Reena Bharti, Ph.D

Post-doctoral Scholar

513 Parnassus Ave. Lab-S1179

Department of Medicine, Moffit Hospital

University of California, San Francisco, USA

Contact Numbers: +1-3322699774, 8638648520
E-mail: reena.bharti@ucsf.edu, reena.cdri@gmail.com

EDUCATION

March 2023-present	Post doc., Depart. of Medicine, University of California, SanFrancisco, California, USA-94107
Jan 2017- June 2022	Ph.D. Life Sciences (biological sciences), Division of Pharmaceutics & Pharmacokinetics, Central Drug Research Institute, Lucknow, India
Aug 2014- Nov 2016	Master of Science (Biotechnology) University of Hyderabad Hyderabad
Aug 2011- June 2014	Bachelor of Science (Life Sciences), Jamila Millia Islamia University, Delhi

RESEARCH EXPERIENCE

Post -doc (2023-present)

Institute: University of California, San Francisco, **Supervisor**: Dr. Daniel Calabrese

CCR5 drives NK cells trafficking to the airways in acute lung injury model induced by endogenous lipid: Acute respiratory distress syndrome is the clinical entity that manifests from severe acute lung injury (ALI) from a variety of precipitating factors. CCR5-dependent natural killer (NK) cell responses mediate ALI in pulmonary ischemia-reperfusion injury, but the involvement of CCR5 and NK cell responses in ALI due to other causes is poorly understood. Innate immune responses to bacterial lipopolysaccharides (LPS) are implicated in ALI due to lung infections and lung storage prior to transplantation. Here, we test the hypothesis that CCR5-dependent NK cell responses mediate LPS-induced ALI. To address this hypothesis, we used a mouse model of endotoxin-induced ALI. 50 ug/uL of LPS or 50 uL of saline (PBS) was delivered by oropharyngeal aspiration with endpoints measured 24 hours later. We collected 1 mL of bronchoalveolar lavage (BAL) and measured concentrations of CCR5 ligand proteins (CCL3/MIP1α, CCL4/MIP1β, CCL5/RANTES) with multiplex ELISA. Lungs were dissociated and BAL and lung compartment NK cells were enumerated and phenotyped with flow cytometry. In a treatment trial, 24 hours preceding ALI, a group of animals were given intraperitoneal 10 mg/kg of Maraviroc (allosteric CCR5 inhibitor) or 10 mg/kg of corn oil vehicle control. Injury was quantified by histopathology, alveolar capillary permeability to I^{131}-

radiolabeled albumin, and arterial oxygenation (PaO_2). Comparisons between endpoints were assessed with the Kruskal-Wallis test and Mann-Whitney U testing.

Our results demonstrate that CCR5 drives NK cell-associated airway damage in LPS-induced acute lung injury. CCR5 inhibition may be a potential therapeutic strategy to mitigate this pathology.

Doctor of Philosophy (PhD) (2017-2022)

Institute: CSIR-Central Drug Research Institute,

Supervisor: Dr. Amit Misra,

Thesis Title: Transient transfection of lung and respiratory epithelium with gamma interferon.

A dry powder inhalation formulation was prepared with plasmids expressing gamma interferon or fluorescent proteins. The formulation was optimized and characterized for inhalation. Stability of plasmid DNA was checked in prepared formulation and MMAD of particles was checked through Cascade impactor. *In- vitro* and *in-vivo* studies were done to investigate the kinetics of expression of IFN-γ and/or reporter genes. Immunohistochemistry was done to investigate the kinetics of induction of autophagy as a consequence of expression of functional IFN-γ in the lungs of *Mtb* infected mice. Efficacy of DPI in terms of reduction of bacterial burden in lungs and spleen of *Mtb* infected mice were shown.

Our study has shown that it is possible to transiently transfect the lung and airway epithelium with gamma interferon for an optimal period of time. Condos et al. reported the clinical efficacy of nebulized gamma interferon (IFN- γ) protein in patients with pulmonary TB, but the prohibitive cost of IFN- γ protein is a hurdle in developing this as a host-directed therapy (HDT) for TB. Our study addressed the transient transfection of the lung and airway epithelium with IFN-γ. A prototype dry powder inhalation (DPI) product was developed for transient gene therapy over an optimal period of gene expression. The formulation is potentially affordable, because it is not a sterile product, does not require cold chain storage, and can be self-administered by outpatients. Transient transfection with IFN-γ did not induce pathological inflammation of the lung and airways. The long story cut to short is that IFN-γ, as expected of host-directed therapy, 'heals the host;' but does not 'kill the bug.'

