

## **New Technologies - Biomarkers and Prediction Models**

### **The role of CTC on prediction of cancer recurrence after transplantation**

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Liver transplantation (LTx) is an effective treatment for hepatocellular carcinoma (HCC), but tumor recurrence after LTx remains a challenge. Therefore, identifying accurate biomarkers to recognize high-risk patients and provide early warning signs of metastasis and recurrence after LTx is paramount importance. Circulating tumor cells (CTCs) are seed cells which potentially lead to early recurrence and metastasis. To investigate the value of CTCs as a predictor of recurrence following LTx in patients with HCC, we included pre- and post-operative CTC from 193 patients with HCC and 38 patients were underwent serial CTC monitoring. At each time point, 5 mL of peripheral blood was collected from each patient and blood sample were analyzed by our self-developed ChimeraX®-i120 platform. To validate the genomic characteristics of CTCs, we performed single-cell whole genome sequencing (WGS). We observed a significant decrease in CTC burden after LTx. Notably, a post-operative CTC count  $\geq 1$  per 5 mL of peripheral blood emerged as a promising biomarker for predicting tumor recurrence after LTx, particularly in patients without detectable CTCs prior to LTx and negative tumor serological biomarkers. This predictive value of a postoperative CTC count  $\geq 1$  per 5 mL of blood remained significant even in patients who did not meet the Milan, University of California San Francisco (UCSF), or Fudan criteria. Moreover, serial post-operative CTC detection may be useful in post-surgical surveillance for HCC recurrence, providing a complementary strategy for early recurrence detection. Overall, our findings suggested that CTC count has the potential to be a useful biomarker to predict post-transplantation recurrence in patients with HCC, and could be employed as a valuable tool to guide LTx management in clinical practice.