Synthetic Cofactor Analogs of S-Adenosylmethionine as Ligatable Probes of Biological Methylation

Published date: March 14, 2017

Technology description

Methylation of nucleic acids and proteins is necessary for normal development and cellular viability of organisms. The most important cofactor in substrate methylation is S-adenosyl-L-methionine (SAM), with SAM-dependent methylation of nucleic acids and proteins playing a crucial rule in the regulation of gene transcription. UW-Madison researchers have developed compounds and methods for specifically labeling the substrates of SAM-dependent methyltransferases. The methods use SAM analogs that have been modified at the C5` position so the analog is transferred by the methyltransferase to a methylation site in a substrate, such as a peptide or nucleic acid. Once anchored to the substrate, these cofactor analogs allow for the addition of a detectable and/or isolable label. The label may contain various moieties that aid in determining the methylation state of the substrate. The SAM analogs can also be used with nucleic acid methyltransferases to allow for the rapid identification of specific DNA or RNA residues that are typically methylated.
The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing compounds and methods for specifically labeling the substrates of SAM-dependent methyltransferases.

Application area

Determining the methylation state of a gene or gene promoter, such as those involved in imprinting and transcription regulation
May be used therapeutically to block DNA methylation or protein recognition of methylated DNA
Allows labeling of known or unknown methylation sites on DNA or proteins
Enables monitoring of methyltransferase activity without radioactivity
Provides a new approach to cancer treatment
May lead to greater understanding of biological methylation

Advantages

Easily synthesized
Stable for long periods
Amenable to labeling with purification and/or reporter moieties

Institution

Wisconsin Alumni Research Foundation

Inventors

Scott Rajski
Lindsay Comstock
Rachel Weller