2020「中技社科技獎學金」

2020 CTCI Foundation Science and Technology Scholarship

境外生生活助學金

Living Grant for International Graduate Students

Co-Culturing, Drug Screening, and Digitized Self-Assembled Cell Array (Digi-SACA) Chip for In-Parallel/ In-Situ Image Analysis, and Cell Capture

Venkanagouda S. Goudar, 6th year Ph.D.. Student, Advisor : Prof. Fan-Gang Tseng

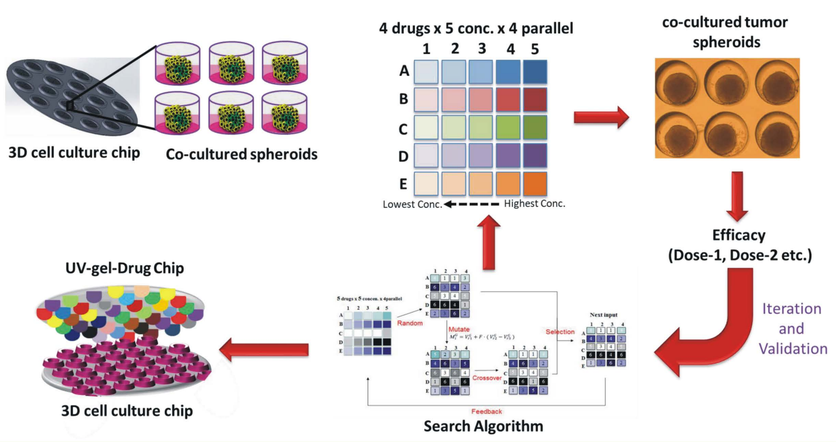
Engineering and System Science Department, National Tsing Hua University, Hsinchu, Taiwan (R.O.C)

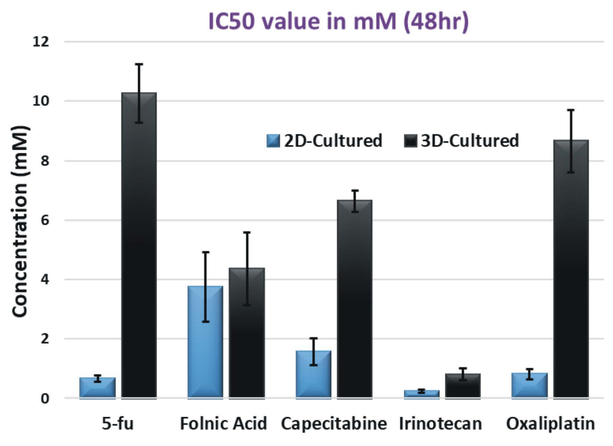
μ-Nano ESS NTHU Taiwan

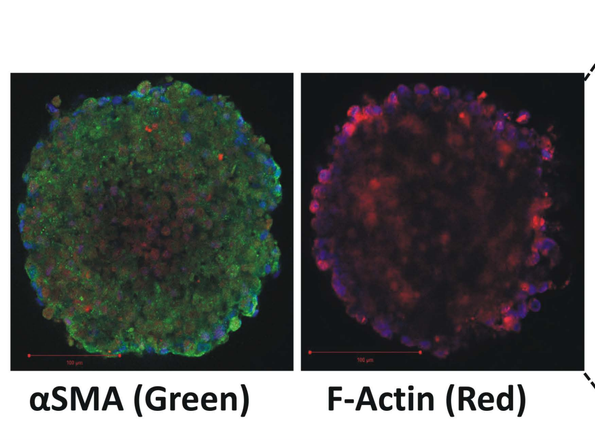
ABSTRACT

Colorectal cancer is the one of the leading cause of cancer related mortality. The development of novel cellular models in vitro shows a promising alternative for animals. Our study introduces a simple photosensitive Poly (ethylene glycol) diacrylate (PEGDA) hydrogel based combinatorial cocktail drug screening platform for high dynamic range testing of 5 different drugs against colon cancer. UV cross linked PEGDA hydrogel drop arrays on Teflon coated glass substrate were employed for rapid and accurate drug dosage selection by search algorithms. Precisely loaded and selected cocktail anticancer drugs are released in-parallel into a 2D and 3D cultured cell chip from PEGDA hydrogel simultaneously. Further, In co-culture we used colon cancer (HCT-116) cells and fibroblast (NIH3T3) cells to study tumor microenvironment. Digi-SACA, an automated workflow to capture CTCs from the whole blood on self assembled cell array chip. The gravity force and lateral driving force based microfluidic chip drive the mononuclear blood cells from 4 ml of samples to form a monolayer without any external fluid control equipment's.

