ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) is characterized by poor prognosis, being commonly diagnosed in the unresectable advanced or metastatic stage which poses an extremely poor prognosis for patients. Hypoxia predominates most pancreatic cancer tumour microenvironments (TME), with HIF-1 signalling being overexpressed in 88% of all pancreatic cancers. Long noncoding RNAs (lncRNAs) have emerged as potential key players in the onset and progression of cancer, by possessing both tumour suppressor and oncogenic functions. Of note, hypoxia inducible lncRNAs are implicated to be either regulate or control HIF-1 signalling in pancreatic cancer. LncRNA X is a novel hypoxia-inducible lncRNA which has been previously studied in other types of cancer, but not PDAC. In these studies, the overexpression of LncRNA X was found to upregulate cancer cell migration and activate HIF-1 signalling pathways. However, due to the tissue-specificity of the effects of most lncRNAs in cancer, it is currently unknown whether these same effects extend to PDAC. Thus, this project aims to validate the effect of LncRNA X overexpression on PDAC migration and signalling pathways it is involved in using transwell migration assays and high-throughput RNA sequencing. Through these methods, LncRNA X was observed to promote PDAC migration and indirectly activate HIF-1 pathways by downregulating mitophagy. Nevertheless, as the data obtained in this project was only sufficient to identify a possible signalling pathway of LncRNA X in HIF-1 activation in PDAC, further functional assays are necessitated to completely elucidate these pathways and obtain a more detailed understanding of how LncRNA X promotes PDAC malignancy.

Keywords: Pancreatic Ductal Adenocarcinoma; LncRNA; Hypoxia; HIF-1; Hypoxia-inducible lncRNA