M.Sc. Biotechnology (2014 - 2016)

Curcumin loaded lactoferrin nanoparticles: development, characterization, stability study and scaling up of lactoferrin.

PROFESSIONAL SKILLS

- Expertise in nanoparticle and micro-particles preparation and characterization.
- Dynamic light scattering and laser diffraction analysis (Zetasizer and Mastersizer)
- Expertise in dry powder formulation preparation and optimization *via* spray drying, spray freeze drying, and super critical fluid technologies
- Expertise in designing novel drug delivery systems (excipient-polymer conjugation) for targeted and controlled release of drug molecules, proteins, and RNA/DNA
- Expertise in flow cytometry and its data analysis.
- Expertise in Cytek and its data analysis

- Knowledge regarding Bioavailability and Bio-equivalence studies
- Expertise in cell culture and isolation of stem cells form bone marrow of small laboratory animals. In vitro evaluation of formulations in various cell lines like THP-1, RAW, A549, MCF-7 using standard procedures. Experimental techniques as ELISA, flow cytometry, western blotting, confocal microscopy and histology.
- Expertise in handling and culture of infectious bacteria under Biosafety level 3 (BSL 3) laboratory
- Expertise in using *in vivo* fluorescent imaging (ILS *in vivo* imaging system) and *intra vital* imaging (Olympus BX61-FV1200-MPE system)
- Expertise in animal handling; oral, IV, intranasal, pulmonary and subcutaneous dosing; Blood & tissue sampling
- Expertise in animal intratracheal instillation using PENCENTURY^{TM} Microsprayer®
- Knowledge of various scientific software programs
- Capable of both collaborative and independent research
- Possession of good communication and efficient management skills
- Proficient in statistical analytical methods using MS Excel, Graph pad prism, Origin pro and data presentation

PUBLICATIONS

a) **R Bharti,** N Greenland, J Santos, SJ Cleary, JR Greenland, DR Calabrese" CCR5 Drives NK Cell Mediated Airway Damage in an Endotoxin-induced Model of Acute Lung Injury" American Thoracic Society, A6837-A6837

b) **Reena Bharti**, Trisha Roy, Sonia Verma, D. V. Siva Reddy, Hasham Shafi, Khushboo Verma, Sunil K Raman, Sampita Pal, Lubna Azmi, Amit K Singh, Lipika Ray, Madhav N Mugale, Amit Misra* Transient transfection of the respiratory epithelium with gamma interferon for host-directed therapy in pulmonary tuberculosis. Molecular Therapy-Nucleic Acids. 2020 Dec 4;22:1121-8

c) **Bharti R**, Roy T, Verma S, Reddy DS, Shafi H, Verma K, Raman SK, Pal S, Azmi L, Singh AK, Ray L. Transient, inhaled gene therapy with gamma interferon mitigates pathology induced by host response in a mouse model of tuberculosis. Tuberculosis. 2022 May 1;134:102198.

d) **Bharti R**, Calabrese DR. Innate and adaptive effector immune drivers of Cytomegalovirus disease in lung transplantation: a double-edged sword. Frontiers in Transplantation. 2024;3:1388393.

e) Tsao T, Qiu L, **Bharti R**, Shemesh A, Hernandez AM, Cleary SJ, Greenland NY, Santos J, Shi R, Bai L, Richardson J. CD94+ Natural Killer cells potentiate pulmonary ischemia-reperfusion injury. European Respiratory Journal. 2024 Jan 1.Roy T, Seth A, Shafi H, Reddy DS, Raman SK, Chakradhar JV, Verma S,

f) **Bharti R**, Azmi L, Ray L, Misra A. Transcriptional regulation of suppressors of cytokine signaling during infection with Mycobacterium tuberculosis in human THP-1-derived macrophages and in mice. Microbes and Infection. 2024 Mar 1;26(3):105282.

g) Tsao T, Qiu L, Shemesh A, Hernandez AM, Shi K, Richardson J, **Bharti R**, Santos J, Lanier L, Looney M, Greenland J. Novel Anti-CD94 Treatment Reduces Mouse and Human Experimental Pulmonary Ischemia-Reperfusion Injury. The Journal of Heart and Lung Transplantation. 2024 Apr 1;43(4):S119.

h) Verma S, Dal NJ, Srivastava A, **Bharti R**, Siva Reddy DV, Sofi HS, Roy T, Verma K, Raman SK, Azmi L, Ray L. Inhaled Adjunct therapy with second-line drug candidates for dose reduction in chemotherapeutic regimens for multi-drug-resistant tuberculosis. AAPS PharmSciTech. 2023 Jun 8;24(5):130.

