

Statement of research achievements on which awards have been received by the applicant

Lung cancer (LC) is a leading cause of cancer-related mortality in India. Discovery of targetable driver alterations and implementation of targeted therapy/immunotherapy has massively improved LC survival globally but is yet to impact India. Epidermal growth factor receptor (*EGFR*) mutations are one of the best characterized driver mutations in primary lung adenocarcinomas (ADCAs), a subtype of non-small-cell lung cancer (NSCLC). The frequency and distribution of somatic *EGFR* mutations in NSCLC varies significantly across the world, with geographical, regional and ethnic differences in prevalence.

For the last 10 years, my laboratory has been involved in predictive biomarker testing of LC patients which not only help in patient management but also provide cost effective solutions to poor patients. My initial research projects from ICMR, DBT, Lady Tata Memorial Trust were utilized in standardizing and validating biomarker testing and ultimately for patient care. Outcome of this work resulted in award winning two publications mentioned below.

One of which is related to the spectrum of *EGFR* gene mutations in over 1000 lung cancer patients and its correlation with responsiveness of targeted inhibitors and outcome of the disease (**Ref 1**). Our cohort of 1227 patients, predominantly from North India, was one of the largest single-institution series from the country where we detected *EGFR* mutations in about a third of NSCLC patients. T790M mutations are considered rare treatment resistant mutations and emerge subsequent to first or second generation Tyrosine Kinase Inhibitors (TKI) therapy. However the study showed a considerable number of baseline T790M mutations occurring both singly and as compound mutations which showed the poorest response rates to both TKIs and chemotherapy. Some of these were germline T790M mutations which hint towards hereditary link of lung cancer. The spinoff of the same work led to current project proposals which are under process to delineate etiopathogenetic link of hereditary lung cancer syndromes.

Ref 1: Singh V, Nambirajan A, Malik PS, Thulkar S, Pandey RM, Luthra K, Arava S, Ray R, Mohan A, Jain D. Spectrum of uncommon and compound epidermal growth factor receptor mutations in non-small-cell lung carcinomas with treatment response and outcome analysis: A study from India. *Lung Cancer*. 2020 Sep 13;149:53-60. (**Impact Factor: 5.705**) (**Cited 11 times**)

The research work was awarded AIIMS Oncology Research Award, under Clinical Sciences category, Second Prize, 2020.

As 70-80% of lung cancer patients are advanced stage patients in which surgery is not a treatment option, only small biopsy specimens and cytology samples are available to perform a large panel of predictive biomarkers. Secondly, due to their progressive disease, at times patients are critically sick and are not able to undergo invasive procedures. For these patients liquid biopsy has been recommended to use for molecular testing. We used blood plasma and urine of these patients to extract cell-free tumor DNA for *EGFR* gene mutation testing (**Ref 2**). Although sensitivity of urine, as a

liquid biopsy resource, was lesser than plasma, it emerged as a powerful tool in absence of tissue and blood of these critically ill patients of clinically and radiologically suspected lung cancer for diagnostic work-up.

Ref 2: Satapathy S, Singh V, Nambirajan A, Malik PS, Tanwar P, Mehta A, Suryavanshi M, Thulkar S, Mohan A, **Jain D**. EGFR mutation testing on plasma and urine samples: A pilot study evaluating the value of liquid biopsy in lung cancer diagnosis and management. *Curr Probl Cancer*. 2021 Dec;45(6):100722. (Impact Factor: 2.6) (Cited 10 times)

The research work was awarded AIIMS Oncology Research Award, under Clinical Sciences, Third Prize, 2021

Best Paper Award was given for platform presentation on “Immunostaining with EGFR mutation specific antibodies in lung adenocarcinomas: a first study from India” by **Indian Society of Oncology** Indian Cancer Congress Delhi, 2013. The work was published **Ref 3**

