

**Supplemental Data 10**  
**Immunohistochemical verification of 14 potential biomarker candidates**

putatively CCC-specific	No.	Gene name	Comparison	AUC	CI	cut-off	Sensitivity	CI	# of samples CCC positive	Specificity	CI	# of samples non- CCC negative
	1	APOA4	vs. hepatocytes	0.45	0.24-0.67	$\infty$	0%	0-23%	0 (14)	100%	77-100%	14 (14)
			vs. cholangiocytes	0.87	0.73-1	3.5	79%	49-95%	11 (14)	92%	62-100%	11 (12)
	2	CLIC1	vs. hepatocytes	0.99	0.98-1	7	100%	77-100%	14 (14)	93%	66-100%	13 (14)
			vs. cholangiocytes	0.59	0.41-0.78	10.5	79%	49-95%	11 (14)	42%	15-72%	5 (12)
	3	GSN	vs. hepatocytes	1	0.99-1	4.5	93%	66-100%	13 (14)	100%	77-100%	14 (14)
			vs. cholangiocytes	0.28	0.11-0.45	$\infty$	0%	0-23%	0 (14)	100%	75-100%	13 (13)
	4	MSN	vs. hepatocytes	0.68	0.55-0.81	1	36%	13-65%	5 (14)	100%	77-100%	14 (14)
			vs. cholangiocytes	0.68	0.55-0.81	1	36%	13-65%	5 (14)	100%	77-100%	14 (14)
	5	PKM2	vs. hepatocytes	0.97	0.94-1	3.5	100%	77-100%	14 (14)	86%	57-98%	12 (14)
			vs. cholangiocytes	0.58	0.34-0.81	10	43%	18-71%	6 (14)	100%	74-100%	12 (12)
	6	PPA1	vs. hepatocytes	0.82	0.67-0.97	7	93%	66-100%	13 (14)	54%	25-81%	7 (13)
			vs. cholangiocytes	0.70	0.50-0.90	7	93%	66-100%	13 (14)	42%	15-72%	5 (12)
7	SERPINH1	vs. hepatocytes	0.99	0.96-1	10	86%	57-98%	12 (14)	100%	77-100%	14 (14)	
		vs. cholangiocytes	0.98	0.96-1	10	86%	57-98%	12 (14)	100%	74-100%	12 (12)	
8	SFN	vs. hepatocytes	1	0.98-1	2.5	93%	66-100%	13 (14)	100%	77-100%	14 (14)	
		vs. cholangiocytes	0.99	0.98-1	2.5	93%	66-100%	13 (14)	100%	77-100%	14 (14)	
9	STIP1	vs. hepatocytes	1	1-1	3	100%	77-100%	14 (14)	100%	77-100%	14 (14)	
		vs. cholangiocytes	1	1-1	3.5	100%	77-100%	14 (14)	100%	77-100%	14 (14)	

putatively hepatocyte-specific	No.	Gene name	Comparison	AUC	CI	cut-off	Sensitivity	CI	# of samples hepatocytes positive	Specificity	CI	# of samples non- hepatocytes negative
	10	ABAT	vs. CCC	1	1-1	10	100%	77-100%	14 (14)	100%	77-100%	14 (14)
	11	ACAA2	vs. CCC	0.79	0.65-0.92	10.5	100%	77-100%	14 (14)	57%	29-82%	8 (14)
	12	BHMT	vs. CCC	1	1-1	1.5	100%	77-100%	14 (14)	100%	77-100%	14 (14)
	13	FABP1	vs. CCC	1	1-1	9	100%	77-100%	14 (14)	100%	77-100%	14 (14)
	14	HMGCS2	vs. CCC	0.95	0.86-1	8.5	86%	57-98%	12 (14)	93%	66-100%	13 (14)

Tissue samples from set 2 (n = 14) were evaluated regarding positive antibody staining. Areas under the curve (AUC) from receiver operating characteristics (ROC) were computed and cut-off values for IRS were optimised according to Youden's criterion. Infinitely high cut-off values ( $\infty$ ) indicate that there is no cut-off value at which groups can be separated meaningfully. In the case of proteins up-regulated in CCC tumour tissue (putatively CCC-specific) the sensitivity represents the proportion of samples positive for CCC cell staining. Specificities were determined for the ability to differentiate CCC tumour cells from normal hepatocytes (vs. hepatocytes) as well as for distinguishing between CCC cells and non-tumorous cholangiocytes (vs. cholangiocytes). AUC and diagnostic values were derived expecting larger values in tumour samples. For down-regulated candidates (putatively hepatocyte-specific) the sensitivity for detecting hepatocytes and the specificity for distinguishing these from CCC cells (vs. CCC) were determined. In this case, AUC and diagnostic values were computed expecting smaller values in tumour samples. Numbers in brackets indicate the numbers of samples which were evaluated regarding staining of the specific cell type since this was not possible in all cases due to technical issues. CI: 95% confidence interval.