Chapter 1

Introduction

1.1 Background

Over the past decades, cancer has been known as a serious public health concern as well as among the leading causes of death worldwide. Pancreatic cancer remains one of the cancer types with a high mortality and morbidity rate. As of 2020, the 5-year survival rate of pancreatic cancer is a mere 10%, resulting in an extremely low prognosis in the five-year time frame due to the late diagnosis and low treatment efficacy. The pancreatic ductal adenocarcinoma (PDAC) accounts for the majority of pancreatic cancer, encompassing 90% of total pancreatic neoplasms (Park et al., 2021). Diagnostic difficulties and a lack of treatment cause the poor prognosis of pancreatic cancer. Prolonged dysregulation of the signaling pathway is suspected further to enhance cancer metastasis, migration, and invasion. The alterations of signaling pathways in PDAC include MAPK/ERK, JAK/STAT, and PI3K/AKT (Javadrashid et al., 2021).

Multiple factors leading to signaling dysregulation, two of which are essential, include growth factors and immune checkpoint inhibitors. Epidermal growth factor (EGF) is found to be a stimulator in cancer cell progression. EGFR gene overexpression in cancer cells is used as a biomarker due to its activation in multiple downstream signaling pathways, such as PI3K/AKT and MAPK/ERK pathways, resulting in cancer cell proliferation and survival (Javadrashid et al., 2021). Those signaling pathway abnormalities lead to the dysregulation of Immune checkpoints. Immune checkpoints are essential hallmarks in cancer cell progression. Abnormal levels in immune checkpoints allow tumour cells to evade immune system surveillance and inhibit apoptosis (Viegas et al., 2023). One of the immune checkpoint overexpressions in pancreatic cancer, resulting in its poor prognosis, is programmed death ligand-1 (PD-L1), which correlates with a lower survivability rate in PDAC patients (Chen et al., 2017).

Through certain molecular pathways such as MAPK/ERK, JAK/STAT, PI3K/AKT, and NF-kB pathways, EGF stimulation can affect PD-L1 expression, resulting in a positive correlation. In various cancers, including non-small cell lung cancer (NSCLC), breast cancer, colon cancer, and esophageal squamous cell carcinoma, EGF stimulation has been found to increase PD-L1 levels (Chen et al., 2019; Zhang et al., 2017; Li et al., 2018). These findings highlight the strong correlation between EGF stimulation and PD-L1 levels. The exact molecular pathway mechanism between EGF stimulation and PD-L1 levels in pancreatic cancer remains unclear. Elucidation of the molecular mechanism allows further development for EGFR inhibitors and opens opportunities for pancreatic anti-cancer drug discovery.

1.2 Objective

To elucidate the involved molecular pathway of PD-L1 expression in pancreatic cancer cell line under EGF stimulation

1.3 Hypothesis

H0 : EGF stimulation will not increase PD-L1 expression through AKT, ERK, or STAT3 in pancreatic cancer cell line

H1 : EGF stimulation will increase PD-L1 expression through AKT, ERK, or STAT3 in pancreatic cancer cell line