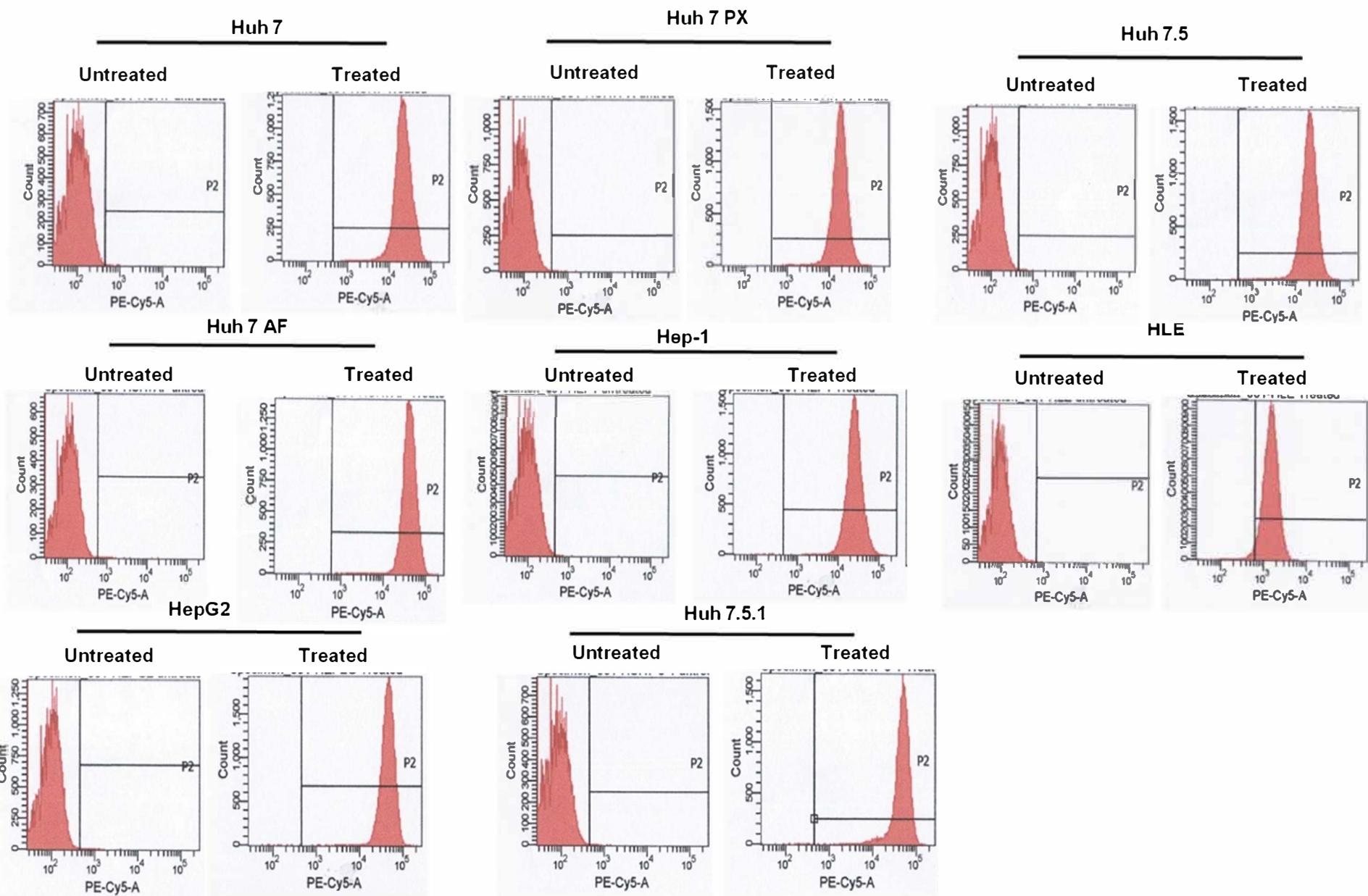
