Merging Femtoliter Fluid Dispensing and Silicon Microsieve Technology

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To gain insight into atomic force microscopy (AFM) based dispensing technology and its applications, a feasibility study was performed on a commercially available AFM system, modified for femtoliter dispensing: the AFM Femtopipette provided by MA3 Solutions. The dispersion of minute amounts (femtoliters) of liquid is enabled by a hollow AFM probe, which can be connected to a pressure controlled liquid reservoir. The study was focused on the dispensing of biofluids onto a microsieve electrode array (µSEA), which acts as a novel readout platform to record in vitro neuronal network activity. To affirm the feasibility of combining bio fluid dispensing with the µSEA platform technology, a technical evaluation of the AFM Femtopipette and a proof-of-principle experiment were performed. The goal of this proof-of-principle was to control the orientation of human neuron outgrowth within a network on the µSEA platform by AFM dispensing fibronectin droplets that act as biological cues. For the first time, we used a commercial hollow AFM probe with an aperture diameter of 300 nm in the AFM Femtopipette. A line of femtoliter-sized droplets of fibronectin was dispensed with the AFM Femtopipette successfully, resulting in droplets with a diameter of 2 to 3 µm on a µSEA substrate. A solution of 50 µg/ml fibronectin in PBS was used as the dispensing liquid. Following fibronectin dispensing on the µSEA, SH-SY5Y human neuronal cells were seeded and cultured overnight. Although no significant response of the cells to the dispensed fibronectin was observed yet, control of droplet dosing was realized. Potentially, patterns of adhesion-specific biocues can be superimposed with the organized seeding of neurons in the microsieve structure of the µSEAs, which can yield unique neurocircuitry. The latter will offer the opportunity to perform advanced brain on a chip studies by applying the AFM Femtopipette in our future research.