List of 10 best papers highlighting the important discoveries/contributions

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)**

   This is a data of over 1000 Indian patients of non-small cell lung carcinoma in which clinical correlations of EGFR gene mutations were established. The results show approximately one fifth of EGFR-mutant patients harbor uncommon and compound mutations. It is important to characterize a particular type of EGFR mutation, as uncommon and compound mutations confer targeted tyrosine kinase inhibitor (TKI) resistance and early disease progression/ poor outcome of the disease.

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)**

   In this project, urine was used as a non-invasive resource for cell free tumor DNA (ctDNA) extraction in predictive biomarker testing and management of Non-Small Cell Lung Carcinoma. Although sensitivity of urine as a liquid biopsy was lesser than plasma, it emerged as a powerful tool with 100% positive predictive value in absence of tissue and blood of these critically ill patients of lung cancer. Urine was used to detect baseline as well as tyrosine kinase inhibitor (TKI) resistant EGFR T790M mutations. Combination of plasma and urine increases sensitivity of detection of mutations and obviated need for invasive biopsies in >60% patients. Work on extracting ctDNA from pleural effusion supernatants (another source of liquid biopsy) has been published as an abstract (Lab Investigation 2023;103:S316) and currently being used for patient care services in addition to blood plasma (J Thorac Oncol. 2022; 17(9): S513).

3. Dutta R, Rathor A, Sharma HP, Pandey HC, Malik PS, Mohan A, Nambirajan A, Kumar R, **Jain D**. Mapping the immune landscape in small cell lung cancer by analysing expression of immuno-modulators in tissue biopsies and paired blood samples. **Sci Rep**. 2023 Mar 6;13(1):3739. (**Impact Factor: 4.996**)

Small cell lung cancer patients show limited benefit to immune-checkpoint-inhibitors/immunotherapy which necessitates identification of potential biomarkers predicting response to immunotherapy. In this work, paired tissue biopsies and peripheral blood was examined of small cell lung cancer/carcinoma (SCLC) patients which revealed immune-suppressive milieu in their peripheral circulation. It is conceivable, taking the observations of the current study in consideration, that patients of SCLC can potentially be benefitted by appropriate immuno-modulatory regimen. IDO1, s-CTLA-4, IFN-γ, TNF-α and IL-2 were identified as prognostic and predictive biomarkers to predict responsiveness to immune-checkpoint inhibitors.

4. Guleria P, Kumar S, Malik PS, **Jain D**. PD-L1 Expression in Small Cell and Large Cell Neuroendocrine Carcinomas of Lung: an Immunohistochemical Study with Review of Literature. **Pathol Oncol Res**. 2020 Oct;26(4):2363-2370 (**Impact Factor: 2.8)**

   Programmed Death-Ligand 1 (PD-L1) expression in tumor cells is a valuable biomarker for the selection of biomarker negative non-small cell lung cancer patients for immunotherapy. However in small cell carcinomas there were no studies in literature at the time of this publication. This work demonstrated PDL1 expression in lower percentage of small cell lung cancer. We proposed to investigate biomarkers other than PD-L1 to be investigated in these tumors. Subsequently NCCN guidelines incorporated immunotherapy in extensive stage SCLC although without PDL1 expression as a biomarker.

5. **Jain D**, Nambirajan A, Chen G, Geisinger K, Hiroshima K, Layfield L, Minami Y, Moreira AL, Motoi N, Papotti M, Rekhtman N, Russell PA, Prince SS, Schmitt F, Yatabe Y, Eppenberger-Castori S, Bubendorf L; IASLC Pathology Committee. Non-small cell lung carcinoma subtyping in conventional cytology: Results of the IASLC Cytology Working Group survey to determine specific cytomorphological criteria for adenocarcinoma and squamous cell carcinoma. **J Thorac Oncol**. 2022 Jun;17(6):793-805. (**Impact Factor: 20.4)**

   It was an international collaborative effort to subtype more than 100 Non-Small Cell Lung Carcinoma (NSCLC) by 13 expert cytopathologists practicing cytopathology worldwide. With the use of machine learning algorithm it was recognized that Non Small Cell Carcinoma –Not Otherwise Specified (NSCC-NOS) is an inevitable morphologic diagnosis which further

emphasized that ancillary immunochemistry is necessary to achieve accurate subtyping of lung cancer on cytology.

