Bevin Engelward, J Biotechnol Biomater 2018, Volume 8
DOI: 10.4172/2155-952X-C4-097

Novel cytotoxicity and broad-spectrum genotoxicity platforms

Bevin Engelward
Massachusetts Institute of Technology, USA

Toxicity and Genotoxicity testing are fundamental to drug safety and drug development. Here, we leverage cell microarray technology to create a robust and highly sensitive cytotoxicity platform and a broad-spectrum genotoxicity platform. Quantification of cell viability is one of the most fundamental and broadly used endpoints in the life sciences. The gold standard is the colony forming assay. While the assay has an impressive dynamic range (over several orders of magnitude), it is relatively low-throughput (10-21days), laborious and requires large dishes/high volumes of media, thus requiring large amounts of test compounds. Microtiter cytotoxicity assay has thus been developed, including the XTT and the CellTiter-Glo assays. The XTT assay suffers from low sensitivity, and the CellTiter-Glo assay is subject to artifacts due to its indirect measure of cell viability. To overcome these limitations, we developed the MicroColonyChip (uCC) assay, which directly measures the ability of cells to divide (like the gold-standard colony forming assay), but with the scale and speed of microtiter assays. Microcolonies grow in a microarray and toxicity is derived using a novel metric, namely the change in the distribution of microcolony sizes. The result is an exquisitely sensitive assay that is robust to artifacts. For genotoxicity testing, the comet assay is a commonly used approach. We recently developed a higher throughput version of the comet assay that exploits a cell microarray. The "CometChip" is more than 1000X faster, far more sensitive and includes automated data analysis. Further, we broadened the spectrum of detectable lesions to include bulky lesions, a class of DNA damaging agents that have the potential to cause cancer. Accurate cytotoxicity and genotoxicity testing hold a central role in drug development. Having reliable and sensitive assays enables identification of untoward deleterious effects of drug candidates, providing immense savings by narrowing the candidate pool. Further, cytotoxicity and genotoxicity assays are also pivotal for the development of novel DNA damaging chemotherapeutics, the mainstay of cancer treatment today.

Biography

Bevin Page Engelward graduated from Yale University in 1988 and from the Harvard School of Public Health in 1996. She continued at Harvard for a one year postdoc, after which she joined the faculty at the Massachusetts Institute of Technology. She is currently Professor of Biological Engineering, Deputy Director of the Center for Environmental Health Sciences, and Director of the MIT Superfund Research Program Center. The main interests of her research is DNA damage and repair, and development of novel technologies relevant to cancer etiology and drug development. In particular, she leads efforts to exploit photolithography to create cell microarrays. Most recently, a high throughput cytotoxicity assay has been developed wherein toxicity is measured by a change in the distribution of microcolony sizes. She has also helped to develop a higher throughput DNA damage assay that is based on the comet assay. The "CometChip" has been further developed to detect diverse classes of DNA damaging agents, including potentially carcinogenic bulky lesions. In addition to studies of cytotoxicity and genotoxicity, her laboratory was the first to develop a mouse model wherein mutations (caused by homologous recombination) can be detected *in situ* via fluorescence.

bevin@mit.edu

Notes: