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DATE OF BIRTH

4TH August, 1975

CITIZENSHIP

INDIA

EDUCATION/RESEARCH EXPERIENCE

National Institutes of Health, National Institutes of Allergy and Infectious Diseases
Principal Investigator: Dr. Clifton E Barry 3rd Feb 2005 – January 2010

Mechanism of action of TB drug currently in clinical trials

- Deazaflavin dependent nitroreductase, Ddn – Biochemical characterization of a novel family of enzymes, Ddn was done. This enzyme was able to activate bicyclic nitroimidazole by reduction of the imidazole ring thereby generating reactive nitric oxide species. Thus, bicyclic nitroimidazoles act as intracellular NO-donors augmenting a killing mechanism intrinsic to innate immune system. We are currently identifying the natural substrates for Ddn and its homologues.
- 3-D-QSAR model for bicyclic nitroimidazoles – We have built a QSAR model for activation of bicyclic nitroimidazoles by Ddn. We have measured enzymatic activation of a ~77 compounds by Ddn and this model should provide rationale for designing more potent bicyclic nitroimidazoles. Structure determination of Ddn alone as well as in complex with nitroimidazoles are currently in progress.

University of Delhi South Campus, Department of Biochemistry, New Delhi, India.

- Ph.D., Biochemistry, 1998-2004

Dissertation title: **“Analysis and characterization of genes associated with pathogenesis of *M. tuberculosis*”**

- Biochemical characterization of mycobacterial protein tyrosine phosphatases (Mptp) was done. Mutant strains of *mptp* were constructed and it was shown that mptp's are involved in virulence of *M. tuberculosis*. I am collaborating with my Ph.D. Supervisor to identify which proteins are being dephosphorylated by Mptp.
- Protective efficacy of recombinant BCG and DNA vaccines – I was also part of the team evaluating the role of rBCG and DNA vaccines in protection against *M. tuberculosis* infections in guinea pig model of tuberculosis. This work was done in collaboration with Tuberculosis Research Centre, Chennai and National JALMA Institute for Leprosy and other Mycobacterial diseases, Agra.

University of Delhi South Campus, Department of Biochemistry, New Delhi, India.

- M.Sc, Biochemistry, 1996-1998

University of Delhi South Campus, Department of Biochemistry, New Delhi, India.

- B.Sc, Biochemistry, 1993-1996

AWARDS & FELLOWSHIPS

- National Bioscience Award for Career Development 2014 from Department of Biotechnology, India.
- Ramalingaswami Fellowship June 2010 – 2015
- FELLOWS AWARD FOR RESEARCH EXCELLENCE by the National Institutes of Health in 2007
- DBT-Wellcome Trust India Alliance Senior Research Fellowship, September 2020 – 2025.

PUBLICATIONS

1. Gosain TP, Chugh S, Rizvi ZA, Chauhan NK, Kidwai S, Thakur KG, Awasthi A and **Singh R***. *Mycobacterium tuberculosis* strain with deletions in *menT3* and *menT4* is attenuated and confers protection in mice and guinea pigs. **Nature Communications**, **15**, 2024, 5467.
2. Chugh S, Bahal RK, Dhiman R and **Singh R***. Antigen identification strategies and preclinical evaluation models for advancing tuberculosis vaccine development. NPJ vaccines, 2024. 9(1): 57.
3. Chugh S, Tiwari P, Suri C, Gupta SK, Singh P, Bouzeyne R, Kidwai S, Srivastava M, Rameshwaram NR, Kumar Y, Asthana S and **Singh R***. Polyphosphate Kinase -1 regulates bacterial and host metabolic pathways involved in pathogenesis of *Mycobacterium tuberculosis*. **Proceedings of the National Academy of Sciences**, 2024, 121(2), e2309664121.
4. Singh P, Kumar A, Sharma P, Chugh S, Kumar A, Sharma N, Gupta S, Singh M, Kidwai S, Sankar J, Taneja N, Kumar Y, Dhiman R, Mahajan D and **Singh R***. Identification and optimization of pyridine carboxamide scaffold as a drug lead for *Mycobacterium tuberculosis*. **Antimicrobial Agents and Chemotherapy**, 2024, 68(2), e00766-23.
5. Gupta V, Sundaramoorthy NS, Bhanwala N, Ambatwar R, Kumar S, **Singh R***, Khatik GL*. Design, synthesis, evaluation, and molecular docking study of novel quinoline hydrazone analogues as anti-tubercular agents. Journal of Computational Biophysics and Chemistry, 2024. * co-corresponding author.
6. Bhanwala N, Sundaramoorthy NS, Gollapudi S, Sharma A, **Singh R*** and Khatik GL*. Design, synthesis, anti-tubercular activity, and computational studies of novel 3-(quinolin-3-yl)-1-phenylprop-2-en-1-one derivatives. Medicinal Chemistry Research, 2024. * co-corresponding author.
7. Tiwari P, Mangubhai GS, Kidwai S, **Singh R*** and Chandrashekhara S*. Design, synthesis and characterisation of ethyl 3-benzoyl-7-morpholinoindolizine-1-carboxylate as anti-tubercular agents: In silico screening for possible target identification. Chem Biol Drug Des, 2024, 103 (4): e14512. * co-corresponding author.

