5-aza, 5,6-dihydro dC (5,6-DHC) is primarily used to modify oligonucleotides slated for use as tools in cytosine-5-methyltransferase research studies. Cytosine-5-methyltransferases are key enzymes involved in methylation of CpG motifs necessary for epigenetic gene regulation in a wide variety of living organisms (1). Defects in the regulation of this set of enzymes are implicated in cancer (2). The reaction mechanism for these enzymes generates a transient dihydrocytosine as a key intermediate. In an oligo modified with 5-aza, 5,6-dihydro dC, the modification acts as a transition-state mimic, and binds non-covalently to the enzyme’s active site with high affinity. As such, it functions as a potent inhibitor of cytosine-5-methyltransferases, which makes them an excellent tool for structural studies, and an attractive alternative to 5-fluoro-cytosine (3).

References