Miniaturized high-throughput cell screening of transfection enhancers using droplet microarrays

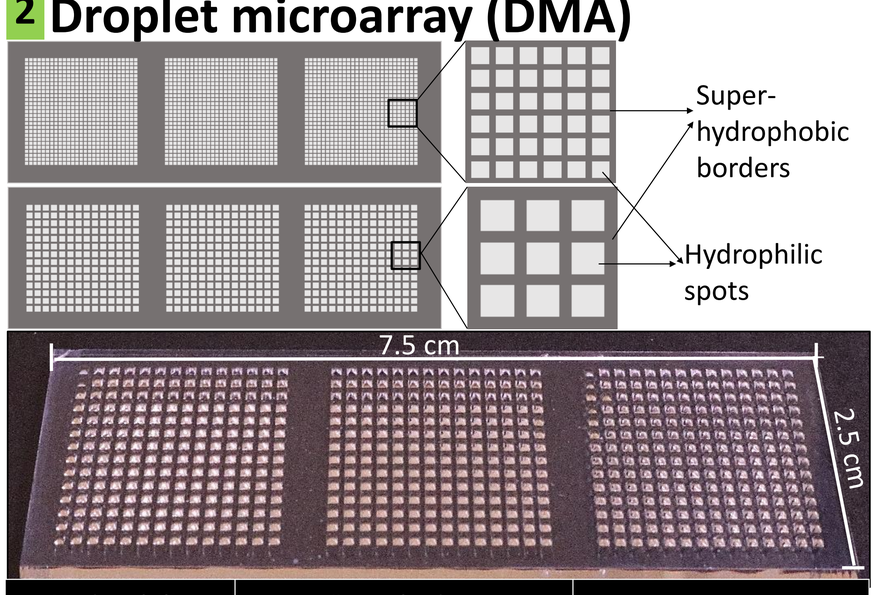
Yanxi Liu[1], Tina Tronser[1], Anna Popova[1], Ravindra Peravali[1], Markus Reischl[2] and Pavel A. Levkin[1,3]*

[1]Karlsruhe Institute of Technology (KIT), Institute of Toxicology and Genetics (ITG), Hermann-von Helmholtz-Platz 1,76344 Eggenstein-Leopoldshafen, Germany
[2]Karlsruhe Institute of Technology (KIT), Institute for Automation and Applied Informatics (IAI), Hermann-von-Helmholz-Platz 1, 76344 Eggenstein-Leopoldshafen, Germany
[3]Karlsruhe Institute of Technology (KIT), Institute of Organic Chemistry, Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany

1 Introduction

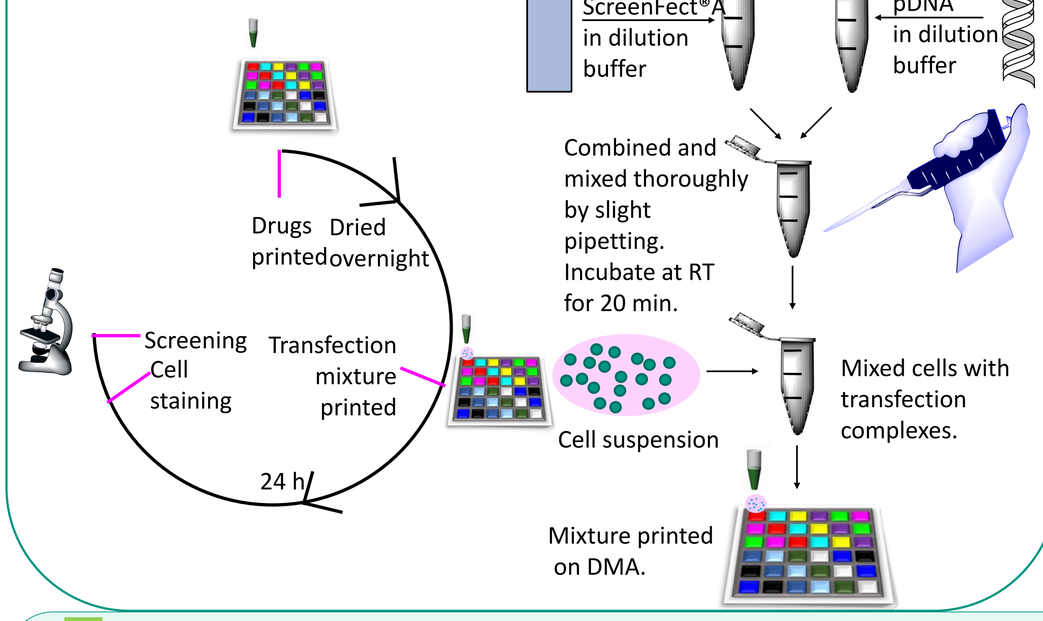
DNA delivery, especially via the non-viral route, has been demonstrated as a powerful research tool for biological research and clinical therapies. However, many transfection reagents have relatively low transfection efficiency due to some unidentified barriers. In this project we hypothesize that by treating CHO-K1 cells with small molecules it is possible to improve transfection efficiency in a safe, efficient and controllable way. In order to identify such transfection enhancer molecules, thousands of structurally diverse molecules are being tested with cells. Current high-throughput screening (HTS) technologies based on microtiter plates cannot be used in such screenings due to prohibitively high costs associated with large volumes required. Our group has recently developed a droplet microarray (DMA) platform based on the superhydrophobic-hydrophilic surfaces, which can be applied to high-throughput screenings of live cells [1-2].