8. Naik L, Patel S, Kumar A, Ghosh A, Mishra A, Das M, Nayak DK, Saha S, Mishra A, **Singh R**, Behura A and Dhiman R. 4-(Benzyloxy)phenol-induced p53 exhibits antimycobacterial response triggering phagosome-lysosome fusion through ROS-dependent intracellular Ca^{2+} pathway in THp-1 cells. *Microbiological Research*, May 2024, 282, 127664.
9. Tiwari, P, Mangubhai GS, Kidwai S, **Singh R*** and Chandrashekhara S*. Design, synthesis and characterization of novel ethyl 3-benzoyl-7-morpholinoindolizine-1-carboxylate as anti-tubercular agents. *Chemical Biology and Drug Design*, manuscript accepted. * co-corresponding author
10. Merugu, SR, Mokoena S, Obakachi V, Shaik BB, Kushawaha B, Kushwaha ND, ike BW, Palkar MB, Bonde CG, Chauhan R, Kajee A, Ghai M, Kidwai S, **Singh R** and Kapoornath R. Novel 4,5-dibromo-N-phenyl-1H-pyrrole-2-carboxamide hybrids as promising DNA gyrase inhibitors: Design, synthesis and antimicrobial evaluation. *Journal of Molecular Structure*, 2024, 1302.
11. Mishra A, Kumar A, Naik L, Patel S, Das M, Behura A, Mishra A, Bhutia SK, **Singh R** and Dhiman R. Soybean lectin-triggered IL-6 secretion induces autophagy to kill intracellular mycobacteria through P2RX7 dependent activation of the JAK2/STAT3/Mcl-1 pathway. *Cytokine*, 2023.
12. Kumar A, Naik L, Patel S, Das M, Nayak DK, Mishra A, Mishra A, **Singh R**, Behura A and Dhiman R. AC-93253 inhibits intracellular growth of mycobacteria in human macrophages by inducing apoptosis in mitochondrial dependent manner. *BBA-General Subjects*, 2023.
13. Deep A, Singh L, Kaur J, Velusamy M, Bhardwaj P, **Singh R** and Thakur KG. Structural insights into DarT toxin neutralization by cognate DarG antitoxin: ss DNA mimicry by DarG C-terminal domain keeps the DarT toxin inhibited. *Structure*, 2023, 31, 1-10.
14. Manav N, Chavda J, Kidwai S, **Singh R**, Mori S and Gupta I. Pd(II) dipyrinato complexes: Synthesis, crystal structure and their antibacterial application. *Journal of Porphyrins and Phthalocyanines*, 2023, 27, 1-9.
15. Shivaprasad K, Kidwai S, Gopavaram S, Saini MS, Reddy K, Chugh S, **Singh R*** and Cahnrashekhara S*. Design, synthesis and *in vitro* antitubercular evaluation of novel 7-methoxy pyrrolo [1,2-a] quinoline analogues as Cyp21 inhibitors. *Journal of Molecular Structure*, 2023. 135439. * co-corresponding author
16. Bhanot A, Lunge A, Kumar N, Kidwai S, **Singh R**, Sundriyal S and Agarwal N. Discovery of small molecule inhibitors of Mycobacterium tuberculosis ClpC1, SAR studies and antimycobacterial evaluation. *Results in Chemistry*, 2023, 100904.
17. Mundhe P, Kidwai S, Saini MS, Singh HR, **Singh R***, and Chandrashekhara S*. Design, synthesis, characterization and anti-tubercular activity of novel ethyl-3-benzoyl-6,8-difluoroindolizine-1-carboxylate analogues. Molecular target identification and molecular docking studies. *Journal of Molecular Structure*, 2023. 135359. * co-corresponding author.
18. Mangla N, **Singh R**, and Agarwal N. HtpG is a metal dependent chaperone which assists DnaK/DnaJ/GrpE chaperone system of *Mycobacterium tuberculosis* via direct interaction with DnaJ2. **Microbiology Spectrum**, 2023, Manuscript accepted.

