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Case number	Gender/ age	Diagnosis	Smoking	Stage	Biomarker finding			Overall survival (months)
					Microsatellite status	TMB (mut/mb)	Gene Alterations	
1	M/58	pleomorphic carcinoma	n/a	IV	Stable	Low(4 mut/mb)	KRAS,CSF1R,DNMT3A,	0.6
2	M/82	pleomorphic carcinoma	YES	IIA	Stable	Intermediate (11 mut/mb)	TP53,MET,NF1 ,INPP4B	7.3
3	M/77	pleomorphic carcinoma	YES	IIIA	Stable	Intermediate (13 mut/mb)	TP53,KRAS,CSF1R ,SMO	3.5
4	M/56	pleomorphic carcinoma	YES	IA3	Cannot determined	Intermediate (13 mut/mb)	TP53,FBXW7,RB	31.2
5	M/52	hepatoid adenocarcinoma	NO	IIIA	Stable	Intermediate (6 mut/mb)	EGFRdel19,MCL1,NOTCH2	22.8
6	M/58	hepatoid adenocarcinoma	YES	IV	Stable	Intermediate (9 mut/mb)	STK11	5.2
7	M/39	pulmonary blastoma	YES	IIB	Stable	Low(3 mut/mb)	CTNNB1	32.3
8	F/68	Pulmonary enteric carcinoma	NO	IIIB	Stable	Low(3 mut/mb)	KRAS,TP53,APC,MSH6	16.4

negative CK7 and TTF1. She also had *KRAS*, *APC*, and *MSH6* mutation. The PET/CT showed irregular border mass at RUL consistent with primary lung cancer, but all histology and molecular profiles trend to support colorectal cancer. We had started to treat her with lung cancer chemotherapy regimen without any responses then we switched to 5-FU-based regimen with partial response until now. Furthermore, we also reported predictive biomarkers for immune checkpoint inhibitor which were MSI and tumor mutation burden (TMB). All cases had stable MSI except case number 4 whom had insufficient tissue. Most of patients had low and intermediate TMB in this study. **Conclusion:** We don't know much about molecular profile data in rare types of lung cancer. However, NGS testing may help identifying potential target genes and provide new therapeutic options for this group of patients. The pooled-data from all regions of the world will be very useful for gathering all information to develop the novel treatment. **Keywords:** Rare type of lung cancer, NGS, genomic alteration profile

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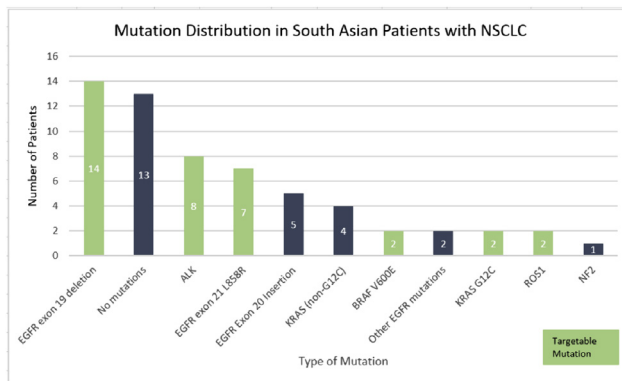
The Mutational Landscape in South Asian Patients with Non-Small Cell Lung Cancer at an US Academic Medical Center



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Introduction: Various molecular underpinnings of lung cancer have been noted in Asian populations, especially with targetable mutations such as *EGFR* and *ALK* (Doval et al., *Ann Oncol* 2014). However, the distribution and prevalence of these mutations have been less well characterized in South Asian/Indian patients, especially those who live outside of South Asia. **Methods:** We performed a retrospective review of NSCLC cases from 2005-2019, at Stanford Cancer Center, USA, and identified seventy-two patients who had a South Asian name. Their ethnicity was confirmed with manual review, with inclusion of patients

noting origin from India, Pakistan, Bangladesh, or Sri Lanka. Patients were excluded if they did not have a confirmation of their ethnicity in the electronic medical record. Molecular testing data and type of methodology used for testing was also collected. **Results:** 72 patients were identified from 2005-2019, of which 63 patients had mutational testing (from 2009-2019) performed. Of the 9 patients who had no mutational testing, 7/9 had non metastatic disease. Demographics and testing characteristics are shown in Table 1. 35 of 63 patients had targetable mutations (55.6%), with 21 patients with *EGFR* activating mutations (exon 19 deletion or exon 21 L858R) (33.3% of 63 patients).. Other mutations included 8 *ALK* rearrangements (12.7%), 6 *KRAS* mutations (9.5%), 2 *ROS1* fusions (3.1%), and 2 *BRAF* V600E mutations (3.1%) (Figure 1). In assessing co-mutations, 3 *ARID1A* and 3 *STK11* mutations were noted.



