C13826: Quantitative Determination of Nucleoside Analogue Drugs in Genomic DNA or RNA

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Technology description

Unmet Need:
Hematologic and epithelial malignancies have been shown to progress by epigenetically silencing genes that code for tumor suppressors, cell cycle regulators or proteins involved in cell-cell interaction. Gene suppression occurs through promoter methylation and modification of histones. Drugs which are able to manipulate promoter methylation and histone modification include DNA methyltransferases (DNMT), as well as inhibitors such as DAC and 5AC. To be effective, these drugs must be incorporated into genomic DNA and RNA. There are, however, multiple factors which affect the degree to which individual drugs can be incorporated. Having a reliable assay for measuring the level of incorporation of these drugs would make it far easier to determine drug doses, drug efficacy, and to help predict toxicity.
Technical Overview:
The efficacy of a DNMT inhibitor is generally measured by its ability to induce demethylation and reactivation of one or a few marker genes. Methylation pattern is a pharmacodynamic effect downstream of DNMTi incorporation, and may vary from person to person. In order to administer the appropriate dose to a particular patient and avoid unnecessary toxicity, it is necessary to predict how patients will respond to these drugs. The JHU inventors developed a novel analytical assay and method that quantifies incorporation of drugs, such DAC, into DNA and RNA. Their quantitative assay has shown great selectivity, precision and accuracy. They have utilized the novel assay to probe the mechanism of action of DAC in preclinical experiments. Their experiments have shown strong correlation between drug incorporation and pharmacodynamics such as l demethylation.
Publication(s):
Anders, et al (2015) Biomed. Chrom.
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