中文題目: 幹細胞標誌 CD133 與胰臟癌惡性度的關係

英文題目: **Pancreatic Tumor Progression Associated With CD133 Overexpression**

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Background: Among the gastrointestinal cancers, Pancreatic ductal adenocarcinoma(PDAC) has the worst median survival prognosis for less than 6 months. The transmembrance protein CD133 has been used as a marker for normal stem cells and is also expressed in a variety of human cancer, including hepatocellular carcinoma, brain tumors, and PDAC. This study aims to investigate the role of CD133 in pancreatic ductal adenocarcinoma malignancy and its involvement in epidermal growth factor receptor (EGFR) signaling.

Methods: The effects of CD133 overexpression on cell proliferation, migration, invasiveness, and angiogenesis were investigated in the human pancreatic ductal adenocarcinoma cell line AsPC-1 in vitro and severe combined immunodeficiency xenografts in vivo.

Results: AsPC-1 cells overexpressing CD133 (AsPC-1 CD133 cells) had elevated cell proliferation, tumorigenesis, cell cycle progression, adhesion, migration, and angiogenesis. AsPC-1 CD133 cells displayed increased survival during treatment with chemotherapeutic agents. CD133 overexpression resulted in decreased EGF expression, increased telomerase reverse transcriptase expression, and increased Akt phosphorylation. Immunoprecipitation assays and immunofluorescent labeling studies revealed that CD133 physically interacts with EGFR. The EGFR inhibitor gefitinib was shown to have potent anti-CD133 activity, decreasing the CD133-induced migration of AsPC-1 CD133 cells. Knockdown of CD133 was also observed to inhibit AsPC-1 CD133 cell proliferation, migration, and invasion.

Conclusion: Our results propse that CD133-induced cancer stem cell activity may arise from enhanced telomerase reverse transcriptase expression and CD133 ligand-independent EGFR activation to exhibit the cancer stem cell phenotype, promoting cancer stem cell proliferation independent of cytokines, with high metastatic potential and the development of chemoresistance.