Milda Nainyte et al., Organic Chem Curr Res 2017, 6:1(Suppl)
http://dx.doi.org/10.4172/2161-0401.C1.017

Improved AdoMet analogs serve as nucleic acids labels

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Biological methylation is a methyl group transfer from *S*-adenosyl-L-methionine (AdoMet) onto N-, C-, O- or S-nucleophiles in DNA, RNA, proteins or small biomolecules. The reaction is catalyzed by enzymes called AdoMet-dependent methyltransferases (MTases). Recently, DNA methyltransferases have been used for the sequence-specific, covalent labeling of biopolymers. To expand the practical utility of this important enzymatic reaction, cofactors with activated sulfonium-bound side-chains have been produced and can serve as surrogate cofactors for a variety of wild-type and mutant DNA and RNA MTases enabling covalent attachment of these chains to their target sites in DNA, RNA or proteins (the approach named methyltransferase-directed Transfer of activated groups, mTAG). Compounds containing hex-2-yn-1-yl moiety has proved to be efficient alkylating agents for labeling of DNA. Two types of MTase catalyzed labeling of biopolymers are known. First is referred as two-step labeling (Fig 1 (a)). In the first step of this type of labeling, biopolymer is alkylated with functionalized AdoMet and in the second step, a reporter group, such as biotin or fluorophores are attached to a functional group, using suitable chemistries of coupling. This approach of labeling is quite difficult and the chemical hitching does not always proceed at the 100%, but in the second step the variety of reporter groups can be selected and that gives the flexibility for this labeling method. In the second type a biopolymer is labeled by one step (Fig. 1 (b)). The AdoMet analog is designed with the reporter group already attached to the functional group. The whole cofactor is used for alkylation of a target nucleotide of a biopolymer. Herein, we present synthetic procedures for the preparation of S-adenosyl-L-methionine analogs containing various functionalities such as "cleavable" bonds, and variety of reporter groups.

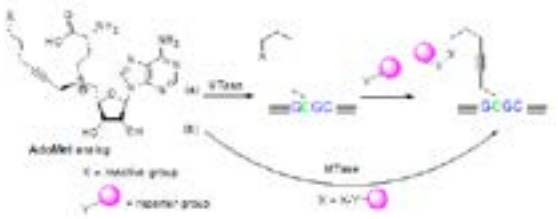

Figure 1: Two types of nucleic acids labeling catalyzed by MTases. (a) Two-step labeling and (b) one-step labeling

Biography

Milda Nainyte has graduated from Vilnius University, obtaining her Master of Science degree in 2015. Currently, she is a PhD student in the group of Professor V Masevičius. Her research interests include organic chemistry, labeling of biopolymers, as well as synthesis and analysis of biologically active compounds.

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