Conclusion: South Asian patients, largely of Indian origin, with NSCLC at an US academic center appear to have a high chance of harboring a driver mutation, emphasizing the importance of molecular testing in this population. These findings corroborate rates of mutations reported from South Asia, and suggest similar trends in mutation prevalence despite different geographical locations. We are collaborating with an institution in Northern India to further compare and report on the molecular landscape of this population. **Keywords:** south asian patients, mutations, nsclc

	N= 72
Female	37 (51%)
Median age of diagnosis, years (range)	64 (38-89)
Non-Smoker	62 (86%)
Country of Origin/ Ethnicity	India- 68 (94%) Pakistan- 3 (4%) Bangladesh-1 (1%)
Pathology	Adenocarcinoma- 63 (88%) Adenocarcinoma with Mixed Features- 4 (6%) Squamous (4%)
Stage of Disease	I or II- 12 (17%) I or II with recurrence- 7 (10%) III- 7 (10%) III with recurrence-1 (1%) IV-45 (63%)
Type of Testing	Fluorescence in situ hybridization (FISH) only – 3 (4%) Next Generation Sequencing (NGS)- 34 (47%) Polymerase Chain Reaction (PCR) (includes ddPCR)- 27 (37.5%)

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Genomic Profiling and PD-L1 Expression Association Analysis in Epstein-Barr Virus (EBV)-infected Lung Cancer Patients



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Introduction: COVID-19, a disease caused by coronavirus SARS-CoV-2, has drawn public attention worldwide. The virus is also associated with carcinogenesis. Epstein-Barr virus (EBV) was reported to be related to

pulmonary lymphoepithelioma-like carcinoma (PLELC), a rare subtype of non-small cell lung cancer (NSCLC). However, the understanding of the treatment for EBV-infected NSCLC was still elusive. Immunotherapy that targets PD-1/PD-L1 has been utilized as a novel clinical treatment in recent years. Here, we focus on the genomic landscapes of lung cancers with EBV-infection and its correlation with PD-L1. **Methods:** Patients with both PD-L1 expression detection and genomic information were screened in HapLab database. HaploX 605-gene panel sequencing, covering 1.31 MB genome, was performed to analyze the genomic data of patients. PD-L1 expression was detected by immunohistochemistry. Bioinformatic analysis of genomic mutations and the correlation with the expression of PD-L1 were studied. **Results:** We analyzed the genomic profiles of 23 EBV-infected NSCLC patients. 11 cases of lung squamous-cell carcinoma (LUSC), 4 cases of lung adenocarcinoma (LUAD), 5 cases of lung pulmonary lymphoepithelioma-like carcinoma (PLELC), and 3 unidentified cases were included in this study. Collectively, 93 genome mutations of 67 genes were detected in 23 EBV-infection cases. Top 3 frequently mutated genes were *TP53* (27%), *CSMD3* (18%) and *KMT2D* (18%). The EBV-infected patients exhibited a low level of tumor mutation burden (TMB). The median TMB was 1.53 Muts/MB (ranging from 0 to 14.5 Muts/MB). Only 3 of 23 patients (13.0%) harbored the canonical driver mutations in NSCLC. Interestingly, 10/23 patients (43.5%) showed high expression of PD-L1, while 13/23 patients (56.5%) showed low expression. We also assessed the expression of PD-L1 in lung cancers with no EBV-infection (867 cases). Only 118/867 (13.6%) patients without EBV-infection presented high PD-L1 expression, while 749/867 (86.4%) presented low PD-L1 expression. **Conclusion:** EBV-infection can occur in different kinds of NSCLC, including LUSC, LUAD, and PLELC. TMB and driver mutations of EBV-infected NSCLC were not frequently observed as normal lung cancers, implying a different mechanism leading to EBV-infected lung cancers. Interestingly, EBV-infected NSCLC tended to have a high correlation with the expression of PD-L1. This may give a hint on the application of checkpoint blockade immunotherapy on EBV-infected NSCLC.

