EGFR nuclear translocation in human lung cancer cells: role of Prostaglandin E2

L. Bazzani[1], F. Finetti[1], S. Donnini[1], M. Ziche[1]

[1]Dept of Life Sciences, University of Siena, Italy

Epidermal growth factor receptor (EGFR) plays a critical role in cancer development and progression. It is highly expressed in human malignancies and correlates with poor prognosis (1). In addition to the classical EGFR signaling pathways initiated at the cell surface, nuclear localization of the receptor has been reported to be involved in cancer resistance to therapies. EGFR can be shuttled from the plasma membrane to the nucleus in a series of well-defined steps through clathrin-mediated endocytosis (major pathway of EGFR internalization) or clathrin-independent endocytosis (2). In the nucleus, EGFR serves as a transcriptional co-activator for a series of genes involved in multiple biological functions, including cell proliferation, tumor progression, DNA repair and replication, and chemo- and radio-resistance (3).
Chronic inflammation is a critical component of EGFR mediated cancer progression (4). The aim of this study was to assess whether PGE_2, a known inflammatory mediator, contributes to EGFR nuclear translocation. Lung cancer cell lines (A549, GLC82) were used. PGE_2 was able to induce the receptor nuclear translocation, inducing its tyrosine phosphorylation mediated by activation of PGE_2 receptor, EP3, and the dowstream tyrosine kinase SFK. Further, we also demonstrated that PGE_2 induced EGFR translocation through Caveolin-endocytosis.
In conclusion the findings demonstrate that PGE2 controls EGFR translocation contributing to sustain its oncogenic drive, and suggest the potential pharmacological targeting of EP3 receptor.

References:

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