INVESTIGATING THE IMPACT OF ELAVL1 INHIBITION ON PANCREATIC CANCER CELL VIABILITY

Joris Dambrauskas[1], Darius Stukas[2]

[1]Faculty of Chemistry and Geosciences, Vilnius University
[2]Surgical Gastroenterology Laboratory, Institute for Digestive Research, Lithuanian University of Health Sciences
joris.dambrauskas@chgf.stud.vu.lt

Introduction

An RNA binding protein, human antigen R (ELAVL1), is a key regulator of a molecular mechanism that is responsible for posttranscriptional gene regulation which is altered in pancreatic ductal adenocarcinoma (PDAC) cells. This, in turn, supports the pro-survival phenotype intrinsic to PDAC cells [1]. Thus, ELAVL1 inhibition could be considered a viable direction for cancer therapeutics [2], yet, it is still not clear how different inhibitors affect the cell.

Aim

This study aimed to investigate the effects of two known natural ELAVL1 inhibitors – 15,16-dihydrotanshinone-I (DHTS) [3] and pyrvinium pamoate (PP) [4] – on expression of ELAVL1 target mRNAs and proteins.

Methods

PDAC (BxPC-3) cells were treated with different concentrations of the two inhibitors for 24 hours. The IC50 doses of both inhibitors were determined through MTT assays. Then, doses that don't affect cell viability were used to evaluate the inhibition of ELAVL1 according to two of its targets – aryl hydrocarbon receptor (AHR) [5] and deoxycytidine kinase (dCK) [6]. Protein expression was assessed through western blot (WB) an lysis and the quantities of respective mRNA transcripts – through quantitative real-time polymerase chain reaction (qRT-PCR).

Results

The results show that both DHTS and PP affect the cell metabolic activity in a similar manner with IC50 doses being comparable between inhibitors. Protein expression of AHR and DCK, was reduced in all cases, while there was an increase in mRNA being transcribed.

Conclusion

Inhibition of ELAVL1 may have a positive impact on the course of PC by decreasing expression of unfavourable proteins such as AHR. On the other hand, ELAVL1 also stabilizes DCK, which is required for gemcitabine to be effective. Thus, although ELAVL1 could potentially be used to contribute to the treatment of pancreatic cancer, it is important to consider the adjacent therapies used.

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