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Short Communication

Somatic Genomic Alterations and Mechanisms of Genomic Instability in Lung Cancer

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DESCRIPTION

Lung Cancer (LC) remains the largest cause of cancer death. Histologically, lung cancer is divided into two subtypes: Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC), which account for 85% and 15% of LC cases, respectively. Adenocarcinoma (50%) is the most common type of NSCLC, followed by squamous cell carcinoma (30%-40%) and large cell carcinoma (10%-20%). Independent of gender, age, or smoking history, adenocarcinoma is the most common subtype of NSCLC, but squamous cell and large cell carcinoma are closely associated with smokers. Although NSCLC is frequently identified as advanced metastatic disease, vascular invasion occurs frequently in the early stages, leading to recurrence and poor survival [1-3]. Surgery for local tumours and platinum-based chemotherapy for systemic illness are common therapies. Notwithstanding recent advancements, NSCLC remains a highly recurring cancer with a 5-year survival rate of roughly 15%. LC has hundreds of somatic mutations, copy number changes, and genome duplications, according to genomic studies. Tobacco carcinogen exposure mixed with germline genomic instability causes in a high somatic mutation rate in LC [4].

The multiple sub clonal populations obtained from a single biopsy demonstrate the considerable genetic diversity within LC malignancies. Tobacco use and DNA repair changes, for example, are extrinsic and intrinsic variables that contribute to frequent genomic abnormalities in LC. Yet, only a small percentage of smokers get cancer, emphasizing the role of germline genetic predisposition in lung carcinogenesis. When compared to other kinds of cancer, LC has a specific genetic signature. Tobacco-related lung cancer ranks second only to melanoma among malignancies with a high somatic mutational load. The high somatic mutation rate (8-10 mutations/Mb) in smokers, independent of histologic subtype, compared to less than 1 mutation/Mb in nonsmokers, confirms tobacco carcinogen causation. Furthermore, transversion rates (C-A) are unusually high in smoking-related LC, both in squamous cell carcinoma and adenocarcinoma, with the highest frequency compared to other cancer types, surpassed only by melanoma rates derived from UV light exposure, whereas transitions are more common in most cancer types. Endogenous mutational processes also result in the complex genome of LC, which exhibits frequent nonsilent mutations, copy number changes (CNA), chromosomal translocations, and genome doublings [5-7].

NSCLC initial tumours have a significant level of genetic variability. Beyond tobacco smoking, increased somatic mutational burden is related with germline polymorphisms, according to the spatial and temporal dynamics of tumour evolution. Tumor driver mutations spread unevenly and might be dominant in some clones while being missing in others. Remarkably, with chronic exposure to tobacco carcinogens, smoking-related mutations fade, and endogenous-derived mutations take over during tumour evolution [8,9]. The specific genomic profile of LC defines various molecular categories of patients and serves as the foundation for customized therapy that target driver mutations. A variety of Tyrosine Kinase Inhibitors (TKIS) have been discovered during the last decade for Epidermal Growth Factor Receptor (EGFR) mutations and Anaplastic Lymphoma Kinase (ALK) fusions, while next-generation sequencing is uncovering additional molecular targets. Results from numerous sequencing experiments reveal distinct genetic landscapes based on histology type. Mutations in receptor tyrosine kinases are common in lung adenocarcinoma but uncommon in squamous or big cell carcinomas. Defective cell cycle control, involving cyclins, cyclin-dependent kinases, tumour suppressors, and oncogenes, is the key molecular mechanism generating genomic instability in LC. Because many of these proteins correlate with cancer cell growth, survival, tumorigenesis, and metastasis in preclinical models both *in vitro* and *in vivo*, and they are overexpressed and/or have prognostic value in LC patients, this represents opportunities for the development of novel biomarkers and targeted therapies [10].

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REFERENCES

1. Zhu X, Li S, Xu B, Luo H. Cancer evolution: A means by which tumors evade treatment. Biomed Pharmacother. 2021;133:111016.
2. Xie S, Wu Z, Qi Y, Wu B, Zhu X. The metastasizing mechanisms of lung cancer: Recent advances and therapeutic challenges. Biomed Pharmacother. 2021;138:111450.
3. Cai L, Bai H, Duan J, Wang Z, Gao S, Wang D, et al. Epigenetic alterations are associated with tumor mutation burden in non-small cell lung cancer. J Immunother Cancer. 2019;7(1):1-1.
4. Gong X, Du J, Parsons SH, Merzoug FF, Webster Y, Iversen PW, et al. Aurora A kinase inhibition is synthetic lethal with loss of the RB1 tumor suppressor gene. Cancer Discov. 2019;9(2):248-263.
5. Nigam R, Babu KR, Ghosh T, Kumari B, Akula D, Rath SN, et al. Indenone derivatives as inhibitor of human DNA dealkylation repair enzyme AlkBH3. Bioorg Med Chem. 2018;26(14):4100-12.
6. Thu KL, Silvester J, Elliott MJ, Ba-Alawi W, Duncan MH, Elia AC, et al. Disruption of the anaphase-promoting complex confers resistance to TTK inhibitors in triple-negative breast cancer. Proc Natl Acad Sci U S A. 2018;115(7):E1570-E1577.
7. Andor N, Maley CC, Ji HP. Genomic instability in cancer: teetering on the limit of tolerance. Cancer research. 2017;77(9):2179-2185.
8. Choi M, Min YH, Pyo J, Lee CW, Jang CY, Kim JE. TC Mps1 12, a novel Mps1 inhibitor, suppresses the growth of hepatocellular carcinoma cells *via* the accumulation of chromosomal instability. Br J Pharmacol. 2017;174(12):1810-18125.
9. Ansari J, Shackelford RE, El-Osta H. Epigenetics in non-small cell lung cancer: from basics to therapeutics. Transl Lung Cancer Res. 2016;5(2):155.
10. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. Eur Respir J. 2016;48(3):889-902.