Abstract

PDAC remains one of the most lethal cancers with a poor prognosis due to late diagnosis, lack of reliable biomarkers, and limited treatment options. One of the essential drivers in cancer progression is the EGF signaling pathway, which leads to cancer cell proliferation and higher PD-L1 expression, resulting in immune surveillance evasion. This study aims to elucidate and analyse PD-L1 expression under EGF stimulation and its molecular pathways. Bioinformatic analysis was done to check EGFR and PD-L1 expression in the PDAC cell line. PDAC cell line, BxPC-3, was treated under various EGF concentrations of 0-100 ng/ml for 24-72 hours. Cell viability assays were done to check cancer cell proliferation. Protein extraction followed by western blot was done to analyse p-AKT, AKT, p-ERK1/2, ERK1/2, p-STAT3, STAT3, and PD-L1 protein expression. Significant proliferation of the BxPC-3 cell line was observed under various EGF stimulations after 24 hours of treatment. There was no significant activation of AKT, ERK, or STAT3 under EGF stimulation, and PD-L1 expression increased in low EGF stimulation. These might be due to transient expression peaks of canonical pathways, possibilities of non-canonical pathways activation, including the NF-kB-inducing kinase, or EGFR degradation through a negative feedback loop. Bioinformatics analysis showed a low baseline of PD-L1 expression in the BxPC-3 cell line. Negative feedback loop for PD-L1 expression might be affected by EGF stimulation. PD-L1 expression through EGFR signaling in PDAC remains unknown, and further optimization using transient time points and KRAS-mutated cell lines, including ASPC-1 and PANC-1, is needed to improve the study.

Keywords: PDAC, EGF, PD-L1, Molecular pathway