Kokand University
Andijon filiali

O‘ZBEKISTON RESPUBLIKASI OLIY TA’LIM, FAN VA INNOVATSIYALAR VAZIRLIGI
QO‘QON UNIVERSITETI ANDIJON FILIALI

“FARMASEVTIKA, BIOTEXNOLOGIYA VA BIOTIBBIYOTDA ZAMONAVIY TADQIQOTLAR VA ILMIY YANGILIKLAR”

MAVZUSIDAGI XALQARO ILMIY-AMALIY

KONFERENSIYA

MATERIALLARI

Kokand University Andijon filiali
Kokand University
TASHKENT INTERNATIONAL UNIVERSITY
ISCAD
The International Strategic Center for Agri-Food Development
TIIAME
ecobiome
Society for Environmental Sustainability
SARTORIUS

Ushbu to‘plam O‘zbekiston Respublikasi Prezidentining 2023 yil 4-iyuldagi PQ-200 qarori hamda Oliy ta`lim, fan va innovatsiyalar vazirligining 2024-yil 27-dekabrdagi 490-son buyrug‘i ijrolarini ta`minlash maqsadida Qo‘qon universiteti Andijon filialida **“FARMASEVTIKA, BIOTEXNOLOGIYA VA BIOTIBBIYOTDA ZAMONAVIY TADQIQOTLAR VA ILMIY YANGILIKLAR”** mavzusida o‘tkazilayotgan xalqaro ilmiy-amaliy konferensiya materiallari asosida tayyorlandi.

To‘plam barcha ta’lim muassasalarida shu soha bo‘yicha shug‘ullanuvchi pedagoglar, mutaxassislar, tadqiqotchilar, talaba-yoshlar va keng jamoatchilik foydalanishlari uchun mo‘ljallangan.

EGFR-ASSOCIATED MOLECULAR MARKERS OF LUNG CANCER IN UZBEKISTAN

Mirakbarova Zebinisa[1,2,3], Turdikulova Shahlo [4]
1.Insititute of biophysics and biochemistry under the National University of Uzbekistan, 100169, Uzbekistan Tashkent. 2. Central Asian University, 111221, Uzbekistan Tashkent. 3. International Agriculture University, Uzbekistan Tashkent. 4. Centre for advanced technologies, 100169, Uzbekistan Tashkent
[*Corresponding author: E-mail: zebyniso@gmail.com]

Abstract

Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), including gefitinib and erlotinib, are reversible competitive inhibitors of the tyrosine kinase domain of EGFR, binding to its adenosine-5'-triphosphate (ATP)-binding site[1]. The presence of somatic activating mutations in the EGFR gene, an increased gene copy number, and specific clinical and morphological tumour characteristics correlate with the high efficacy of these inhibitors, leading to significant tumour regression and improved clinical outcomes in patients with non-small-cell lung cancer (NSCLC)[2].

Lung cancer remains one of the leading causes of cancer-related mortality worldwide, including in Uzbekistan. The epidermal growth factor receptor (EGFR) is one of the most frequently mutated driver genes in lung cancer. However, unlike lung adenocarcinoma, EGFR mutations are relatively rare in squamous cell lung carcinoma (SCC), with a reported prevalence ranging from 3% to 18%[3]. The objective of this study was to investigate the prevalence of activating EGFR mutations (L858R mutation and E746_A750 deletion) in patients with SCC.

The study included formalin-fixed paraffin-embedded (FFPE) tumour tissue samples from 39 patients with SCC and 79 healthy individuals as a control group. DNA was extracted from these samples using nucleosorption with prior paraffin removal, followed by polymerase chain reaction (PCR) amplification to detect the L858R mutation and E746_A750 deletion in the EGFR gene. Genotyping analysis revealed the following results: in the case group, the genotype distribution was TT - 15 (38.5%), TG - 6 (15.4%), GG - 18 (46.1%), whereas in the control group, all individuals exhibited the TT genotype - 79 (100%) ($p<0.0001$). The frequency of the E746_A750 deletion in the case group was 26 (66.6%), while the wild-type EGFR genotype was present in 13 (33.3%). In contrast, no EGFR deletions were detected in the control group ($p<0.0001$).

Further studies on the role of EGFR activating mutations in different populations, including European and Asian cohorts, have demonstrated their impact on survival and response to targeted therapies[4-6]. In particular, EGFR mutations, especially exon 19 deletions and the L858R mutation in exon 21, have been associated with high response rates to targeted treatments[7]. Additionally, patients with EGFR L858R mutations who received anti-angiogenic therapy as part of their treatment regimen exhibited a significantly prolonged overall survival (OS) compared to those who had never received an anti-angiogenic agent[8].

Analysis of this polymorphism provides an opportunity for the primary prevention of NSCLC and the personalization of treatment in this patient group. It facilitates early diagnosis, individualized therapy, and improvements in overall survival (OS) and progression-free survival (PFS). The findings of this study further confirm the critical role of EGFR mutations in SCC pathogenesis and their potential as prognostic biomarkers, which could aid in the development of more effective therapeutic strategies. However, large-scale studies in this cohort are necessary to further elucidate the underlying mechanisms and therapeutic potential of these mutations.

References

1. Seshacharyulu P, Ponnusamy MP, Haridas D, Jain M, Ganti AK, Batra SK. Targeting the EGFR signaling pathway in cancer therapy. Expert Opin Ther Targets. 2012 Jan;16(1):15-31.

2. Bethune G, Bethune D, Ridgway N, Xu Z. Epidermal growth factor receptor (EGFR) in lung cancer: an overview and update. J Thorac Dis. 2010 Mar;2(1):48-51

3. Jin R, Peng L, Shou J, Wang J, Jin Y, Liang F, Zhao J, Wu M, Li Q, Zhang B, Wu X, Lan F, Xia L, Yan J, Shao Y, Stebbing J, Shen H, Li W, Xia Y. *EGFR*-Mutated Squamous Cell Lung Cancer and Its Association With Outcomes. Front Oncol. 2021 Jun 14;11:680804

4. Liu J, Xu WY, Ye M, Liu Z, Li C. Genetic Alteration Profiling of Chinese Lung Adenocarcinoma and Its Effect on Targeted Therapy Efficacy. Front Oncol. 2021 Dec 14;11:726547

5. Clinical Lung Cancer Genome P. Network Genomic M . A Genomics-Based Classification of Human Lung Tumors. Sci Transl Med (2013) 5(209):209ra153

6. Osmani L, Askin F, Gabrielson E, Li QK. Current WHO Guidelines and the Critical Role of Immunohistochemical Markers in the Subclassification of Non-Small Cell Lung Carcinoma (NSCLC): Moving From Targeted Therapy to Immunotherapy. Semin Cancer Biol (2018) 52(Pt 1):103–9.

7. Harrison PT, Vyse S, Huang PH. Rare epidermal growth factor receptor (EGFR) mutations in non-small cell lung cancer. Semin Cancer Biol. 2020 Apr;61:167-179

8. You L, Zheng X, Deng D, Pan H, Han W. The benefit of anti-angiogenic therapy in EGFR exon 21 L858R mutant non-small cell lung cancer patients: a retrospective study. Sci Rep. 2022 Aug 26;12(1):14624