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

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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.