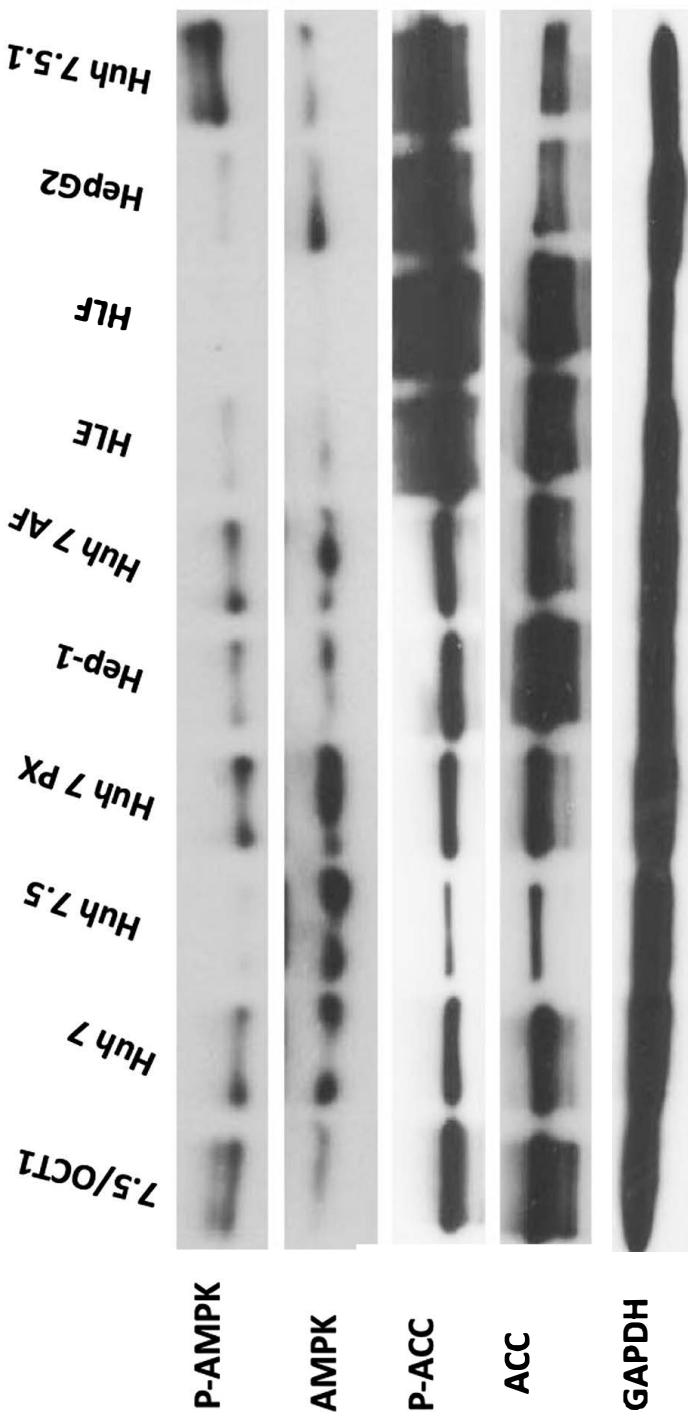


