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Abstract #1806

Genetic mutations in PIK3CA predict liver metastases in patients with lung adenocarcinoma

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BACKGROUND

Liver is a common metastatic site of lung cancer, and patients with liver metastases will progress rapidly. This study aims to access whether certain genomic features could predict the presence of liver metastasis.

METHODS

A total of 253 patients with lung adenocarcinoma were divided into three groups: A (50 cases with liver metastases), B (88 cases without distal metastasis) and C (115 patients with other distal metastases). Their tumor tissue samples and matched peripheral blood were collected to perform next-generation sequencing of 1021 cancer-related genes. Their genomic features, including single-nucleotide variants (SNVs), small insertions and deletions (Indels), copy number variants (CNVs), structural variants (SVs), tumor mutation burden (TMB), were retrospectively reviewed. TMB was calculated as the number of somatic non-synonymous SNVs and Indels per Mb in the coding region.

RESULTS

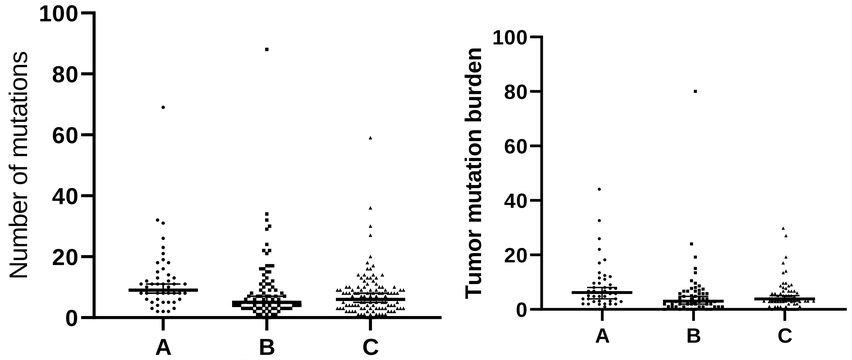

Figure. Comparison of number of mutations and tumor mutation burden among three groups

The number of mutations in group A was significantly higher than that in group B and C, with the median number of mutations of 9, 5, and 6, respectively (P =0.001, P =0.0001). The same trends were observed in terms of TMB (median: 6.24, 3, 3.84 muts/Mb; p=0.0022, p=0.0157), SNV (median: 8, 4, 5; p=0.0015, p=0.0005) and CNV (median: 1, 0, 0; p=0.0011, p=0.0002). There was no difference in the number of SV among three groups.

Differential mutated genes were analyzed using Fisher's exact test. The results showed that the mutation rate of PIK3CA was higher in group A than in group B and C (26%, 4.65%, 2.65%; P =0.0007, p=0.0001). TP53 mutation rate in group A and C was significantly higher than that in group B (72%, 60.18%, 39.53%; P =0.0003, P =0.0044).

Table. Analysis of differential mutated genes among three groups

Group A vs. Group B					
gene	Group A-mutations	Group A-mutation rates	group B-mutations	Group B-mutation rates	p
TP53	36	72.00%	34	39.53%	0.00034
PIK3CA	13	26.00%	4	4.65%	0.00068
MS4A1	4	8.00%	0	0.00%	0.01689
ABCC11	3	6.00%	0	0.00%	0.04780
Group A vs. Group C					
gene	Group A-mutations	Group A-mutation rates	group C-mutations	Group C-mutation rates	p
PIK3CA	13	26.00%	3	2.65%	0.00002
BRCA2	8	16.00%	6	5.31%	0.03409
ATR	6	12.00%	3	2.65%	0.02470
PTEN	5	10.00%	2	1.77%	0.02875
ACIN1	3	6.00%	0	0.00%	0.02766
CTNNB1	0	0.00%	10	8.85%	0.03239
Group B vs. Group C					
gene	Group B-mutations	Group B-mutation rates	group C-mutations	Group C-mutation rates	p
TP53	34	39.53%	68	60.18%	0.00435
MLL2	8	9.30%	2	1.77%	0.02126
ATM	1	1.16%	9	7.96%	0.04533

CONCLUSIONS

These results suggested that PIK3CA mutation may play a non-negligible role in the development of liver metastasis. TP53 mutation may play a role in the distal metastasis of lung adenocarcinoma, but it is not a specific predictive biomarker for liver metastasis.