N3-Methyl deoxycytosine (N3-Me-dC) is a methylated nucleoside base, and is primarily used in the study of DNA damage and repair mechanisms related to alkylation damage. N3-Modified lesions are highly toxic and mutagenic in all three domains of life (prokaryotes, eukaryotes, and archaea) (1). The N3-Me-dC lesion is primarily generated by SN2 alkylating reagents such as methyl methane sulfonate (MMS), dimethylsulfate and methyl halides, which react with the N3 position of cytosine (2,3). In cells, N3-methyl-dC acts as a lethal DNA replication block and is highly mutagenic, being 30% mutagenic in AlkB(-) E. coli (mostly C to T and C to A), and 70% mutagenic in E. coli that is both AlkB(-) and expresses SOS bypass enzymes (4,5). N3-Methyl-dC is restored to dC by a novel direct reversal repair mechanism. This mechanism removes the N3-methyl via oxidative demethylation catalyzed by the AlkB protein, and requiring AlkB-bound non-heme Fe(2+), molecular oxygen, and alpha-ketoglutarate (6,7).

References