Aims: To investigate the smooth muscle nature of the stromal cells in the capsule of hepatocellular carcinomas.

Methods: Immunohistochemical analysis using monoclonal antibody to high molecular weight caldesmon (HCD), a highly specific marker for smooth muscle cells, was performed in 33 encapsulated hepatocellular carcinomas and adjacent hepatic tissues.

Results: HCD positive stromal cells were detected in the capsule of 21 of the 33 hepatocellular carcinomas examined.

Conclusions: The capsule of hepatocellular carcinomas contains smooth muscle cells.

Caldesmon is a major calmodulin binding protein that also interacts with actin filaments. Two molecular weight forms of caldesmon—high molecular weight caldesmon (HCD) and low molecular weight caldesmon—have been purified. In particular, HCD, with a molecular weight 120–150 kDa, is associated with smooth muscle contraction and is localised exclusively to smooth muscle cells. In contrast to smooth muscle actin, HCD is not detected in myofibroblasts, indicating that HCD could be used as a highly specific marker for smooth muscle cells and smooth muscle tumours. In the colorectum, pericryptal fibroblasts are positive for HCD.

α Smooth muscle actin is an excellent marker for myofibroblasts and transformed hepatic stellate cells, but is not specific for smooth muscle cells. To investigate the presence of smooth muscle cells in hepatic stroma, immunostaining for HCD should be performed. There are no reports regarding immunohistochemical analysis for HCD positive stromal cells in liver neoplasms.

RESULTS
HCD positive stromal cells were detected in the capsule of 21 of the 33 hepatocellular carcinomas, whereas no HCD positive cells were found in the fibrous septa of the adjacent hepatic tissues examined (fig 1). Of the 21 hepatocellular carcinomas with HCD positive stromal cells, four were HBV associated lesions, nine were HCV associated lesions, and the remaining eight had an unknown aetiology.

DISCUSSION
The presence of intermediately differentiated smooth muscle cells in the capsule of hepatocellular carcinomas is suggested by immunohistochemical analysis using various smooth muscle markers (desmin, smooth muscle actin (clone 1A4, HHF35, CGA7), and smooth muscle myosin heavy chain (SM1, SM2)) and electron microscopy. Unfortunately, the antibodies used in the above mentioned study are not specific for smooth muscle cells, but are also positive in myofibroblasts. Therefore, to confirm the presence of smooth muscle cells, immunostaining for HCD should be performed.

Abbreviations: HBV/HCV, hepatitis B/C virus; HCD, high molecular weight caldesmon

Figure 1 Immunostaining for high molecular weight caldesmon (HCD) in hepatocellular carcinoma. HCD positive stromal cells were detected in the tumour capsule; HCD was also positive in the vessel walls (vascular smooth muscle cells; lower right hand corner).
Immunohistochemical analysis using various smooth muscle markers has suggested that smooth muscle cells are present in the capsule of hepatocellular carcinomas, although the antibodies used were not specific.

We have confirmed this by the use of a monoclonal antibody to high molecular weight caldesmon, which is specific for smooth muscle cells.

Further molecular and biological analyses are needed to elucidate the origin of these cells.

**Take home messages**

- Immunohistochemical analysis using various smooth muscle markers has suggested that smooth muscle cells are present in the capsule of hepatocellular carcinomas, although the antibodies used were not specific.
- We have confirmed this by the use of a monoclonal antibody to high molecular weight caldesmon, which is specific for smooth muscle cells.
- Further molecular and biological analyses are needed to elucidate the origin of these cells.

In conclusion, HCD positive stromal cells, namely smooth muscle cells, were detected in the capsule of hepatocellular carcinomas. To elucidate the origin of the capsular smooth muscle cells, further molecular and biological investigations are needed.

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High molecular weight caldesmon positive stromal cells in the capsule of hepatocellular carcinomas

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