Ref 3: Jain D, Iqbal S, Walia R, Malik P, Cyriac S, Mathur SR, et al. Evaluation of epidermal growth factor receptor mutations based on mutation specific immunohistochemistry in non-small cell lung cancer: A preliminary study. *Indian J Med Res*. 2016 Mar;143(3):308-14. (Impact Factor: 4.2) (Cited 23 times)

During COVID-19 pandemic, my team in collaboration with IIT Delhi successfully characterized transcriptome in lung-tissues of severe COVID-19 patients for which I received **AIIMS Excellence Research Award** in January 2024. The work was published **Ref 4**

Ref 4: Budhraja A, Basu A, Gheware A, Abhilash D, Rajagopala S, Pakala S, Sumit M, Ray A, Subramaniam A, Mathur P, Nambirajan A, Kumar S, Gupta R, Wig N, Trikha A, Guleria R, Sarkar C, Gupta I, **Jain D**. Molecular signature of postmortem lung tissue from COVID-19 patients suggests distinct trajectories driving mortality. *Dis Model Mech*. 2022 May 1;15(5):dmm049572. doi: 10.1242/dmm.049572. (Impact Factor: 4.3) (Cited 20 times)

Other Awards and Honours

International

1. Fellow Royal College of Pathologists (FRCPath) by published work 2022
2. Listed in Stanford University California list of world's top 2% of scientists 2021, 2022
3. Editorial Board Member, IAC-IARC International System for Reporting Lung Cytopathology 2022
4. Editorial Board Member World Health Organization Classification of Thoracic Tumors 5th edition 2021
5. Mary J. Matthews Pathology/ Translational Research Award, International Association for the Study of Lung Cancer (IASLC), Sep 2021
6. Member International Collaboration on Cancer Reporting (ICCR) Thymic Epithelial Tumours dataset authoring committee
7. PPS Travel award Pulmonary Pathology Society, USA. Dubrovnik, Croatia, June 2019

8. Geraldine C. Zeiler Pulmonary Pathology and Cytopathology Fellowship May 2018 Mayo Clinic Scottsdale, Arizona, USA
9. PPS Travel award Pulmonary Pathology Society, USA. Chicago, USA June 2017
10. The AMP International Membership Grant Association of Molecular Pathology 2017
11. Fellow International Academy of Cytology (FIAC) 2016
12. IASLC International Mentorship Award at 17th world conference on lung cancer Vienna, Austria 2016
13. Bursary award International Academy of Pathologists, 2012 Cape Town, South Africa
14. Young Pathologist Award in 7th Asia pacific IAP congress, Taipei, Taiwan May 20-23, 2011

National

15. SERB Women POWER Fellowship March 2021
16. ICMR Travel grant 20th International Congress Cytology, Sydney, Australia, May 2019
17. Young Researcher Award Lady Tata Memorial Trust 2015
18. Member, National Academy Sciences of India (NASI)
19. UGC Travel Grant 16th World Conference on Lung Cancer, September 6-9, 2015 Denver, Colorado
20. Talented Young Pathologist Award, IAPM, Delhi chapter, April 2008
21. Member National Academy of Medical Sciences (MNAMS)
22. Bronze Medal (Second order) in MD, Post Graduate Institute of Medical Education & Research, Chandigarh, 2002
23. Prof R Nath Gold medal for best research work in bio medical sciences for year 2002, Post Graduate Institute of Medical Education & Research, Chandigarh, 2005
24. Dr. Mrs. Veena Gosain Gold Medal for First in Gynaecology and Obstetrics, GR Medical College, Gwalior, 1998
25. Dr. K.V. Waugh Gold Medal for First in Gynaecology and Obstetrics, GR Medical College Gwalior, 1998
26. Capt. Dr. S. S. Sapre Gold Medal for First in Final Professional MBBS, GR Medical College Gwalior, 1998
27. Pfizer "Medallion in Medicine and scroll of honour" award for First in Final Professional MBBS, Gwalior, 1998
28. Certificate of Merit for First in Final Professional MBBS, GR Medical College Gwalior, 1998
29. Certificate of Merit for Third in Second Professional MBBS, GR Medical College Gwalior, 1997