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21. Tiwari P, Gosain TP, Chugh S, Singh M, Sankhe GD, Arora G, Kidwai S, Agarwal S, Saini DK, and **Singh R***. Exopolyphosphatases PPX1 and PPX2 from *Mycobacterium tuberculosis* regulate dormancy response and pathogenesis. **Microb Pathog**, Dec 173 (Pt B), 2022: 105885.
22. Gosain TP, Singh M, Singh C, Thakur K, and **Singh R***. Disruption of MenT2 toxin impairs the growth of *Mycobacterium tuberculosis* in guinea pigs. **Microbiology**, 168 (11) 2022, 001246.
23. Singh P, Rawat S, Agrahari AK, Singh M, Chugh S, Gurcha S, Singh A, Abrahams K, Besra, GS, Asthana S, Rawat DS and **Singh R***. NSC19723, a Thiacezone-like Benzaldehyde Thiosemicarbazone Improves the Efficacy of TB Drugs *In Vitro* and *In Vivo*. **Microbiology Spectrum**, 10 (6), 2022, e02592-22.
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29. Mishra BB, Essafi M, **Singh R**, Gupta S, and Parihar SP. Repurposed drugs as Immune-Modulators to combat Infectious Diseases. **Frontiers in Immunology**, 2022, 1-3.

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33. Khurana H, Srivastava M, Chaudhary D, Gosain TP, Kumari R, Bean AC, Chugh S, Maiti T, Stephens CE, Asthana S, and **Singh R***. Identification of diphenyl furan derivative via high throughput and computational studies as ArgA inhibitor of *Mycobacterium tuberculosis*. **International Journal of Biological Macromolecules**, 193, 2021, 1845-1858.
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35. Bouzeyne R, Chugh S, Gosain TP, Barbouche MR, Haoues M, Rao KVS, Essafi M, and **Singh R**. Co-administration of anticancer candidate MK-2206 enhances the efficacy of BCG vaccine against *Mycobacterium tuberculosis* in mice and guinea pigs. **Frontiers in Immunology**, 12, 2021, 1-18.
36. Gagandeep, Singh M, Kidwai S, Das US, Velpandian T, **Singh R**, and Rawat DS. Monocarbonyl curcuminoids as antituberculosis agents with their moderate *in-vitro* metabolic stability on human liver microsomes. **Journal of Biomolecular and Molecular Toxicology**, 35(6), 2021, 1-10.
37. Singh M, Schiavone N, Papucci L, Maan P, Kaur J, Singh G, Nandi U, Nosi D, Tani A, Khuller G, Priya M, **Singh R**, and Kaur IP. Streptomycin sulphate loaded solid lipid nanoparticles show enhanced uptake in macrophages, lower MIC in *Mycobacterium* and improved oral bioavailability. **European Journal of Pharmaceutics and Biopharmaceutics**, 160, 2021, 100-124.
38. Mishra A, Behura A, Kumar A, Ghosh B, Naik L, Mawatlal S, Mohanty SS, Mishra A, Saha S, Bhutia SK, **Singh R**, and Dhiman R. Soybean lectin induces autophagy through P2RX7 dependent activation of MF-kB-ROS pathway to kill intracellular mycobacteria. **Biochimica et Biophysica Acta** 1865 (2), 2021, 1-15.
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40. Jadhav P, Sinha VK, Chugh S, Kotyada C, Bachhav D, **Singh R**, Rothweller U and Singh M. 2.09Å resolution structure of *E. coli* HigBA toxin-antitoxin complex reveals

an ordered DNA-binding domain and intrinsic dynamics in antitoxin. **Biochemical Journal** 477(20), 2020, 4001-4019.

