Karlsruhe Institute of Technology

IBCS-FMS Functional-Molecular-Systems

Heinrich Heine Universität Düsseldorf

AQUARRAY

Miniaturizing Drug-Induced Differential Gene Expression Analysis for Precision Oncology on Droplet Microarray

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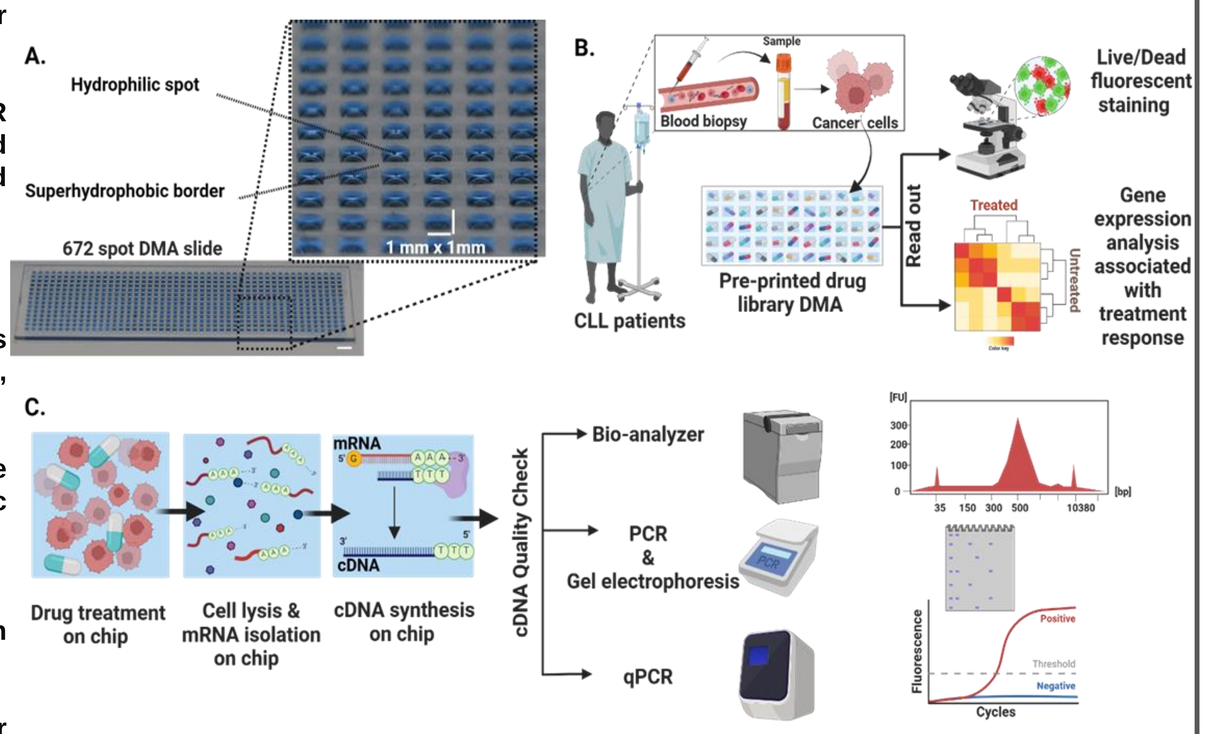
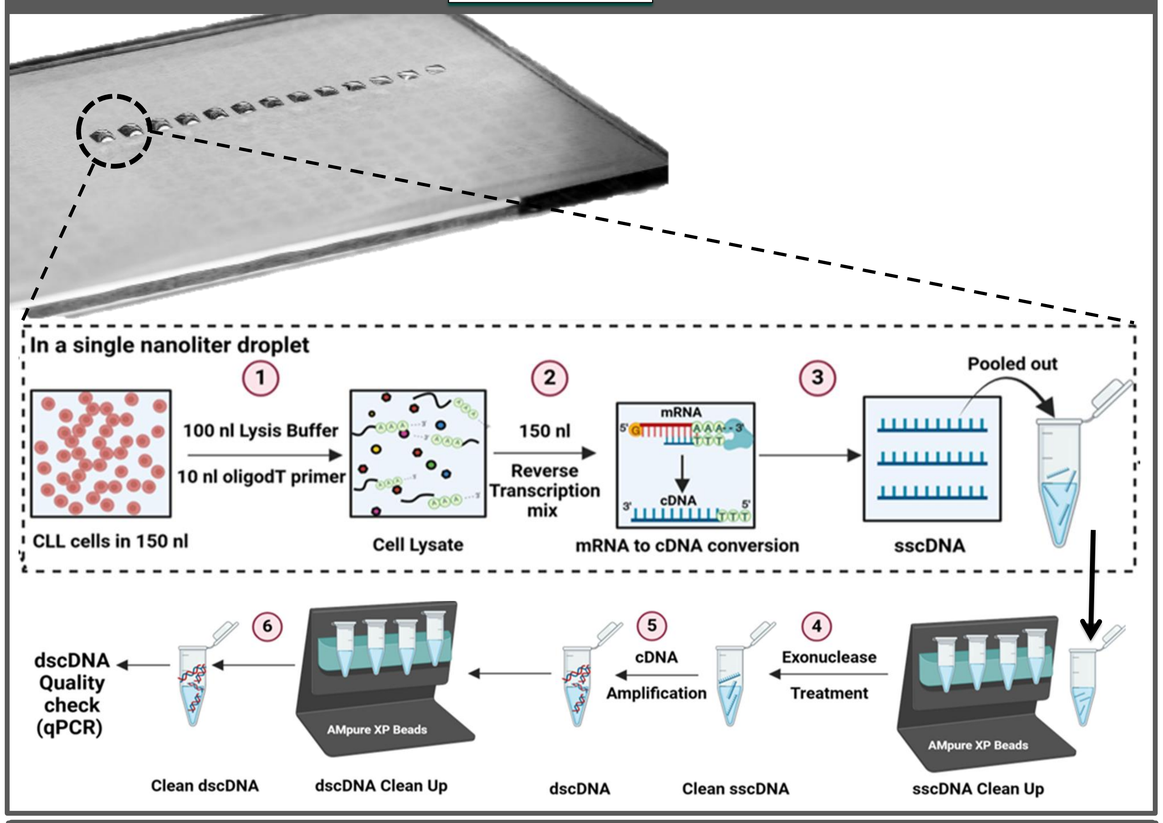
Introduction:

- Understanding the molecular basis of drug-induced phenotypic changes is crucial for unravelling drug mechanisms and enhancing personalized oncology treatment approaches.
- High-throughput differential gene expression analysis (DGEA) using mRNA-seq and RT-PCR is the most commonly employed tool in this field. However, challenges including costly and labor-intensive sample preparation are particularly relevant when dealing with limited patient-derived cells and in high throughput manner.
- Proposed solution: Miniaturized Droplet-Microarray (DMA) platform for efficient DGEA.
- DMA platform consists of hydrophilic spots on a superhydrophobic background and allows for formation of arrays of stable nanoliter droplets for cell culture, drug treatment, microscopy, and sample preparation.
- Our study focuses on demonstration and validation of protocol for high throughput sample preparation and DGEA in both established cell lines and primary patient-derived Chronic Lymphocytic Leukemia (CLL) cells.
- Successful cDNA generation within individual droplets on DMA chip was demonstrated.
- Results show upregulation of SYK and GADD45β genes upon Doxorubicin treatment in both cell lines and patient-derived CLL cells.
- DMA platform offers scalable, cost-effective solution for molecular profiling of tumor responses in personalized oncology treatment.



Method:



Conclusion:

Our study presents a significant advancement in the field of drug-induced DGEA, particularly focusing on addressing the challenges associated with high-throughput screening and limited cell availability, especially in the context of patient-derived cancer cells. By using DMA platform, we have developed a streamlined protocol for DGEA that significantly reduces the required amount of reagents and enables analysis of minute cell. Our work demonstrates the successful implementation of this protocol on both cell lines and primary patient-derived CLL cells, showcasing its adaptability and relevance in clinical settings. Importantly, our findings reveal comparative and correlative results between the DMA platform and conventional methods, highlighting the reliability and accuracy of our approach. Furthermore, we provide evidence of the platform's efficacy by identifying upregulation of key genes, such as SYK and GADD45β, upon treating CLL cells with the Doxorubicin drug. With this our research not only introduces a novel methodology for drug-induced DGEA in a miniaturized format, but also underscores its potential for broader applications in a high throughput manner. Using a 672-DMA drug library for precision oncology ultimately contributes to the advancement of personalized medicine and the improvement of patient outcomes.

