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Spatio-temporal profiling of IgE receptor-mediated pathway using an integrated microfluidic platform

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Traditional biochemical techniques for studying cellular behavior rely on multiple manual steps leading to hard-to-reproduce results, loss of sample, and poor temporal resolution. We are developing a microfluidic platform that integrates and automates the various steps required (e.g., cell culture, cell preparation, challenge, and measurement) to systematically interrogate cellular signaling process at a single cell level with high-sensitivity and minimum reagent consumption. The monolithic serpentine microfluidic chip is about 250 μm in width and 30 μm in depth, which holds up to a thousand cells per chamber. The accessories including pneumatic control units, electronic control valves, digital heaters and optical detectors are assembled into a bench-top, semi-automated platform that maintains cell viability and enables quantitative measurement of signaling events in single cells using high-resolution imaging and on-chip flow cytometry. The platform is being validated using rat basophilic leukemia cells (RBL-2H3), a mast cell model used to understand fundamental mechanisms that lead to allergic responses and asthma. Following on-chip cross-linking of the high-affinity receptor FcεRI for IgE by multivalent antigen, we examined early, intermediate, and late stages of signaling events including protein phosphorylation, calcium mobilization and the release of inflammatory mediators and synthesis and secretion of cytokines, demonstrating the ability of our platform to make quantitative measurements on a cell by cell basis from just a few hundred cells. The new platform enables analysis of the heterogeneity of cellular responses and makes it possible to analyze rare primary cells and tissue samples.