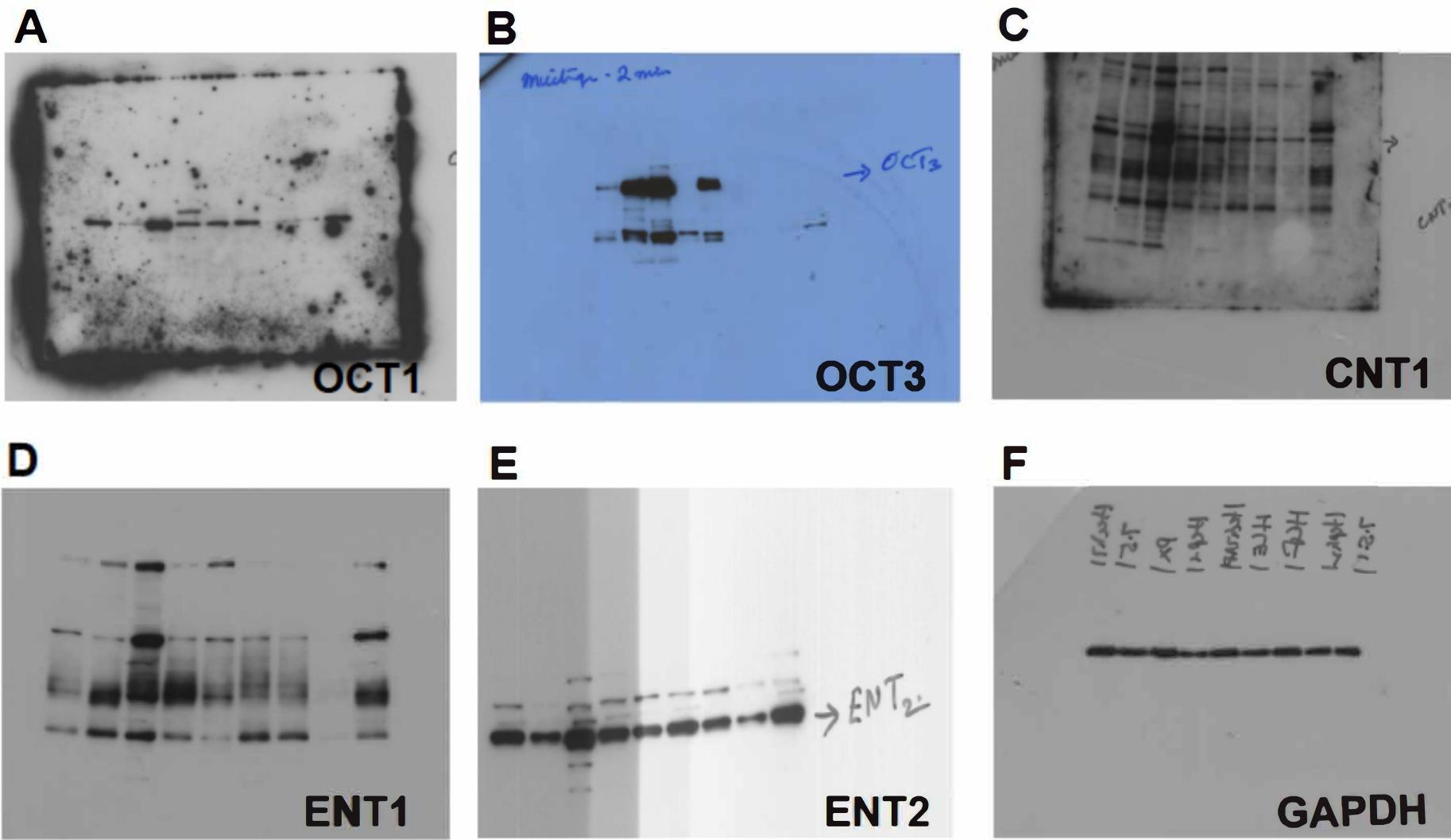
**Supplemental Figure 1:** MTT assay of SR Huh 7.5 and SS Huh 7.5.1 cells treated with increasing concentrations of doxorubicin.



