OLIGONUCLEOTIDE ANALOGUES INCORPORATING 5-AZA-CYSTOSINE THEREIN

ABSTRACT

Oligonucleotide analogues are provided that incorporate 5-aza-cystosine in the oligonucleotide sequence, e.g., in the form of 5-aza-2'-deoxycytidine (decitabine) or 5-aza-cytidine. In particular, oligonucleotide analogues rich in decitabine-de-oxyguanosine islets (DpG and GpD) are provided to target the CpG islets in the human genome, especially in the promoter regions of genes susceptible to aberrant hypermethylation. Such analogues can be used for modulation of DNA methylation, such as effective inhibition of methylation of cytosine at the C-5 position. Methods for synthesizing these oligonucleotide analogues and for modulating nucleic acid methylation are provided. Also provided are phosphoramidite building blocks for synthesizing the oligonucleotide analogues, methods for synthesizing, formulating and administering these compounds or compositions to treat conditions, such as cancer and hematological disorders.

No suitable figure.