References:

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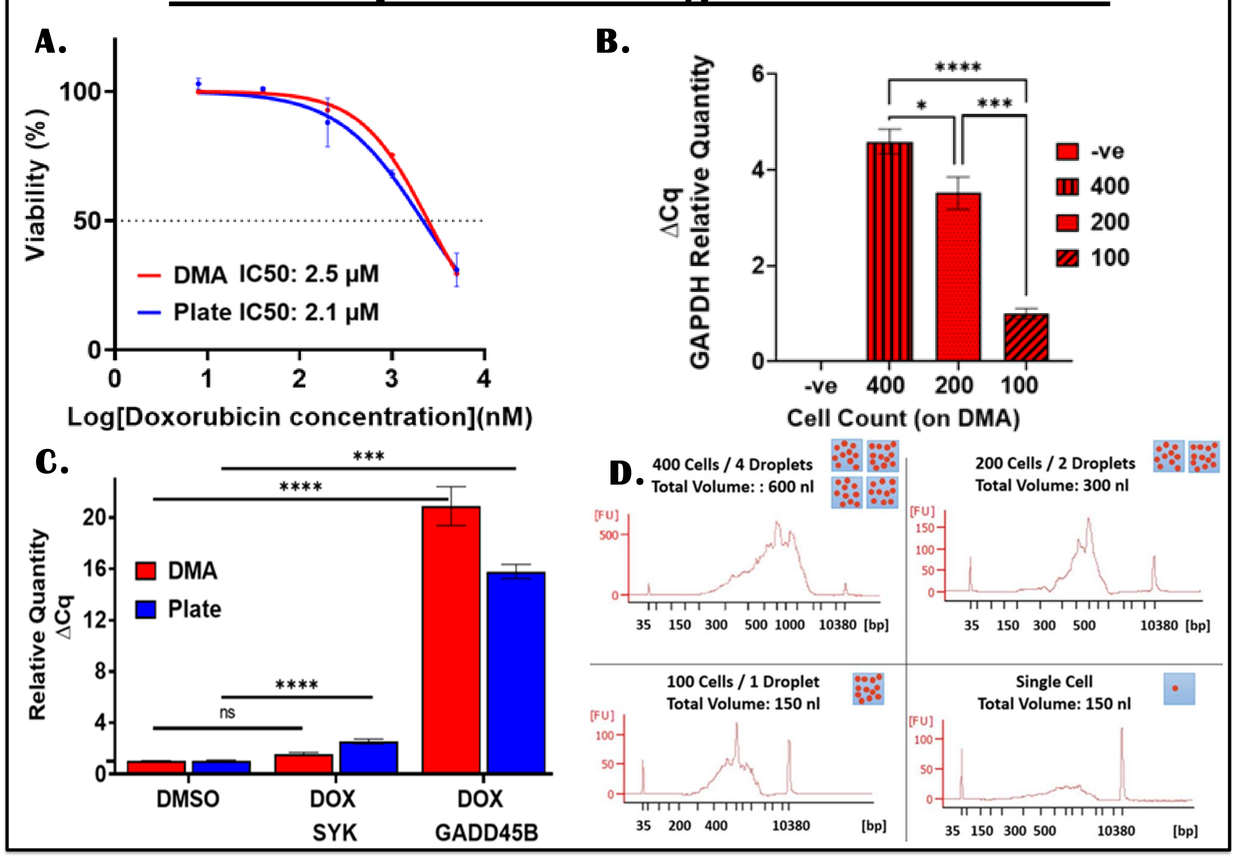
Acknowledgment:

This research was supported by Excellence University Project KIT Future Fields stage 2 "Screening Platform for Personalized Oncology (SPPO)". The authors are grateful to Dr. Dietrich (Heinrich-Heine-University Düsseldorf) for providing CLL patient-derived cells for the study.

The manuscript is ready for publication.

Results:

Protocol optimization using SU-DHL-4 Cell line :



Patient-derived CLL Results on DMA :