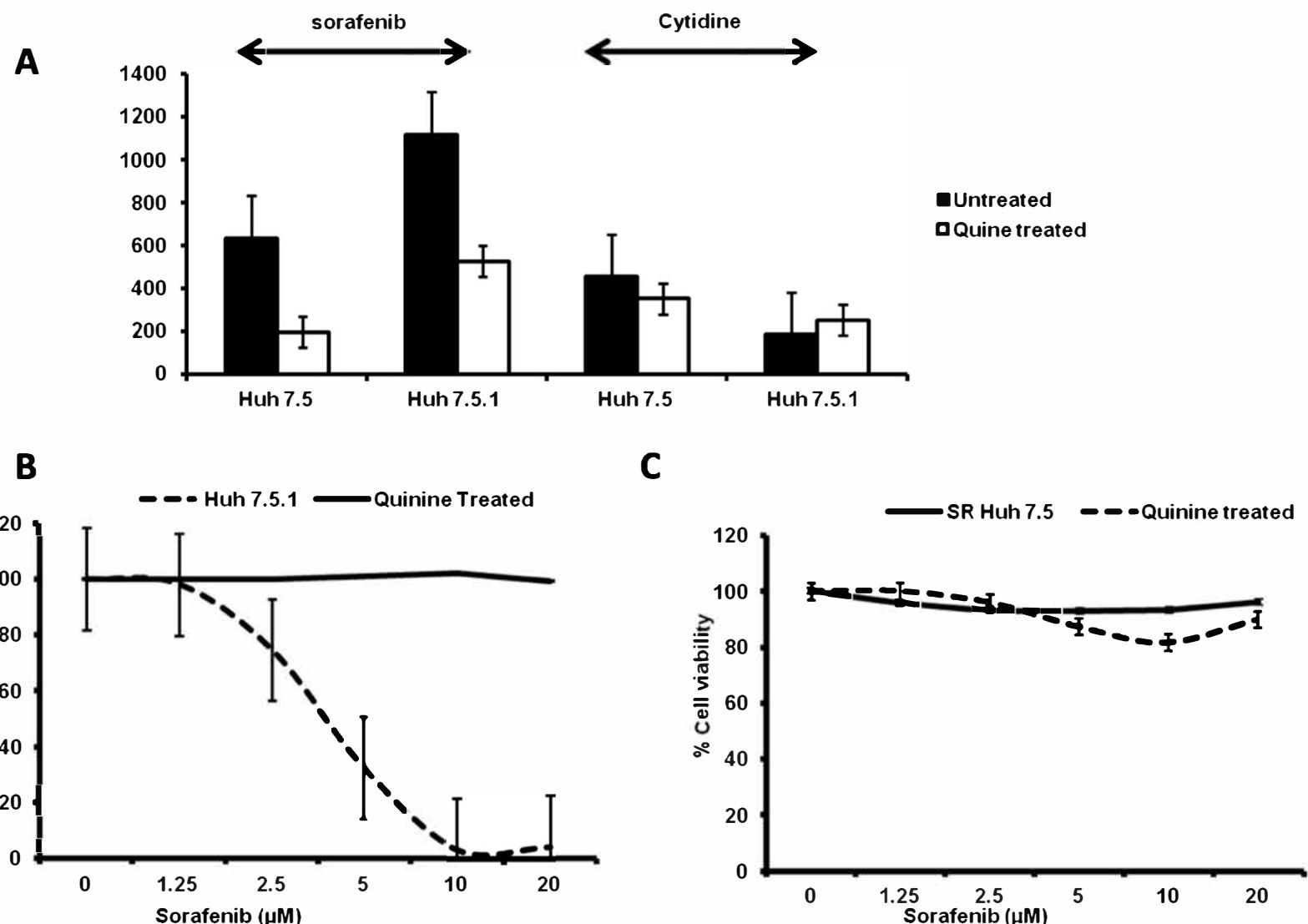
Supplemental Figure 2: Doxorubicin uptake of HCC cells determined by flow cytometry. Cells were treated with 200  $\mu$ g of doxorubicin and after 4 hours cells were washed and analyzed by flow cytometry. Cells without doxorubicin treatment used as negative control.



