

PIK3CA AS A PROGNOSTIC BIOMARKER IN CLEAR CELL RENAL CELL CARCINOMA: A BIOINFORMATIC ANALISYS

Clívia Vitória dos Santos da Silva¹, José Cleyton Nascimento Glins²

¹Pharmacy student, at Universidade da Amazônia (UNAMA), Pará, Brazil

²Chemistry, Master in Medicinal Chemistry and Molecular Modeling, Researcher at Bionorte (BIONORTE), Pará, Brazil

Introduction: Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer in adults and presents variable clinical behavior, with risks of late recurrence and metastasis. The PIK3CA gene, which encodes the p110 α subunit of PI3K, is involved in signaling pathways related to cell proliferation and survival, and is frequently altered in cancers. In ccRCC, PIK3CA is not listed among genes with known prognostic value, making its analysis relevant to investigate its potential as a prognostic biomarker. **Objectives:** To analyze the expression of the PIK3CA gene in clear cell renal cell carcinoma (ccRCC) and its association with patient overall survival (OS), based on bioinformatic data from public databases. **Methods:** This is an observational, descriptive, and exploratory study based on bioinformatic analysis of public databases. PIK3CA gene expression and its association with OS and DFS were evaluated using the Gene Expression Profiling Interactive Analysis 2 (GEPIA2) platform, based on Cancer Genome Atlas (TCGA) and Genotype-Tissue Expression (GTEx) data. Survival analysis was performed using Kaplan–Meier curves, with statistical comparison by log-rank test, as provided by the GEPIA2 platform. Protein expression was assessed through the Human Protein Atlas (HPA), based on immunohistochemistry data available using the antibody HPA009985, including analysis of staining intensity, proportion of positive tumor cells, and subcellular localization in renal tumor tissues. **Results:** Gene expression analysis in GEPIA2 revealed that the PIK3CA gene exhibits significantly higher expression in the tumor tissues of ccRCC compared to normal tissues (n=523 vs. n=100). In overall survival (OS) analysis, patients with high PIK3CA expression had a better prognosis (HR=0.58; p=0.00066), with a statistically significant difference (Log-rank p=0.00056; n=257 for high expression and n=258 for low expression). In DFS (although a trend towards better survival was observed for patients with high expression (HR=0.72; p=0.078), this difference was not statistically significant (Log-rank p=0.075). The analysis of PIK3CA protein expression in ccRCC, revealed that among 12 samples evaluated, 5 (41.7%) showed medium expression, 2 (16.7%) low expression, and none showed high expression, while 5 samples (41.7%) exhibited no detectable protein expression. Regarding staining intensity, 5 samples (41.7%) showed moderate staining, 3 (25%) weak staining, and 4 (33.3%) were negative. As for the proportion of positively stained

tumor cells, 3 samples (25%) had over 75% positive cells, 4 (33.3%) showed positivity in 25%–75% of cells, 1 (8.3%) had less than 25% positivity, and 4 (33.3%) showed no positive staining. In terms of subcellular localization, 8 of the 12 samples (66.7%) exhibited a cytoplasmic and/or membranous staining pattern, while 4 (33.3%) had no detectable staining; nuclear staining was not observed. **Conclusion:** The results demonstrate that the PIK3CA gene is overexpressed in tumor tissues of ccRCC and is associated with better overall survival outcomes, suggesting a potential prognostic role. However, the analysis of protein expression revealed heterogeneous and partially undetectable protein levels, which may reflect post-transcriptional regulatory mechanisms or methodological limitations of immunohistochemistry. Therefore, although the findings indicate the potential of PIK3CA as a prognostic biomarker in ccRCC, further studies are needed to validate its clinical applicability.

Keywords: Tumor biomarkers; renal cell carcinoma; gene expression.