NOVEL FUNCTIONALITYS OF ADOMET ANALOGS FOR NUCLEIC ACIDS LABELING

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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).

To expand the practical utility of this important enzymatic reaction, cofactors containing sulfonium-bound side-chains with various functional or signal groups instead of methyl group were synthesized. These AdoMet analogues serve as cofactors for a variety of wild-type and mutant DNA, RNA or protein 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 sulfonium-bound propargyl moiety has proved to be efficient alkylating agents for labeling of DNA and RNA alike. While DNA MTases even engineered ones like E119H M.HhaI efficiently uses AdoMet analogues with only medium size side-chains, some RNA MTazes e.g. Hen1 can use as cofactors even large signal groups (Biotin, Cy3) possessing AdoMet analogues.

Herein we present latest AdoMet analogues for labeling of nucleic acids.