2 Droplet microarray (DMA)

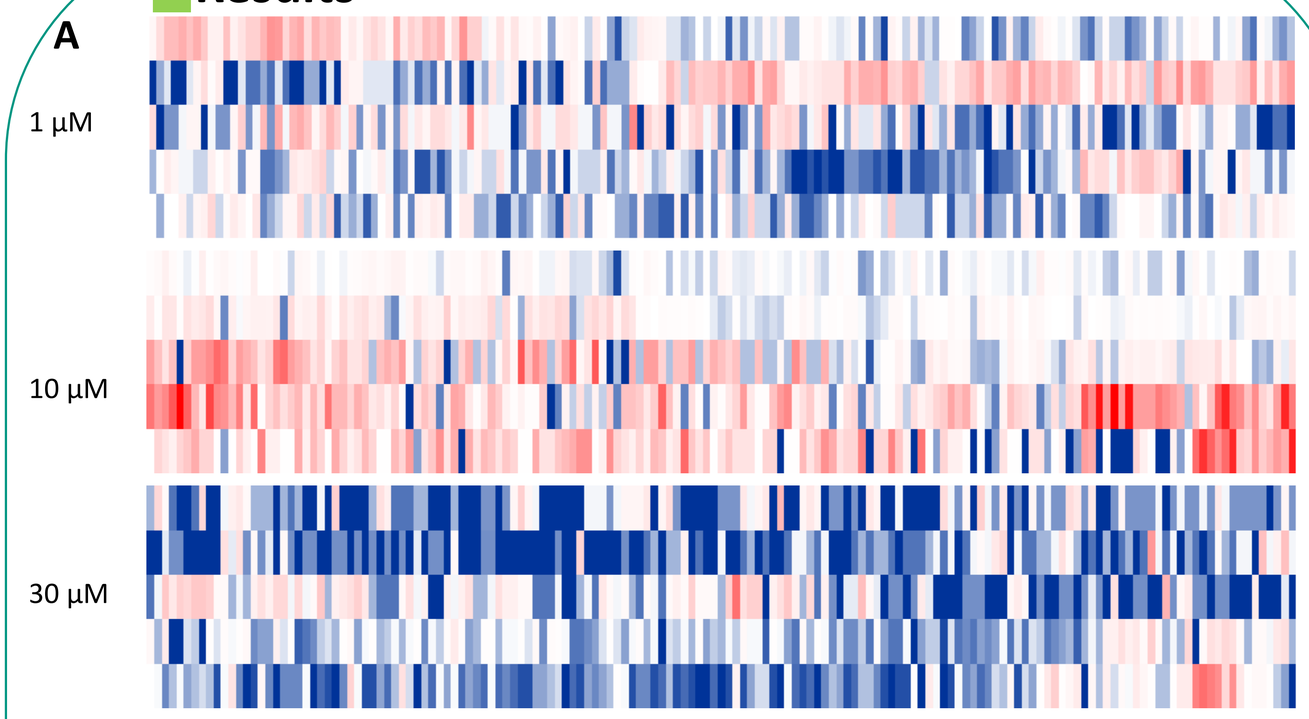


Hydrophilic spots	Superhydro-phobic borders	Spots per array
500 μm	250 μm	27×27×3=2187
1000 μm	500 μm	14×14×3=588