Keywords: Epstein-Barr virus (EBV), PD-L1 expression, non-small cell lung cancer (NSCLC)

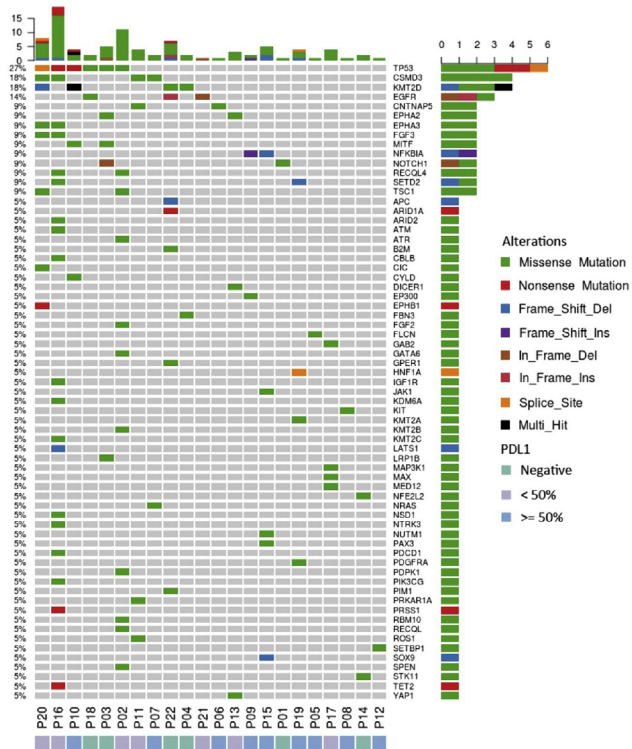
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Comprehensive Genomic Profiling of Lung Metastases in Cancer Patients



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Introduction: Lung is one of the most common sites of cancer metastases. However, the molecular characterization of the lung metastases in patients with different tumor types remained unclear. **Methods:** Tissue samples of the lung metastases were obtained from patients with solid tumors other than lung cancer. Targeted next-generation sequencing (NGS) with a panel of over 381 cancer genes was performed on the lung metastases in 3DMed laboratory. **Results:** A total of 184 lung metastases samples were screened and included for analysis. The sites of origin included colorectal cancer (n=51), breast cancer (n=24), gynecologic cancer (n=20), sarcoma (n=17), kidney cancer (n=14), head and neck carcinoma (n=14), and hepatocellular carcinoma (n=13), etc. In overall, the most frequently mutated genes fell in *TP53* (54.9%), *KRAS* (21.2%), *APC* (19.0%), *PIK3CA* (16.8%), *PTEN* (7.1%), *ERBB2* (6.5%), *CDKN2A* (5.4%), and *VHL* (5.4%). Distinct molecular mutational patterns were observed in lung metastases from different tumor types. Lung metastases from colorectal cancer exhibit the highest prevalence of gene alterations (*TP53*, 92.2%, *APC*, 62.7%, and *KRAS*, 58.8%), followed by breast cancer (*TP53*, 70.8%, *PIK3CA*, 45.8%, *ERBB2*, 25%, and *MCL1*, 25%), hepatocellular carcinoma (*TP53*, 69.2% and *AX1N1*, 30.8%) and renal carcinoma (*VHL*, 57.1%). The lowest mutation prevalence were obtained from the lung metastases from gynecologic cancer (*PIK3CA* and *TP53*, 30% for each), head and neck carcinoma (*TP53*, 35.7% and *PIK3CA*, 28.6%), and sarcoma (*FRS2* and *MDM2*, 23.5% for each). Amongst all, mutations in *EGFR* kinase domain were found only in two lung metastases samples, with one patient with primary urothelial cancer and the other one with primary melanoma. The other sensitizing mutations in the driver genes of lung cancer were rarely observed, including *ALK* fusion (*ALK-SMYD3*) in one 34-year-old female with primary clear cell renal cell carcinoma, *MET* gain in one male with primary hepatocellular carcinoma, and *RET* fusion (*KIF5B-RET*) in one female with primary neuroendocrine carcinoma. **Conclusion:** In general, the mutational patterns of the lung metastases were more likely to depend on that of the corresponding primary tumors. A subset of patients harboring lung cancer related targetable driver mutations in the lung metastases may benefit from targeted TKIs therapies. **Keywords:** Lung metastases, next-generation sequencing



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