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Author(s)	Chan, S.H
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Use of Monoclonal Antibodies for the Diagnosis of Liver Cancer

S. H Chan*

* WHO Immunology Centre, Faculty of Medicine,
National University of Singapore

Mouse monoclonal antibodies (McAb) were generated by fusion by P3/NS1/1-Ag4-1 or SP2/O-Ag-14 cells with spleen cells from Balb/c mice immunized with fresh local hepatocellular carcinoma (HCC) cells or with established HCC cell lines. From a total of 263 McAb against liver cells, 5 reacted only with human HCC. An immunofluorescence antibody inhibition assay using PLC/PRF/5 liver cancer cell lines as target cells was developed in which circulating antigens that reacted with these McAb could be detected. The reaction of one of the McAb 3H11 and its corresponding antigens 3H11 Ag is shown in Table 1. 3H11 Ag was detected in 7/30 (23.3%) HCC sera compared to 1/40 (2.5%) control sera ($P=.009$; $RR=12$). The one positive serum from the control group was from a patient with chronic hepatitis/cirrhosis, a premalignant condition. We are following up this patient to see whether he will develop HCC. We are increasing the sensitivity of the assay by converting it to ELISA.

Table 1. 3H11 Ag in hepatocellular carcinoma and control sera

	Presence of 3H11-Ag		
	+	-	
HCC	7	23	30
Cirrhosis/Hepatitis/ Normal	1	39	40
	8	62	70

$P=0.009$ $RR=12$

CA-50 Ag AS A DIAGNOSTIC MARKER FOR HEPATOCELLULAR CARCINOMA

The CA-50 antigen is a tumour-associated sialylated glycoprotein/ganglioside antigen

(CA-50 Ag) detected by a mouse monoclonal antibody, C-50, raised against a colorectal adenocarcinoma cell line¹. A radioimmunoassay for detecting CA-50 Ag in serum has been developed.

A blind study was conducted between Sweden and Singapore whereby sera (various cancers, premalignant conditions, family members of cancer patients and normals) were sent to Sweden under code and the diagnosis revealed only after the sera were tested. In some studies the coded sera (coded by a third party) were tested in Sweden as well as in Singapore. Hidden controls (split samples and multiple bleeds from the same patient) were also included. The results from the hidden controls were good and the concordance rate between results from Sweden and Singapore was 95%.

CA-50 AND HCC

The level of CA-50 Ag was expressed in units and an elevated level was defined as one greater than two standard deviation above the mean level of normal health controls. The frequency of raised CA-50 Ag in HCC and control sera is shown in Table 2. Raised levels of CA-50 Ag was observed in 77.8% of HCC patients, 21.5% of patients with cirrhosis/chronic hepatitis, 6.3% non-cancer (thyrotoxicosis, diabetes, SLE, thyroiditis etc.) patients and 3.4% of normal family members of cancer patients. The frequency of elevated CA-50 Ag was significantly higher in HCC patients compared to non-cancer patients and normal family members ($P<.0001$; $RR=65$) or to patients with cirrhosis/chronic hepatitis ($P<.0001$, $RR=13$; Table 3).

Table 2. Elevated CA50-Ag in serum of hepatocellular carcinoma patients and controls

	No. Tested	Elevated CA50-Ag	
		No.	%
HCC AFP + ve	84	64	76.2
HCC AFP - ve	69	55	79.7
HCC Total	153	119	77.8
Cirrhosis/Ch. Hepatitis	47	10	21.3
Non Cancer Patients	128	8	6.3
Normal Family Members of Ca Patients	88	3	3.4

Table 3. CA50 Antigen in hepatocellular carcinoma and controls

	Elevated CA50		
	+	-	
Liver Cancer	119	34	153
Non Cancer Patients and Normal Family Members	11	205	216
	130	239	369

$X^2 = 207$
 $P < 0.0001$
 $RR = 65$

	Elevated CA50		
	+	-	
Liver Cancer	119	34	153
Chronic Hepatitis/ Cirrhosis	10	37	47
	129	71	200

$X^2 = 50$
 $P < 0.0001$
 $RR = 13$

Table 4. CA50 Ag in AFP negative HCC and controls

	CA50 Ag		
	+	-	
AFP-ve HCC	55	14	69
Controls	11	205	216
	66	219	285

$X^2 = 163.6$
 $P < 0.0001$
 $RR = 73.2$

correlation between CA-50 Ag and AFP, α_1 antitrypsin, α_1 acid glycoprotein, GGT or CEA.

REFERENCES

- 1) Lindholm L, Holmgren J, Svennerholm L, Fredman P, Nilsson O, Person B, Hyrvold H, Lagergard T. Monoclonal antibodies against gastrointestinal tumor-associated antigens isolated as monosialoganglioside. *Int Archs Allergy Appl Immunol* 71 : 178-181, 1983.

CA-50 AND AFP AND OTHER MARKERS

The frequency of elevated CA-50 Ag was equally marked in AFP-positive (76.2%) or in AFP-negative (79.7%) HCC patients (Table 2). This suggests that CA-50 Ag may be a good test for the diagnosis of AFP-negative HCC patients. Elevated CA-50 Ag was observed in 55/69 (79.7%) AFP-negative HCC patients compared to 11/216 (5.1%) on cancer controls ($P < .0001$, $RR = 73.2$; Table 4). There was no