

# High expression of pyruvate dehydrogenase kinase in cholangiocarcinoma patients

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### ABSTRACT:

In our previous demonstration, we found the differential mitochondrial proteome between CCA and adjacent non-cancerous tissues assessed by mass spectrometry. Cancer cells are well-known for their altered metabolic state and the main cause under this phenomenon is mitochondrial metabolic enzyme permutation. So in this study, the glucose metabolism-involved proteins were selected from data and fold-change analysis was performed. The data showed the overexpression of pyruvate dehydrogenase kinase (PDK) isoform 2 and 3 in CCA compared to its adjacent non-cancerous tissues. Especially, PDK3 showed the highest fold-change at 13. PDK is a Ser/Thr kinase that inactivates mitochondrial pyruvate dehydrogenase and plays a keystone of Warburg effect that lead cancer cells survive in hypoxia condition. PDK isoforms consist of PDK1, PDK2, PDK3 and PDK4. All PDK isoforms notably express on specific tissues and there is no report of PDK pattern in CCA yet. In this work, all PDK isoforms immunohistochemistry was performed in CCA and adjacent non-cancerous tissues to confirm mass spectrometric data. The results showed the pattern of PDK isoform expression where PDK1, PDK2 and PDK3 exhibited high expression on CCA tissues at H-score  $240\pm 69$ ,  $210\pm 30$  and  $262\pm 28$  respectively (maximum H-score=300), while the weak staining was observed in adjacent tissues. In contrast, PDK4 showed no staining in CCA tissues. Taken together, the specification of PDKs pattern in CCA may provide a good tumor marker for CCA. Furthermore, PDK1 and PDK3 may be considered as potential prognostic markers for CCA patients due to their tumor progression involvement.

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