DNA Strand Cleavage near a CC Mismatch Directed by a Metalloinsertor

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Abstract:

Reagents for recognition and efficient cleavage of mismatched DNA without photoactivation were designed. They contain a combination of a mismatch-directing metalloinsertor, [Rh(bpy)2(chrysi)]3+ (bpy = 2,2'-bipyridyl, chrysi = 5,6-chrysenequinone diimine), and an oxidative cleavage functionality, [Cu(phen)2]+ (Cu). Both unconjugated (Rh+Cu) and conjugated (Rh-Cu) frameworks of the Rh insertor and Cu were prepared. Compared to Cu, both constructs Rh+Cu and Rh-Cu exhibit efficient site-specific DNA scission only with mismatched DNA, confirmed by experiments with 32P-labeled oligonucleotides. Furthermore, these studies indicate that DNA cleavage occurs near the mismatch in the minor groove and on both strands. Interestingly, the order of reactivity of the three systems with a CC mismatch is Rh+Cu > Rh-Cu > Cu. Rh binding appears to direct Cu reactivity with or without tethering. These results illustrate advantages and disadvantages in bifunctional conjugation.

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