

# National Institutes of Health

- Fall 2007—Fall 2011:
- Biological Micro-Electro-Mechanical Systems (Bio-MEMS) for pharmaceutical drug discovery
- Collaborators: Louisiana State University, Tulane University

## *High Throughput Modular Microfluidic Systems for Drug Discovery/Development*

BioMEMS (Biological-MicroElectroMechanical Systems) are seen as the next generation platform for performing many different biologically-based assays in areas such as drug discovery, due to their potential for providing improved performance and low assay cost. However, in reports to date of BioMEMS used in high throughput screening (HTS), the potential improvements in throughput and costs have yet to be realized. This research focuses on developing new highly integrated polymer BioMEMS platforms to achieve advantages in the screening of libraries of drug candidates using parallelized infrared fluorescence assays. As a demonstration of the efficacy of the technology, inhibitors of L1 endonuclease (L1-EN) will be screened. L1-EN induces doublestrand breaks via a TTTT'AA consensus sequence and can contribute to genetic damage responsible for cellular aging, cancer formation or progression. Therefore, discovery of inhibitors of L1-EN, of which there is currently none, could play an important role in minimizing genetic instability during cancer therapies or certain aspects of aging. The platforms to be developed have several enabling technologies that will allow the dissemination of HTS capabilities into the broader drug-discovery community by significantly reducing equipment demands and minimizing consumable costs. The system will consist of a large number of fluidic processors (96-192) configured on a 6" polymer wafer produced using micro- replication. Each fluidic processor will consist of (1) interconnected chip(s) to feed compounds directly from titer plates to the main processor wafer; (2) micromixer that speeds reagent mixing; (3) high surface area bioreactor in which the target is immobilized; and (4) grouped fluidic flow-cells for identifying potential leads using multi-channel fluorescence detection. A substrate of L1-EN will be dual-labeled with new, near-IR fluorescent phthalocyanine dyes, which provide high sensitivity and low background. Parallel fluorescence readout from the fluidic flow cells will be carried out by imaging a group of tightly spaced channels onto a CCD camera. Simulation and modeling will guide the selection of an appropriate readout format and optical configuration. In its finished format, the system will be able to screen -190,000 drug candidates in 24 hr. Fluid handling will be accomplished via microfluidics with minimal robotic intervention, as only a single sample transfer step is required to load the system with drug candidates.