CTCatch™ Clinical Applications in Liver Cancer

1	2	3
Diagnosis	**Monitoring**	**Surgical Guidance**
• ASGPR	• CSV	• CSV

Consult your physicians about CTCatch™ test.

CTCatch™ Test Process

1. Consult your physicians about CTCatch™ test
2. Collect 7.5mL whole blood
3. Analyze samples in Abnova Diagnostics Japan lab
4. Generate your report in 7 days
5. View test results under physician guidance

Diagnostics Abnova 上元株式会社

Address: National Cancer Center Research Institute
3F, 5 Chome-1-1 Tsukiji, Chuo-ku,Tokyo 104-0045, Japan
Tel: + 81 3 6264 3448 Fax: + 81 3 6264 3449
www.abnovadx.com

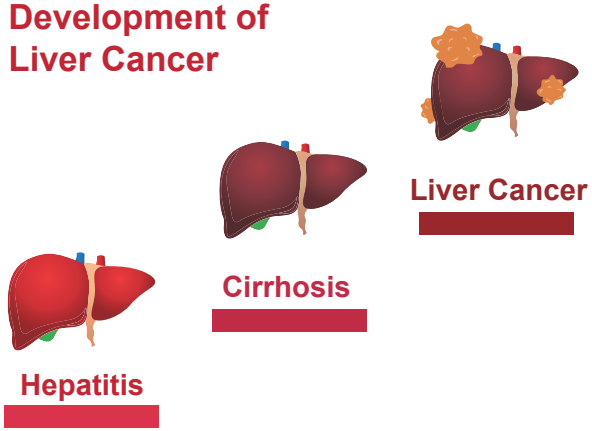
CTC Liquid Biopsy for Liver Cancer

Abnova Diagnostics Japan
CTCatch™ Test

Liver Cancer

Liver cancer is the sixth most common cancer in the world, with 782,000 new cases diagnosed in 2012. Hepatitis B and hepatitis C viruses are causes of liver cancer. The former appears to act directly by damaging cells and their DNA. The latter shows an indirect effect, mediated by cirrhosis. There is convincing evidence that greater body fatness, consumption of alcoholic drinks, and higher exposure to aflatoxins and consumption of aflatoxin-contaminated foods are causes of liver cancer[1].

Development of Liver Cancer



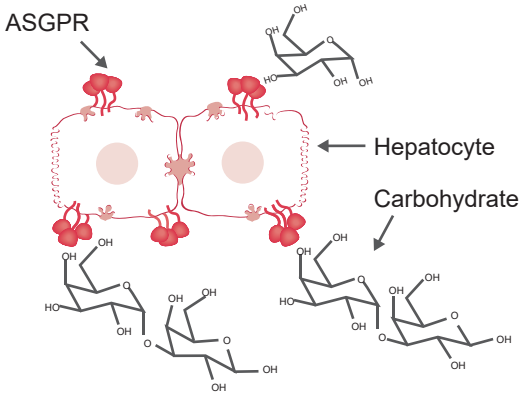
1 Diagnosis

ASGPR

The function of asialogycoprotein receptor (ASGPR) is building bonds with carbohydrates in blood in order to process carbohydrate uptake and metabolization[2].

- ASGPR is primarily expressed on hepatocytes or liver cancer cells, but rarely on extra-hepatic cells.
- The expression on hepatocytes is up to 500,000 ASGPR molecules per hepatocyte.
- Because of its tissue specificity, ASGPR is generally used in hepatocyte clinical research.

Detecting whether circulating tumor cells (CTCs) express ASGPR can identify the origin of cancer cells.



2 Monitoring

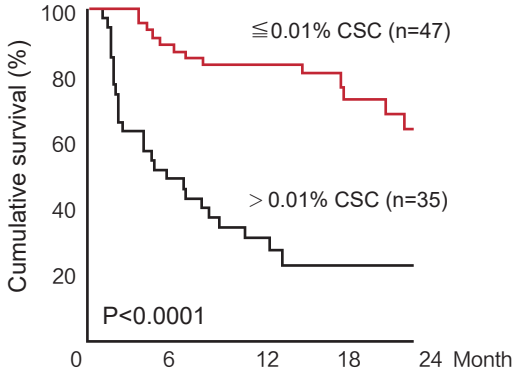
Recurrence and Metastasis

The development of liver cancer is considered as a downstream effect of cirrhosis and fibrosis which are resulted from chronic diseases and viral infection over decades. Even with aggressive treatments such as liver transplantation, chemoembolization or hepatectomy, patients with hepatocellular carcinoma (HCC) still have high risk of recurrence during their life span. Studies have found the relationship between recurrence and cancer stem cells (CSCs), which have displayed drug resistance in different types of tumors. CSCs with epithelial-mesenchymal transition (EMT) phenotypes are more aggressive and could cause recurrence. Additionally, cell surface vimentin (CSV) is considered as a marker on cancer cells with EMT phenotypes. CSV positive CTCs also have stem-like properties and they are statistically associated with recurrence[3].

3 Surgical Guidance

Poor prognosis and massive recurrence remain leading causes of primary HCC mortality. Early HCC has a limited prognosis due to recurrence rates of more than 50% after hepatectomy. The spread of CTCs in blood leads to metastasis initiation and tumor recurrence after surgery. CTCs with stem cell properties might be the origin of cancer recurrence and distant metastasis. Research has indicated that circulating cancer stem cells detected in patients before hepatectomy account for an elevated risk of HCC recurrence three months after surgery[4,5,6].

- CSV can be used in identification of CTCs with stem cell properties.
- By detecting circulating cancer stem cells, the prediction of HCC recurrence after hepatectomy is more accurate.
- Monitoring the number of CTCs and circulating cancer stem cells after surgery reduces the risk of recurrence and metastasis.



If circulating cancer stem cells are detected before hepatectomy, HCC patients have shorter recurrence-free survival (RFS).

Reference

1. World Cancer Research Fund International
2. D'souza, Anisha A., and Padma V. Devarajan. "Asialoglycoprotein receptor mediated hepatocyte targeting—strategies and applications." Journal of Controlled Release 203 (2015): 126-139.
3. Mitra, Abhisek, et al. "Cell - surface Vimentin: A mislocalized protein for isolating csVimentin+ CD133− novel stem - like hepatocellular carcinoma cells expressing EMT markers." International journal of cancer 137.2 (2015): 491-496.
4. Correnti, Margherita, and Chiara Raggi. "Stem-like plasticity and heterogeneity of circulating tumor cells: current status and prospect challenges in liver cancer." Oncotarget 8.4 (2017): 7094.
5. von Felden, Johann, et al. "Circulating tumor cells as liquid biomarker for high HCC recurrence risk after curative liver resection." Oncotarget 8.52 (2017): 89978.
6. Fan, Sheung Tat, et al. "Prediction of posthepatectomy recurrence of hepatocellular carcinoma by circulating cancer stem cells: a prospective study." Annals of surgery 254.4 (2011): 569-576.