



○ Innovative Science

○ Breakthrough Therapies

○ Clinical Advances

A Rapid Sensitive Multiparameter Flow Cytometric Assay of Whole Blood for Pharmacodynamic Monitoring of Histone Deacetylase Inhibitors



TEDCO/NIH/NCI Technology Showcase

Min-Jung Lee

September 25, 2007

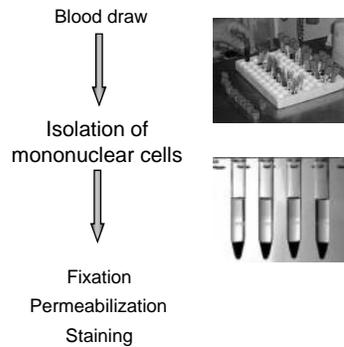


Technology

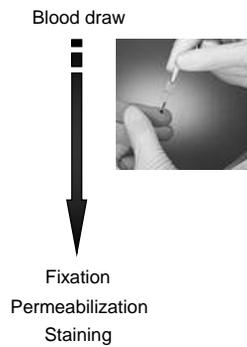


Preparing Patient Blood for Flow Cytometry

Conventional protocol

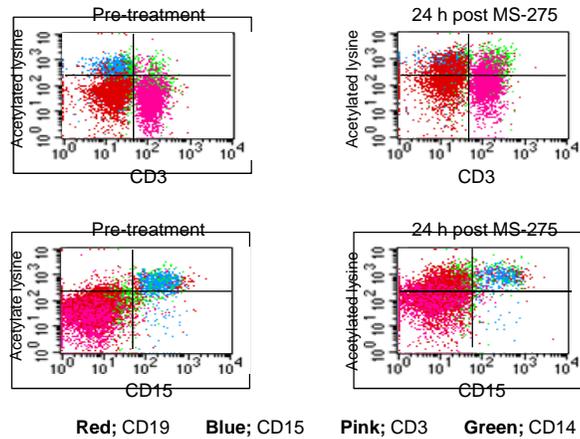


New protocol



Technology

7-parameter flow PD response

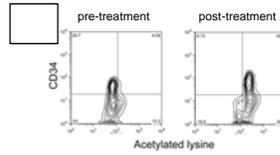


Technology Applications

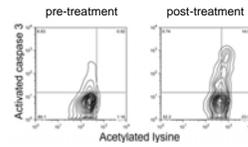
- The technology can be used in multiparameter format to study HDAC inhibitor combination therapy by developing separate PD assays for each drug component
- The technology can be used to examine system effects of HDAC inhibitors by its ability to analyze rare cells in complex mixtures, e.g. the effect of hyperacetylation on angiogenesis, indicated by circulating endothelial cells and circulating endothelial progenitors
- The technology can be used to answer questions important for HDAC inhibitor drug development including:
 - (1) Does hyperacetylation occur preferentially in tumor cells in response to HDACi
 - (2) Does hyperacetylation correlate with induction of apoptosis
 - (3) Does hyperacetylation correlate with regulated gene expression

Technology Applications

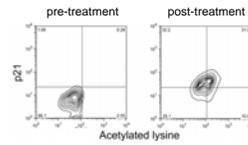
hyperacetylation in tumor cells



hyperacetylation & apoptosis



hyperacetylation & gene expression



Commercial Applications

- A kit for the pharmacodynamic analysis of HDAC inhibitors:

PD assessment from a fingerstick



Collaboration Opportunities

Licensing and CRADA opportunities:

- Use of the PD assay for **development of novel HDAC inhibitors**. Minimal blood volume required enables rodent studies with repeated sampling to determine optimal dose and scheduling
- Use of the PD assay for **development of optimal combination therapy protocols**. Using multiparameter flow cytometry and individualized assays for each drug component, it can be determined readily if drug combinations are antagonistic or cooperative

Contact Information

Jane Trepel

- Medical Oncology Branch, CCR, NCI
- Building 10, Room 12N230
- NIH, Bethesda, MD 20892
- Phone: 301-496-1547
- Fax: 301-402-0172
- E-mail: trepel@helix.nih.gov