# Combining Miniaturized Chemical Synthesis with Biochemical Screening for High-Throughput Drug Development

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Drug Development is an expensive field with a high risk of failure after investing money and time. Yet, there is a need to continue developing new therapeutics to improve our wellbeing. To identify new drug candidates, compounds are synthesized and tested for biological activity. Biochemical assays provide a fast readout for multiple targets, when looking for inhibitors for known enzymes. Testing a broad range of reagents causes high material consumption and time for synthesis of each molecule. In addition, enzymes and substrates are expensive and the total amount is summing up, if 5-10 µL are used for each sample.

Here, droplet microarrays (DMAs) are used to miniaturize and combine all steps of early drug development on one platform using an enzymatic assay to characterize a synthesized library (Figure 1). The platform is based on a microscopic glass slide with special surface wettability. Organic solvents or buffer solutions can be dispensed to omniphilic spots with a diameter of 900 µm to form droplets separated by an omniphobic border. Synthesis optimization, library synthesis and the analysis in a biochemical assay are performed using low volumes from 50 to 100 nL. Up to 840 experiments are performed on one DMA, using 42 µL of reaction solution and 84 µL of buffer solution in total. With small amounts of reagents for each sample, different reaction conditions are tested for different combinations of starting materials, while the high density of reactions allows to cover a large chemical space by combining a range of starting materials.

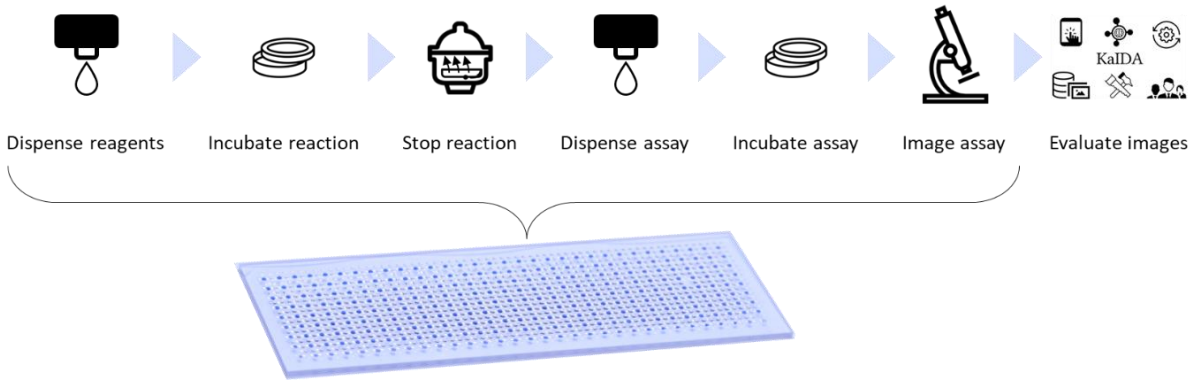


**Figure 1:** Workflow on the droplet microarray

Using DMAs in early-stage drug development, the number of synthesized compounds can be increased covering a larger chemical space, while the amount of reagent is reduced. The biochemical assay can be used as a combined readout for a well working chemical reaction and high biochemical activity and can help to identify promising drug candidates as well as suitable reaction conditions more efficiently.