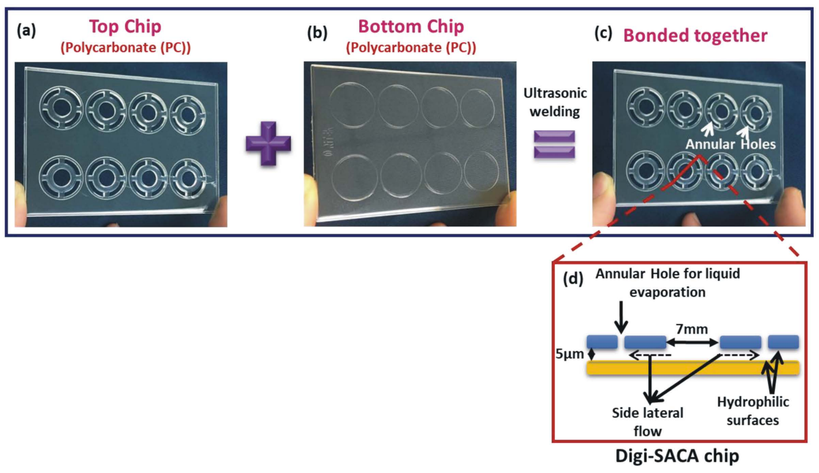
RESULTS AND FOCUS

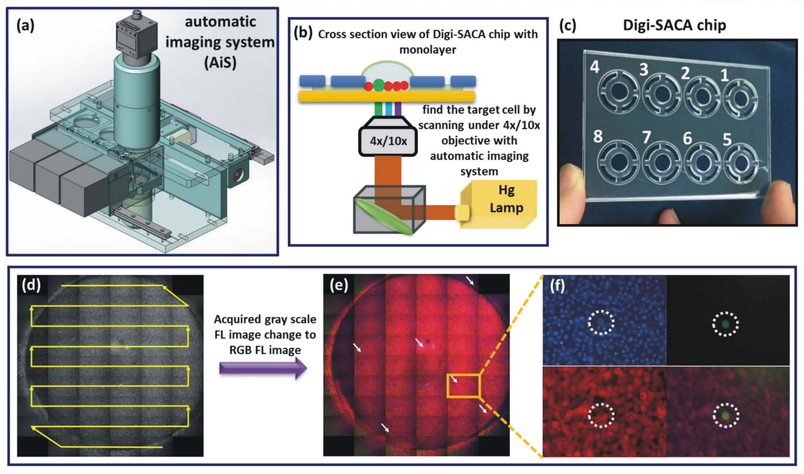


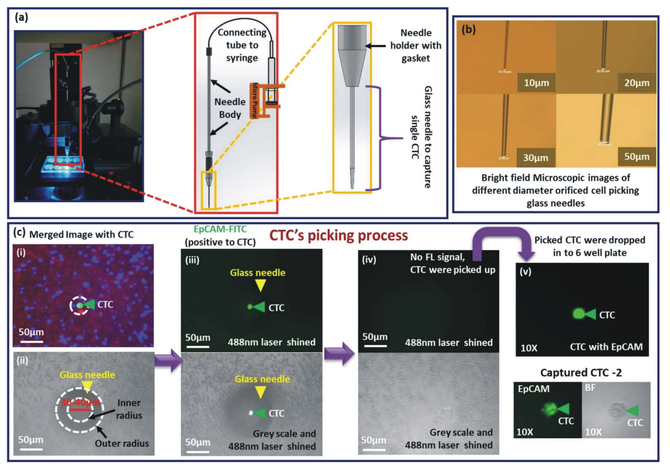




In summary, The current platform provide a better operation of cocktail drug testing in some aspects over the traditional petri dishes ones:
Much less wastage of drugs during the drug testing (Now a days, in conventional way drug usage is 1-10 µl. But, our drug chip containing only 12 nL/drop. So, with this 10 fold of drug can be saved), More accurate drug releasing time/dosage control, Reduce the labouring individual dosage preparation and drug-well registration issues from pipetting process (10-15 mins. Is needed for conventional 96 well experiment. In contrast, 1-2 mins. Is more than enough for our platform), and Capable for programmed delay-time releasing process for each drug.







