

Mucin 5B, carbonic anhydrase 9 and claudin 18 are potential theranostic markers of gallbladder carcinoma

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Aims: Gallbladder cancer (GBC) is an aggressive tumour that is usually diagnosed at advanced stages and is characterised by a poor prognosis. Using public data of normal human tissues, we found that mRNA and protein levels of mucin 5B (MUC5B) and carbonic anhydrase 9 (CA9) were highly increased in gallbladder tissues. In addition, previous evidence has shown that claudin 18 (CLDN18) protein expression is higher in GBC. The aim of this study was to perform an analysis of these cell surface proteins during the histological progression of GBC in order to identify their theranostic potential. **Methods and results:** MUC5B expression, CA9 expression and CLDN18 expression were examined by immunohistochemistry in a series of 179 chronic cholecystitis (including 16 metaplastic tissues), 15 dysplasia and 217 GBC samples by the use of tissue microarray analysis. A composite staining score was calculated from staining intensity and

percentage of positive cells. Immunohistochemical analysis showed high expression of MUC5B and CA9 among normal epithelium, metaplastic tissues, and dysplastic tissues. However, expression of both proteins was observed in roughly 50% of GBC samples. In contrast, CLDN18 was absent in normal epithelium, but its expression was higher in metaplastic cells. Among GBC cases, approximately half showed high CLDN18 expression. No associations were found between MUC5B, CA9 and CLDN18 expression and any clinicopathological features. Conclusions: CLDN18 is a new metaplasia marker in gallbladder tissues, and is conserved in approximately half of GBC cases. MUC5B and CA9 are highly conserved during GBC histological progression. The three markers are potential theranostic markers, in particular CA9 and CLDN18, for which there are already targeted therapies available. © 2018 John Wiley & Sons Ltd

biomarker

CA9

CLDN18

Gallbladder cancer

MUC5B

theranostic

carbonate dehydratase IX

claudin 18

messenger RNA

mucin 5B

protein p53

proteome

transcription factor Cdx2

transcriptome

tumor marker

CA9 protein, human

carbonate dehydratase IX

claudin

CLDN18 protein, human

mucin 5B

tumor antigen

tumor marker

adult

advanced cancer

aged

Article

bile duct carcinoma

cancer growth

cancer patient

carcinogenesis

chronic cholecystitis

clinical feature

cohort analysis

dysplasia

female

gallbladder carcinoma

gallbladder epithelium

human

human cell

human tissue

immunohistochemistry

major clinical study

male

molecular pathology

mRNA expression level

priority journal

protein expression level

tissue microarray

biosynthesis

gallbladder tumor

middle aged

pathology

procedures

theranostic nanomedicine

Adult

Aged

Antigens, Neoplasm

Biomarkers, Tumor

Carbonic Anhydrase IX

Claudins

Female

Gallbladder Neoplasms

Humans

Male

Middle Aged

Mucin-5B

Theranostic Nanomedicine