An Innovative Platform for Early Detection of Circulating Tumor Cells for Colorectal Cancer

一個創新的平臺以靈敏地偵測循環癌細胞來提早預警大腸直腸癌

Wen-Sy Tsai[1], Ying-Chih Chang[2], Ben Hsieh[3], Hung-Jen Shao[3], Jen-chia Wu[3], Jr.-Ming Lai[3], Mana Javey[3], Rui Mei[3]*

1 Chang Gung Memorial Hospital, #5, Fuxing St, Guishan Dist, Taoyuan, Taiwan 333
2 Academia Sinica Genomics Research Center, No. 128, Section 2, Academia Rd, Nangang Dist, Taipei, Taiwan 115
3 CellMax Life Taiwan, 18F-1, #3, Park St, Nangang Dist, Taipei, Taiwan 115

* Corresponding author: rui@cellmaxlife.com

蔡文司[1], 張瑛芝[2], 謝煌彬[3], 邵宏仁[3], 吳仁家[3], 賴志明[3], Mana Javey[3], 梅蕊[3]*

1長庚紀念醫院大腸直腸肛門外科, 桃園市龜山區復興街5號
2中央研究院基因體研究中心, 台北市南港區研究院路二段 128號
3合度精密生物科技, 台北市115南港區園區街3號18樓之一

* 通訊作者: rui@cellmaxlife.com

Purpose: Mortality of colorectal cancer (CRC) continues to rise in Taiwan despite a trend of gradual decrease in other industrialized countries. The increasing mortality rate is due to the lack of an easy-to-use and highly sensitive screening test to identify pre-cancer or cancer at earlier stages when it is curable. An ideal screening test should be simple and convenient for patients, such as a routine blood draw, since many patients fail to comply with current methods especially those that require a bowel prep or utilize stool-based testing. It has been shown that circulating tumor cells (CTCs) shed from CRC primary tumors from the beginning of tumor development into the bloodstream. However, detecting CTCs from whole blood in the early stages of CRC hasn't been thoroughly demonstrated. Here we present clinical studies, where we utilized a unique, highly sensitive microfluidic chip platform for CTC enumeration for early CRC detection.

Materials & Methods: 2mL peripheral blood was processed using the CellMax microfluidic platform (CMx), which possesses following unique characteristics: 1.Proprietary micro-patterns that maximize cell contacts, 2.Biomimetic surface that minimizes non-specific EpCAM antibody binding to blood cells and promotes dynamic capture of epithelial cells, 3.Gentle CTC release via an air-foam technique without disrupting antibody-antigen bonds. CTCs on immunofluorescent images were enumerated by trained technicians.

Results: Two IRB-approved, blinded clinical studies (N=170, N=304 human subjects) were performed for CRC detection. The CTC enumeration results were then correlated with the disease status evaluated by a standard clinical protocol. Probability of CRC risk was assessed by an age-adjusted regression model. The CMx test sensitivities were 91%/95% for N170/N304 studies based on ROC-curves analyses with accuracies at 89%/93%. Based on disease prevalence, the studies also achieved high PPV and NPV (94%/91%). The area-under-the-curve (AUC) for both studies were 0.92 and 0.95.

Conclusion: A CRC early detection test based on the CMx platform has been clinically validated in two separate blind clinical studies. Its performance (AUCs >0.9) is significantly above the prevailing CRC screening method iFOBT (AUC=0.68). The CMx test provides a non-invasive, easy-to-use and highly sensitive method to screen for CRC at an early stage.