In Summary, The gravity force and lateral driving force based microfluidic chip drive the mononuclear blood cells from 4 ml of samples to form a monolayer without any external fluid control equipment. The subsequent immunostaining and automated image acquisition, image processing, CTC enumeration and CTC harvest can be completed within 4 hours. Sensitivity of Digi-SACA chip is 1 in ten million leukocytes which is very promising for early detection of the CTC. To isolate the CTCs from whole blood without cellular damage a glass micropipette is employed and delivered on to the cell cultural chip and Tissue culture plate for further analysis.

Research Experience

Basically, I pursued my degrees in Life sciences i. e. in Microbiology as major from Karnataka University (top 3rd in Karnataka) Dharwad, Karnataka, India. There I under took "Isolation and phenotypic characterization of *Staphylococcus aureus* from Bovine mastitis" as the problem for my Master's thesis, for that I obtained 90% of marks. Further, I joined as a project assistant in a multidisciplinary team at the Indian Institute of science (IISc, one of the esteemed institute in India). Here demonstrated the potential of PEMs in the large-scale, roll-to-roll manufacturing of fluorescence enhancements substrates for developing disposable, low-cost devices for fluorescence based diagnostic methods. During these days, **I have authored and co-authored Six peer review journal papers, one International Conference paper, and one Indian patent.** I have come to the most important decision in my career, the choice of university to pursue my PhD studies, have been motivated by my eventual objective of undertaking meaningful research in the field of nano biosensors and lab-on-chip (low cost devices in biomedical engineering). In this direction, **I have joined BioNEMS and Nano/Micro Fluidics Lab. Group in ESS, NTHU, Taiwan.** In last 4 years, I have been focused on in vitro colon cancer research (mimicking in vivo tumor model in in vitro) and building up of bioengineering and Bio-MEMS technologies. The colon cancer circulating tumor cell (CTC's) detection and culturing. **Here, I have authored and co-authored in two SCI peer journal papers *[RSC advances (IF:3.9) and Applied Material and Interfaces (IF:8.097)]* and ten international conferences. In addition, recently we have filed the Taiwan and US patent.**

In Conclusion, This co-cultured spheroid model can be used to investigate crucial factors involved in EMT and to evaluate the potential agents to inhibit stroma-secreted factors and overcome drug resistance and tumor invasion. with present Digi-SACA system, we have detected rare cancer cells from liquid biopsy safely and subjected for further downstream applications, which may be useful in patient stratification and therapeutic selection. However, CTC incubation helps to study molecular characteristics, heterogeneity and drug resistance towards chemotherapies of the different cancers. This efficient, rapid, and cost effective integrated system has potential to be used for regular clinical oncology studies and applications.

References

[1] T. J. Chen, J. K. Wu, Y. C. Chang, C. Y. Fu, T. P. Wang, C. Y. Lin, H. Y Chang, C. C. Chieng, C. Y. Tzeng, F. G. Tseng, High-efficiency rare cell identification on a high-density self-assembled cell arrangement chip. Biomicrofluidics, 8 (2014) 036501. doi:10.1063/1.4874716.

[2] W. Cho, R. Pradhan, H. Y. Chen, Y. H. Weng, H. Y. Chu, F. G. Tseng, C. P. Lin, J. K. Jiang, Author Correction: Rapid Staining of Circulating Tumor Cells in Three-Dimensional Microwell Dialysis (3D-μDialysis) Chip. Scientific Reports, 8 (2018). doi:10.1038/s41598-018-26548-5.

財團法人中技社 CTCI FOUNDATION