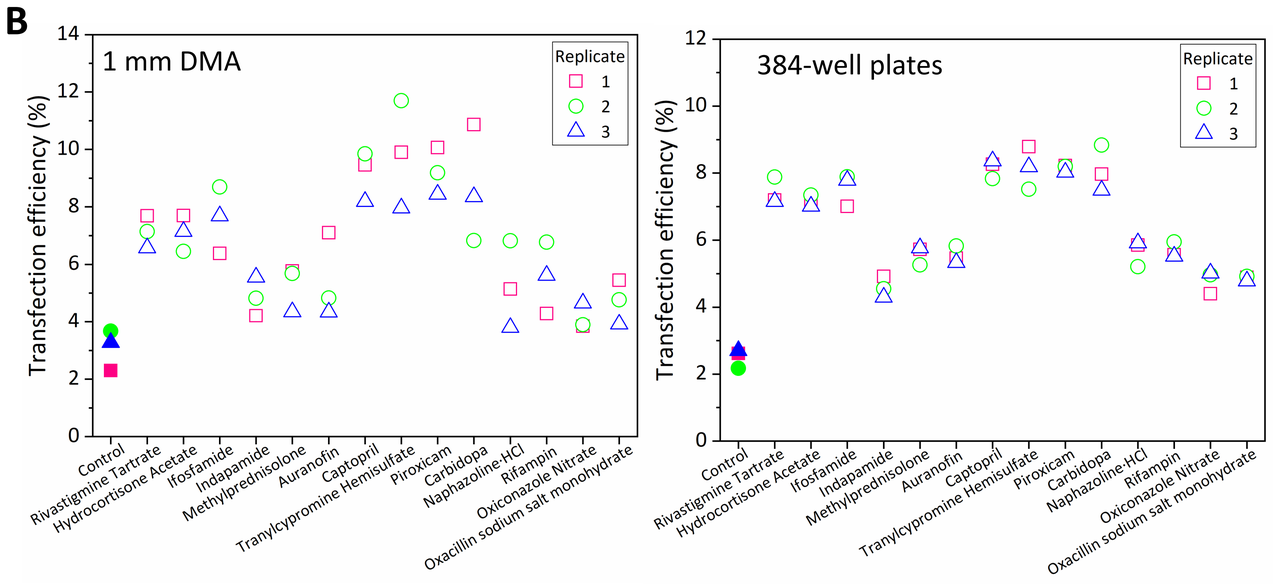
3 Method

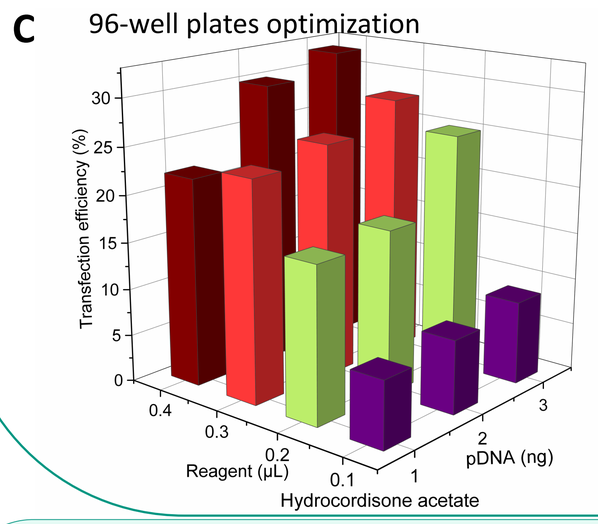


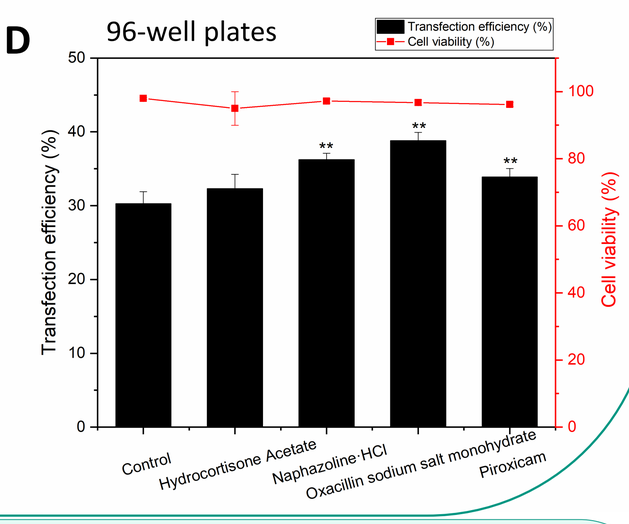
4 Results



Relative transfection enhancement on DMA. Red demonstrated higher transfection efficiency compared to drug free control and blue demonstrated lower transfection.







5 Conclusion

- 774 FDA-approved drugs were screened: 42,000 individual experiments, 20 nL/spot, 200 pmoles of drugs/spot (in total 0.02 moles), 2,500 times smaller than in 384-well plates.
- On DMA: hydrocortisone acetate, naphazoline·HCl, oxacillin sodium salt monohydrate and piroxicam showed 2-4 fold increasing of transfection efficiency.
- Transfection enhancement by four hit compounds can be observed in a optimized condition in 96-well plates.
- The potential of the DMA platform to perform HTS in an economic and time-saving way.

6 References & acknowledgements

1. Popova, Anna A., et al. "Droplet-Array (DA) Sandwich Chip: A Versatile Platform for High-Throughput Cell Screening Based on Superhydrophobic–Superhydrophilic Micropatterning." *Advanced Materials* 27.35 (2015): 5217-5222.
2. Tronser, Tina, et al. "Droplet Microarray Based on Patterned Superhydrophobic Surfaces Prevents Stem Cell Differentiation and Enables High-Throughput Stem Cell Screening." *Advanced healthcare materials* 6.23 (2017): 1700622.

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