High Content Imaging for predictive toxicology: discriminating between adverse and adaptive outcomes

Chairs:
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Presentation #4
Title: Using HCI to analyze cellular tipping points
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Overview: Translating results obtained from high-throughput screening to risk assessment is vital for reducing dependence on animal testing. A challenge to using in vitro data is differentiating adaptive from adverse cellular responses. We studied the effects of hundreds of chemicals in HepG2 cells using high-content imaging (HCI) to measure dose and time-dependent perturbations in p53, JNK, oxidative stress, cytoskeleton, mitochondria, and cell cycle. A novel computational model was developed to describe the dynamic response of the system as cell-state trajectories based on multidimensional HCI datastreams. Cell-state trajectories produced by multiple concentrations chemicals showed resilience of the HepG2 system in many cases, however, we also found "*tipping points*" in system recovery. Further analysis of trajectories identified dose-dependent transitions, or critical points, in system recovery. The critical concentration was generally much lower than the concentration that produced cell loss. We believe that HCI can be used to reconstruct cell state trajectories, and provide insight into adaptation and resilience for *in vitro* systems.