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42. Singh P, Khurana H, Yadav SP, Dhiman K, Singh P, Ashish, **Singh R**, and Sharma D. Biochemical characterization of ClpB protein from *Mycobacterium tuberculosis* and identification of its small molecule inhibitors. **International Journal of Biological Macromolecules** 165 (Pt A), 2020, 375-387
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44. Agarwal S, Sharma A, Bouzeyen R, Deep A, Sharma H, Mangalaparthu K, Datta KK, Kidwai S, Gowda H, Varadarajan R, Sharma RD, Thakur KG and **Singh R**. VapBC22 toxin-antitoxin system from *Mycobacterium tuberculosis* is required for pathogenesis and modulation of host immune response. **Science Advances** 2020, 1-15.
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46. Bouzeyen R, Haoues M, Barbouche MR, **Singh R**, and Essafi M. FOXO3 transcription factor regulated IL-10 expression in mycobacteria-infected macrophages, tuning their polarization and the subsequent adaptive immune response. **Frontiers in Immunology** 10, 2019, 2922.
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48. Tandon H, Sharma A, Wadhwa S, Varadarajan R, **Singh R**, Srinivasan N, and Sandhya S. Bioinformatic and mutational studies of related toxin-antitoxin pairs in *M. tuberculosis* predict and identify key functional residues. **Journal of Biological Chemistry** 294 (23), 2019, 9048-9063.
49. Maurya SS, Gosain TP, Kidwai S, **Singh R**, and Rawat DS. Synthesis of 1,3,4-oxadiazole and imidazo [1,2-1] pyridine based molecular hybrids and their *in vitro* antituberculosis and cytotoxicity studies. **Indian Journal of Chemistry** 58B, 2019, 1005-1018.
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- MtrB of *Mycobacterium tuberculosis* regulates hypoxic survival and establishment of infection. **Journal of Biological Chemistry** 294 (52), 2019; 19862-19876.
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Book Chapters

1. **Singh R**, Kumar P and Tahlan K. Drugs against *Mycobacterium tuberculosis*. Book Chapter in Drug discovery targeting drug-resistant bacteria. Elsevier Press. 2020.

2. Tyagi AK, **Singh R** and Gupta V. Role of Mycobacterial Kinases and Phosphatases in bacterial growth and pathogenesis in "The Mycobacterial Cell Envelope, an overview" edited by Dr. Mamadou Daffe and Dr. Jean Marc Reyrat, 2008.
3. Boshoff HI, **Singh R** and Barry CE^{3rd}. Virulence and Persistence mechanisms of *Mycobacterium tuberculosis*, in Handbook of Tuberculosis: Molecular Biology and Biochemistry edited by Dr. Stefan H. E. Kaufmann and Dr. Eric J Rubin, 2008.

PATENT

- Mutants of mycobacteria and process there off (US Patent filed on 9th July 2004).
- Recombinant BCG- Ag85C based immunization against Mycobacterium (Indian patent filed).
- 1. 7-substituted 2-nitro 6,7- dihydroimidazo [2,1-b][1,3] oxazine derivatives of their optical isomers, pharmaceutical composition containing the same as an active ingredient (Korean Patent filed)
- 5-Nitro-1,10, phenanthroline derivatives and pharmaceutical composition for prevention and treatment of tuberculosis containing the same (Korean Patent filed)
- Novel pyridine carboxamide compounds with anti-tubercular activity (Indian Patent filed).

INVITED TALKS

1. Present a talk at Society of Biological Chemists meeting, December 2023.
2. Presented a talk at National Symposium on Strategies for Impediment of Emerging Infectious Diseases, Jan 2023.
3. Presented a talk at Novel insights into pathogenesis of Tuberculosis for the development of vaccines, diagnostics and therapeutics, May 2023.
4. Presented a talk at Towards End TB: Achievements, challenges and future directions, March 2023.
5. Presented a talk at Drug discovery workshop, Translational Health Science and Technology Institute: Identification of hit molecules against Tuberculosis using different screening strategies, December 2021.
6. Presented a talk at TUPMAS, National Institute of Technology, Rourkela, February 2020.
7. Presented a talk at EMBO meeting, February 2020.
8. Presented a talk at Report TB meeting: Biomarkers and Beyond at Chennai, February 2019.
9. Presented a talk at 4th Indo-Swedish Workshop on Tuberculosis and other infectious diseases at Evolve Back, Coorg, February 2019.
10. Presented a talk at conference entitled "Genes to Networks: Recent Trends in Cell Signaling" at Amity University, Manesar, December 2018.
11. Presented a talk at Symbiosis International University, Pune, August 2018.
12. Presented a talk at NCR Biotech Science Cluster Series, July 2018.
13. Presented a talk at 100th year celebration of Bose Institute, October 2017.

14. Presented a talk under Science Setu Program at ANDC College and Maitreyi College 2016.
15. Presented a talk at TB conference held at Indian Institute of Science, 2016
16. Presented a talk at Association of Microbiologists of India, 2016 held at JNU, New Delhi
17. Presented a talk at conference entitled "Emerging themes in Tuberculosis Research: Creating a Network" held at Indian Institute of Science, Bangalore. July 2013.
18. Presented a talk at conference entitled "*Tuberculosis 2012: moving towards strategies for prevention and intervention*" held at Bose Institute, Kolkata, December 2012.
19. Presented a **short talk** entitled "Suicide and Survival of *Mycobacterium tuberculosis*" at Gordon Research Conference 2007 on Tuberculosis Drug Development held at Magdalen College, Oxford, United Kingdom.