 onwards, Pre-PhD Course, MCARS, Jamia Millia Islamia
2. Data management, Analysis and statistics (4 credit) Semester 2019 onwards, PGDMD course MCARS, Jamia Millia Islamia

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## **Awards and Honours**

- Awarded Early Career Academic Grants by The Association of Commonwealth Universities, UK, 2017
- Selected for UGC-FRP Assistant Professor in Biological sciences 2015
- Awarded DBT's Bio-Care Women Scientist Fellowship 2011 .
- Awarded Travel Fellowship by the Dept of Science and Technology, Govt of India to attend the 48th Biophysical society annual meeting, February 14th -18th 2004 at Baltimore, Maryland, USA.
- Awarded summer fellowship by IISc, IIA and RRI for summer training in Astrophysics, 1997
- Associate Faculty Member of F1000, Theory and Simulation section.
- Editorial board member in the journal Science Matters

## **Publications**

- Sanjeev BS, Chitara D, **Madhumalar A**. Physiological models to study the effect of molecular crowding on multi-drug bound proteins: insights from SARS-CoV main protease. **J Biomol Struct Dyn.** **2021** Oct 26:1-17. doi: 10.1080/07391102.2021.1993342. Epub ahead of print. PMID: 34699337.
- Bhat ZA, Chitara D, Iqbal J, Sanjeev BS, **Madhumalar A**<sup>#</sup>. Targeting allosteric pockets of SARS-CoV-2 main protease Mpro. **J Biomol Struct Dyn.** **2021** Feb 27:1-16. doi: 10.1080/07391102.2021.1891141. Epub ahead of print. PMID: 33645457.
- Coffill CR, Lee AP, Siau JW, Chee SM, Joseph TL, Tan YS, **Madhumalar A**, Tay BH, Brenner S, Verma CS, Ghadessy FJ, Venkatesh B, Lane DP. (2016) The p53-Mdm2 interaction and the E3 ligase activity of Mdm2/Mdm4 are conserved from lampreys to humans. **Genes Dev.** Jan 21. [Epub ahead of print].
- Abad MA, Medina B, Santamaria A, Zou J, Plasberg-Hill C, **Madhumalar A**, Jayachandran U, Redli PM, Rappsilber J, Nigg EA, Jeyaprakash AA. (2014) Structural basis for microtubule recognition by the human kinetochore Ska complex. **Nat Commun.** 2014;5:2964. doi: 10.1038/ncomms3964.
- Lane DP, **Madhumalar A**, Lee AP, Tay BH, Verma C, Brenner S, Venkatesh B. Conservation of all three p53 family members and Mdm2 and Mdm4 in the cartilaginous fish. (2011). **Cell Cycle.** 10(24):4272-9.
- Fuentes, G., Dastidar, S. G., **Madhumalar, A.** and Verma, C. S. Role of protein flexibility in the discovery of new drugs. **Drug Dev. Res.** (2011), 72: 26–35. doi: 10.1002/ddr.20399.

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- Fraser JA, **Madhumalar A**, Blackburn E, Bramham J, Walkinshaw MD, Verma C and Hupp TR. A novel p53 phosphorylation site within the MDM2 ubiquitination signal: II. A model in which phosphorylation at SER269 induces a mutant conformation to p53. (2010) *J Biol Chem.* (2010) 285(48):37773-86.
  - Joseph TL, **Madhumalar A\***, Brown CJ, Lane DP and Verma C. Differential binding of p53 and nutlin to MDM2 and MDMX: Computational studies. (2010) *Cell Cycle*, 9:1167-1181.  
**Comments in: The molecular dynamics of MDM2 Targeting. Judith Nicholson and Ted R.Hupp Cell Cycle, 2010; 10: 1878 – 1881.**
  - Lane DP, Cheok CF, Brown C, **Madhumalar A**, Ghadessy FJ and Verma C. The Mdm2 and p53 genes are conserved in the Arachnids. (2010) *Cell cycle*, 9:748-754.
  - Lane DP, Cheok CF, Brown C, **Madhumalar A**, Ghadessy FJ and Verma C. Mdm2 and p53 are highly conserved from placozoans to man. (2010), *Cell cycle*, 9:540-547.
  - Dastidar SG, **Madhumalar A**, Fuentes G, Lane DP, Verma CS. Forces mediating protein--protein interactions: a computational study of p53 "approaching" MDM2. (2010), *Theoretical Chemistry Accounts*, 125:621-35.
  - Jagadeesh MN, **Madhumalar A\***, Beuerman RW, Lane DP, Verma CS. Differences in the transactivation domains of p53 family members: a computational study. (2010), *BMC genomics* (2010), 10 Feb, S5.
  - **Madhumalar A**, Lee HJ, Brown CJ, Lane DP, Verma CS. Design of a novel MDM2 binding peptide based on the p53 family. (2009). *Cell Cycle*, 8:2828-36.  
**Comments in: Targeting protein interactions of p53 for therapeutic intervention: Success in a frustrated landscape. Tom L. Blundell and Victor M. Bolanos-Garcia Cell Cycle News, 2009; 8: 3631 – 3635.**  
**Faculty of 1000 Biology: evaluations for Madhumalar A et al Cell Cycle (2009) Sep 1 8 (17):2828-36 <http://www.f1000biology.com/article/id/1166641/evaluation>**
  - **Madhumalar A**, Lee HJ, Lane DP and Chandra S.Verma. Dimerisation of the core domain of p53 family: A Computational study. (2009). *Cell Cycle* 8:137-148.
  - **Madhumalar A**, Smith, D J and Chandra S.Verma. Stability of the core domain of p53: Insights from computer simulations. (2008), *BMC Bioinformatics*, 13 Feb, S17.
  - **Madhumalar A** and Bansal. M. Sequence dependent BI/BII Conformation: Evidences from MD study and crystal structures. (2005). *J. Biomol. Struct. Dyn.* 23: 13-27.