**Supplemental Figure 3:** Western blot analysis results show metformin uptake results of nine different HCC cell line. Stable OCT1 expression increased metformin uptake of SR Huh 7.5 cells and induced pAMPK level and pACC level.



Supplemental Figure 4 : Original Western Blood Images of Figure 3B



**Supplemental Figure 5:** Sorafenib uptake and MTT assay between resistant cell line (SR Huh 7.5) and sensitive (SS Huh 7.5.1) cells in the presence and absence of quinine. (A). Show the results of sorafenib uptake of the resistant and sensitive cell line with or without quinine treatment. Show the results of cytidine uptake between resistant and sensitive cells. (B). Show the MTT assay showing pre-treatment of quinine reduced sorafenib cytotoxicity in sensitive cell line (SS Huh 7.5.1). (C). Show that quinine treatment did not alter the sorafenib sensitivity of the resistant cell line (SR Huh 7.5 cells).

**Supplemental Table 1: Evaluation of OCT1 expression in HCC patient samples**

Samples	HCV	Diagnosis	Non-tumor				Tumor					
			No	Status	H&E stained	Score	Staining pattern	Percentage	Total score	Score	Staining pattern	Percentage
1	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	50%	150			
2	(-)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	30%	60			
3	(-)	Cirrhosis/HCC	2	Homogenous	100%	200	Focal	5%	5			
4	(-)	Cirrhosis/HCC	3	Homogenous	100%	300	Negative	0%	0			
5	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	20%	20			
6	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	40%	120			
7	(-)	Cirrhosis/HCC	2	Patchy	30%	60	Homogenous	100%	300			
8	(-)	Cirrhosis/HCC	3	Homogenous	100%	300	Homogenous	100%	300			
9	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	30%	90			
10	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Patchy	80%	240			
11	(-)	Cirrhosis/HCC	3	Homogenous	100%	300	Negative	5%	5			
12	(-)	Cirrhosis/HCC	3	Homogenous	100%	300	Homogenous	100%	100			
13	(-)	Cirrhosis/HCC	1	Homogenous	100%	100	Negative	0%	0			
14	(+)	Cirrhosis/HCC	3	Patchy	60%	180	Patchy	60%	180			
15	(+)	Cirrhosis/HCC	3	Homogenous	100%	300	Negative	0%	0			
16	(-)	Cirrhosis/HCC	2	Patchy	50%	100	Negative	0%	0			
17	(-)	Cirrhosis/HCC	3	Homogenous	100%	300	Focal	20%	20			
18	(+)	Cirrhosis/HCC	1	Patchy	40%	40	Patchy	50%	150			
19	(+)	Cirrhosis/HCC	2	Homogenous	100%	200	Negative	0%	0			
20	(+)	Cirrhosis/HCC	3	Homogenous	100%	300	Patchy	60%	180			

No staining-0, Weak staining-1, Medium staining-2, Strong staining-3

**Supplemental Table 2: Evaluation of OCT3 expression in HCC patient samples**

Samples	Diagnosis	Non-tumor				Tumor			
No	H&E stained	Score	Staining pattern	Percentage	Total score	Score	Staining pattern	Percentage	Total score
1	Cirrhosis/HCC	3	Homogenous	100%	300	3	Patchy	100%	300
2	Cirrhosis/HCC	2	Homogenous	100%	200	2	Patchy	100%	200
3	Cirrhosis/HCC	2	Homogenous	20%	200	2	Focal	10%	30
4	Cirrhosis/HCC	3	Homogenous	80%	300	2	Negative	40%	80
5	Cirrhosis/HCC	2	Homogenous	100%	200	2	Patchy	80%	160
6	Cirrhosis/HCC	3	Homogenous	100%	300	2	Patchy	30%	60
7	Cirrhosis/HCC	2	Patchy	100%	200	2	Homogenous	100%	200
8	Cirrhosis/HCC	2	Homogenous	100%	200	2	Homogenous	20%	40
9	Cirrhosis/HCC	3	Homogenous	100%	300	2	Patchy	100%	200
10	Cirrhosis/HCC	1	Homogenous	100%	200	1	Patchy	20%	100
11	Cirrhosis/HCC	2	Homogenous	100%	200	1	Negative	10%	10
12	Cirrhosis/HCC	2	Homogenous	100%	200	1	Homogenous	70%	70
13	Cirrhosis/HCC	2	Homogenous	100%	200	2	Negative	100%	200
14	Cirrhosis/HCC	2	Patchy	100%	200	2	Patchy	100%	200
15	Cirrhosis/HCC	2	Homogenous	100%	200	1	Negative	100%	100
16	Cirrhosis/HCC	2	Patchy	100%	200	2	Negative	70%	140
17	Cirrhosis/HCC	3	Homogenous	100%	300	1	Focal	10%	10
18	Cirrhosis/HCC	2	Patchy	100%	200	1	Patchy	50%	50
19	Cirrhosis/HCC	3	Homogenous	100%	300	2	Negative	100%	200
20	Cirrhosis/HCC	3	Homogenous	100%	300	2	Patchy	100%	200

No staining-0, Weak staining-1, Medium staining-2, Strong staining-3