6. Kakkar A, Satapathy S, Sikka K, Tanwar P, Deo S, **Jain D**. Evaluation of high-risk human papillomavirus in sinonasalpapillomas and squamous cell carcinomas. **Virchows Arch.** 2023 Jul 15. doi: 10.1007/s00428-023-03601-x. (**Impact Factor: 4.548**)

   First study from India to show that only a small proportion of sinonasal squamous neoplasms in the Indian population harborhigh risk-Human Papilloma Virus (HR-HPV), unlike West where a substantial number of sinonasal neoplasms are etiopathogenetically linked to HR- HPV.

7. Kakkar A, Rathor A, Ashraf SF, Singh V, Sikka K, **Jain D**. IDH1/2 Mutations in Sinonasal Undifferentiated Carcinomas: Previously Undescribed IDH2 R172K and R140x Variants. **Am J Surg Pathol**. 2022 Sep 1;46(9):1284-1290. (**Impact Factor: 5.6)**

   Our work on a rare subset of Sinonasal Undifferentiated Carcinomas (SNUC) demonstrate novel IDH2 R172K and IDH2 R140x variants which were previously not described. Algorithmic and appropriate testing methods to detect and cover all relevant mutations in IDH gene are demonstrated and discussed in this work.

8. Kakkar A, Ashraf SF, Rathor A, Adhya AK, Mani S, Sikka K, **Jain D**. SMARCA4/BRG1-Deficient Sinonasal Carcinoma: Morphologic Spectrum of an Evolving Entity. **Arch Pathol Lab Med**. 2022 Sep 1;146(9):1122-1130. (**Impact Factor: 5.686)**

   Sinonasal undifferentiated carcinoma (SNUC) used to be a wastebasket diagnosis. Characterization of these enigmatic tumors into molecularly defined entities is tremendously helpful for patient management. In this unique series of patients of SNUC, we characterized these tumors into SMARCA4/BRG1-Deficient Sinonasal Carcinoma and described their morphologic spectrum. This is valuable information for pathologists and clinicians adding into literature of rare spectrum of these tumors.

9. Budhraja A, Basu A, Gheware A, Abhilash D, Rajagopala S, Pakala S, Sumit M, Ray A, Arulselvi S, 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. (**Impact Factor: 4.3)**

We performed whole-transcriptome sequencing and metatranscriptomics of lung autopsies from 31 patients with severe COVID-19 and ten uninfected controls. The results suggest two distinct models of lung pathology in severe COVID-19 patients, which can be identified through complement activation, presence of specific cytokines and characteristic microbiome.

10. Gheware A, Ray A, Rana D, Bajpai P, Nambirajan A, Arulselvi S, Mathur P, Trikha A, Arava S, Das P, Mridha AR, Singh G, Soneja M, Nischal N, Lalwani S, Wig N, Sarkar C, **Jain D**. ACE2 protein expression in lung tissues of severe COVID-19 infection. **Sci Rep**. 2022 Mar 8;12(1):4058. (**Impact Factor**: **4.996**)

    Angiotensin-converting enzyme 2 (ACE2) is considered a key host protein by which severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)/COVID-19 enters and initiate multiplication. However, there was no study available in literature to find out protein expression in normal and COVID-19 affected tissues. In this work, ACE2 protein expression was studied in lung tissues of severe COVID-19 patients who died due to infection. In addition, immunohistochemical expressionof ACE2 across all normal body tissues was analyzed which was unique feature of this study to add important piece of information in the literature. Significantly higher ACE2 protein expression was found in lung tissues of COVID-19 patients.

11. Nambirajan A, Sood R, Khatoon W, Malik PS, Mohan A, **Jain D**. Concordance of immunohistochemistry and fluorescence in-situ hybridization in the detection of anaplastic lymphoma kinase (ALK) and Ros-protooncogene 1 (ROS1) gene rearrangements in non-small cell lung carcinoma: a 4.5-year experience highlighting challenges and pitfalls. **Archives of Pathology and Laboratory Medicine** (**IF**: **5.686**) **Accepted for publication**

    Extensive information on ALK and ROS1 gene rearrangement testing in approximately 1800 non-small cell lung carcinomas for general as well as specialized pathologists.