i) Reddy DS, Shafi H, **Bharti R**, Roy T, Verma S, Raman SK, Verma K, Azmi L, Ray L, Singh J, Singh AK. Preparation and evaluation of low-dose calcitriol dry powder inhalation as host-directed adjunct therapy for tuberculosis. Pharmaceutical Research. 2022 Oct;39(10):2621-33.

j) Roy T, Seth A, Shafi H, Reddy DS, Raman SK, Chakradhar JV, Verma S, **Bharti R**, Azmi L, Ray L, Misra A. Transcriptional regulation of suppressors of cytokine signaling during infection with Mycobacterium tuberculosis in human THP-1-derived macrophages and in mice. Microbes and Infection. 2024 Mar 1;26(3):105282.

k) Rajeev Ranjan, Ashish Shrivastava, **Reena Bharti**, Lipika Ray, Jyotsna Singh, Amit Misra; Preparation and optimization of a dry powder for inhalation of second-line anti-tuberculosis drugs, *International Journal of Pharmaceutics*.,547(1-2):150-157,2018

l) Ranjan R, Srivastava A, **Bharti R**, Roy T, Verma S, Ray L, Misra A. Preclinical Development of Inhalable D-Cycloserine and Ethionamide To Overcome Pharmacokinetic Interaction and Enhance Efficacy against *Mycobacterium tuberculosis*. Antimicrob Agents Chemother. 2019 May 24;63(6):00099-19. doi: 10.1128/AAC.00099-19. PMID: 30962335; PMCID: PMC6535545

m) kumar Raman S, Roy T, Verma K, Yadav C, Verma S, Devireddy VS, Sofi HS, **Bharti R**, Sharma R, BANSODE H, Kumar A. Dry Powder Inhalation of Lytic Mycobacteriophages for Adjunct Therapy in a Mouse Model of Infection with Mycobacterium tuberculosis. Authorea Preprints. 2024 Jul 21.

n) Azmi L, **Bharti R**, Reddy S. Metabolic Engineering Approaches to Produce Compounds of Interest in Plants. InMetabolic Engineering in Plants 2022 Jun 2 (pp. 359-374). Singapore: Springer Nature Singapore.

Extracurricular Activities

- Participated in drawing competition
- Participated in 5K campus run Marathon and won a medal.
- Participated as volunteer in Airtel need help marathon in university of Hyderabad
- Participated in badminton tournament
- Got 2nd position at CSIR-CDRI campus run,2019.
- Won tug of war,2019 at CDRI Campus and got a medal.

PROFESSIONAL RECOGNITION/ AWARD/ CERTIFICATE, FELLOWSHIP RECEIVED

- Received **Dr. Swarn Nitya Anand early career achievement award -2021**, for women research scholars in recognition for her journal article.
- Received travel-ship award for **attending international conference at 5th International TB- Meeting**, Groningen, August 25-27, 2019 by Council of Scientific and Industrial Research (HRDG).
- Received **CSIR-Net Fellowship** for the period of five years.
- Made an oral presentation titled with Transient transfection of lung and airway epithelium with gamma interferon **in 5th International TB-Meeting, Groningen**, August 25-27, 2019.
- Attended 7th International Symposium on **Current Trends in Drug Discovery Research** at CSIR-CDRI, Lucknow from 20th to 23rd February 2019
- Attended and participated in a poster discussion session in an **International conference, ATS-2024, San Diego, USA** on CCR5 drives NK cells mediated acute lung injury.
- Presented a poster in **ImmunoX 2023, at UCSF, Asilomar,USA.**

- Participated in India International Science Fest (**IISF 2018**).

- Attended **GIAN course** on "New Approaches in Tuberculosis Research and drug development during 11-15 December 2017 organized by Centre for Continuing Education, IISc. Bengaluru- 560012.
- Qualified national eligibility test (June 2016) for **Junior Research Fellowship** and eligibility for lecturership conducted by Council of scientific and industrial research (CSIR- Govt. of india) with All India Rank 122.
- Qualified **GATE 2016** (Graduate Aptitude Test in Engineering)
- Participated in "**Bio-quest 2015**" held in University of Hyderabad and got best poster presentation award.
- Industrial visit in "**Doctor's Reddy's lab**".
- Participated in international conference in the **2015 NextGen Genomics**, Biology, Bioinformatics and Technologies (NGBT) Conference