Automated Cell Biology in Drug Discovery: Extracting Biological Information from Images of Cells.

E. Vaisberg

Cytokinetics Inc., 280 East Grand Avenue, South San Francisco, CA 94080, USA

Microscopy, in conjunction with immunohistochemical techniques, has been one of the key methodologies of modern cell biology. The ability of humans to extract information from multiple images of populations of cells is, however, limiting. Automated quantitative image analysis, in conjunction with multivariate statistical techniques, enables extraction of a wealth of information about the physiological states of cell populations. We have developed a platform that allows thorough analysis of a large number of images at high throughput. In addition to identification of cells and extraction of multiple features related to morphological and texture changes in cells and sub-cellular compartments, this system allows classification of cells into multiple biologically relevant subpopulations and measurement of changes in each of these populations independently. Resulting datasets are analyzed with a combination of unsupervised and supervised methods to extract information about the biological mode of action of a variety of drugs and other chemical compounds, even in cases for which the biological assay has little or no apparent relationship to the compounds' molecular mechanisms of action. Thus, a small number of relatively simple immunohistochemical assays allow detection and characterization of broad spectrum of physiological alterations and mechanisms of action. This system has been successfully used in basic research and in various stages of drug discovery. We will present examples of its use in high throughput phenotype based screening of compound libraries, compound profiling, characterization of mechanisms-of-action, and for prediction of adverse effects.