487d Study of Heat Shock Effects on Inflammatory Signaling Using a Microfluidic Living Cell Array

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Cellular physiological states can be characterized by gene expression profiles from DNA microarrays; however, their utility in capturing transient expression dynamics is limited. We have recently developed a tool – the Living Cell Array (LCA) – that uses live cell sensors to profile gene expression dynamics of signaling pathways in a non-invasive and combinatorial manner. We are currently using the LCA for comprehensively characterizing the molecular basis of inflammation in hepatocytes. Hepatocyte reporter cell lines were engineered to monitor different genes involved in inflammatory signaling pathways. Each cell line contains a plasmid with a minimal promoter and a DNA binding response element, which together drives expression of EGFP. Multiple engineered cell lines were seeded in parallel in the LCA for combinatorial analysis of their response to multiple inflammatory stimuli. Here, we present results from the dynamic profiling of 6 regulatory molecules including NFκB, HSP and STAT3 that are involved in the heat shock response and inflammation. The data show a dynamic protection window from heat shock against TNF-α induced apoptosis. We are currently screening anti-inflammatory molecules to correlate their effectiveness to this cytoprotection window. Understanding the mechanism underlying this protection using the LCA allows us to monitor multiple different expression events simultaneously and dynamically in one experiment, leading to a better understanding of gene expression dynamics and the development of novel therapeutic approaches.