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Article

Expansion of Circulating Tumor Cells from Patients with Locally Advanced Pancreatic Cancer Enable Patient Derived Xenografts and Functional Studies for Personalized Medicine

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Abstract: Improvement in pancreatic cancer treatment represents an urgent medical goal that has been hampered by the lack of predictive biomarkers. Circulating Tumor Cells (CTCs) may be able to overcome this issue by allowing the monitoring of therapeutic response and tumor aggressiveness through ex vivo expansion. The successful expansion of CTCs is challenging, due to their low numbers in blood and the high abundance of blood cells. Here, we explored the utility of pancreatic CTC cultures as a preclinical model for treatment response. CTCs were isolated from ten patients with locally advanced pancreatic cancer using the Labyrinth, a biomarker independent, size based, inertial microfluidic separation device. Three patient-derived CTC samples were successfully expanded in adherent and spheroid cultures. Molecular and functional characterization was performed on the expanded CTC lines. CTC lines exhibited KRAS mutations, consistent with pancreatic cancers. Additionally, we evaluated take rate and metastatic potential in vivo and examined the utility of CTC lines for cytotoxicity assays. Patient derived expanded CTCs successfully generated patient derived xenograft (PDX) models with a 100% take rate. Our results demonstrate that CTC cultures are possible and provide a valuable resource for translational pancreatic cancer research, while also providing meaningful insight into the development of distant metastasis, as well as treatment resistance.

Keywords: circulating tumor cells; biomarkers; pancreatic cancer; personalized medicine

1. Introduction

Pancreatic cancer is the third leading cause of cancer-related death in the United States [1]. The survival probability with this disease has not improved substantially over nearly 40 years [1,2].