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- **Madhumalar A** and Bansal. M. Structural Insights into the Effect of Hydration and Ions on A-Tract DNA: A Molecular Dynamics Study. (2003). *Biophysical Journal*. 85:1805-1816.

\* **Equal contributions**

# **Corresponding author**

### Book Chapter

**A.Madhumalar** and Bansal. M. Sequence dependent structural features of A<sub>3</sub>T<sub>3</sub> vs (AT) from Molecular Dynamics study. 2003. *Recent Trends in Biophysical Research*. (Ed.M.Maiti), 10-16.

### Oral Presentations

- **Cooperativity in binding of p53 to DNA: a computational study.** **A.Madhumalar**, Hui Jun Lee, David P.Lane and Chandra S.Verma at the Biomolecular simulations 2008: The second CCPB annual conference, *Bristol, UK. Jan 7<sup>th</sup>-9<sup>th</sup>, 2008.*
- **Dimerization of core domain of p53 family: a computational study.** at a Workshop on Computational System Biology approaches to analysis of Genome Complexity and Regulatory Gene networks, *Singapore, November, 2008.*
- **Dissecting MDM2-p53 peptide interactions through computer simulations.** **Madhumalar A**, David P Lane, Chandra Shekhar Verma at **MM2009, Gold coast, Australia, July 26<sup>th</sup>-29<sup>th</sup>, 2009.**
- **Designing therapeutic peptides: based on the p53 family.** **Madhumalar A**, Jagadeesh Mavinahalli N, David P Lane and Chandra Verma at **SHANGHAI SOCIETY OF BIOPHYSICS, Shanghai, August 8<sup>th</sup>-12<sup>th</sup>, 2010.**

### Poster Presentations

- **The role of BII nucleotides in C form DNA.** **A. Madhumalar** and Manju Bansal at the 48<sup>th</sup> Biophysical society annual meeting, February 14<sup>th</sup> -18<sup>th</sup> 2004 at *Baltimore, Maryland, USA.*
- **Stability of core domain of p53: Insights from computer simulations.** **A.Madhumalar**, David P.Lane and Chandra S.Verma at the Joint Third AOHUPO and Fourth Structural Biology and Functional Genomics Conference, *National University of Singapore, December 4<sup>th</sup>-7<sup>th</sup>, 2006 at Singapore.*
- **Computational Characterizations of p53-MDM2 interactions.** **A.Madhumalar**, Hui Jun Lee, David P.Lane and Chandra S.Verma at the Biological Diffusion and Brownian Dynamics Brainstorm, March 26<sup>th</sup>-29<sup>th</sup>, 2007 at *Heidelberg, Germany.*

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- **Understanding p53 interactions for therapy.** Madhumalar A, J. T. Leonard, S. G. Dastidar, H. J. Lee, M. Hui, C.S. Verma, A\*star scientific conference, November 2008, *Singapore*.
  - **Functional characterisation of p53 and Mdm2 in the ancient eukaryotes *Trichoplax adhaerens* and *Lethenteron japonicum*.** Siau Jia Wei, Cindy Coffill, Juliane Hundt, Boon-Hui Tay, Byrappa Venkatesh, Arumugam Madhumalar, Chandra Verma, David Lane, Farid Ghadessy at the 6th International **p53 Workshop**, Stockholm, June **2014**.
  - **“Adaptive dynamics of p53 DNA binding domain: Insights from Sequence and Molecular Dynamics studies”** by Arumugam Madhumalar at the “The 17 th international p53 workshop”, Singapore from 8 th -12 th July, **2017**.