

Letter to the Editor

Ischemia Effect on the Level of Steroid Hormone Receptors in Hepatocellular Carcinoma and Adjacent Liver Tissue

WING-YIU LUI,* FANG-KU P'ENG,* TAI-JAY CHANG,* HWA-LI KAO,* TSUNG-YUN LIU† and CHIN-WEN CHI†

Departments of *Surgery and †Medical Research, Veterans General Hospital, Taipei 11217, Taiwan, Republic of China

RECENT STUDIES have shown that estrogen, progesterone, androgen and glucocorticoid receptors are present in human hepatocellular carcinoma tissues different levels of receptors were observed between the tumor and adjacent liver samples [1]. Moreover, variations in receptor levels were observed among various reports [2-4]; this could be the result of different sampling techniques. Hepatic lobectomy usually takes a few hours, and the blood supply to the resected liver and tumor is gradually reduced during the operation. Yet, the effect of ischemia on the physiology of the resected hepatocellular carcinoma has not been examined. The objective of the present study was to determine whether ischemia has any effect on the receptor levels in liver samples. Normal and hepatoma samples were obtained either as biopsy samples before tumor resection or collected after lobectomy (usually 1-2 h). The samples were immediately frozen in liquid nitrogen and assayed for estrogen, androgen, progesterone and glucocorticoid receptors on the same day. The dextran-coated charcoal assay was used for receptor determination as described previously [1], and the result was analyzed by a Scatchard plot [5].

In seven paired comparisons, no detectable receptor was found in either the pre-ischemia or the post-ischemia samples. Of the other 13 paired samples, receptor level was lower in 11 post-ischemia samples

Table 1. Effect of ischemia on levels of steroid hormone receptors

Group	Receptor level (fm/mg protein)			
	GR	PR	ER	AR
N1-Pre	0	52.2	102.8	47.9
N1-Post	0	10.8	32.5	2.8
H1-Pre	37.6	21.4	166.0	0
H1-Post	6.7	40.3	46.3	0
N2-Pre	0	0	30.2	35.5
N2-Post	0	0	10.5	0
H2-Pre	68.7	74.5	55.6	0
H2-Post	29.3	0	5.5	0
H3-Pre	79.9	0	6.5	0
H3-Post	88.4	0	4.0	0

GR: glucocorticoid receptor; ER: estrogen receptor; PR: progesterone receptor; AR: androgen receptor. Tumor (H) or liver (N) samples were obtained either before (Pre) or after (Post) ischemia occurred.

than their corresponding pre-ischemia controls. The averaged decrease in receptor level was 73.5%. In comparison, only two post-ischemia samples had receptor levels higher than their pre-ischemia samples (88.4 vs 79.9 and 40.3 vs. 21.4) (Table 1).

The results from this preliminary study show that the level of steroid hormone receptors in pre-ischemia samples is higher than that of the post-ischemia specimens. Since most of the surgical specimens used for receptor assays were collected after complete resection of the tumor, consequently, tissue samples were already ischemic for a period of time. It is known that ischemia could result in significant alteration in both the structure and

Accepted 19 January 1989.

Address for correspondence and reprints: Dr. Chin-Wen Chi, Department of Medical Research, Veterans General Hospital, Taipei 11217, Taiwan, Republic of China.

function of mitochondria, and subsequently the reduction of cellular ATP levels [6, 7]. Although specimens were frozen in liquid nitrogen immediately after tissue resection, receptor degradation

may have already occurred during surgical operation. Whether the reduction of measurable receptor in tissue was directly related to ischemia was not clear; the mechanism remains to be elucidated.

REFERENCES

1. P'eng FK, Lui WY, Chang TJ *et al.* Glucocorticoid receptors in hepatocellular carcinoma and adjacent liver tissue. *Cancer* 1988, **62**, 2134–2138.
2. Iqbal MJ, Wilkinson ML, Johnson PJ, Williams R. Sex steroid receptor proteins in foetal, adult and malignant human liver tissue. *Br J Cancer* 1983, **48**, 791–796.
3. Nagasue N, Ito A, Yukaya H, Ogawa Y. Androgen receptors in hepatocellular carcinoma and surrounding parenchyma. *Gastroenterology* 1985, **89**, 643–647.
4. Ohnishi S, Murakami T, Moriyama T *et al.* Androgen and estrogen receptors in hepatocellular carcinoma and in the surrounding noncancerous liver tissue. *Hepatology* 1986, **6**, 440–443.
5. Scatchard G. The attraction of proteins for small molecules and ions. *Ann NY Acad Sci* 1949, **51**, 660–672.
6. Mitnacht S, Sherman SC, Farber JL. Reversal of ischemic mitochondrial dysfunction. *J Biol Chem* 1979, **254**, 9871–9878.
7. Lanir AL, Jenkins RL, Caldwell C *et al.* Hepatic transplantation survival: correlation with adenine nucleotide level in donor liver. *Hepatology* 1988, **8**, 471–475.