Recognition of Abasic Sites and Single Base Bulges in DNA by a Metalloinsertor

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Biochemistry, 2009, 48 (5), pp 839–849
DOI: 10.1021/bi801885w
Publication Date (Web): January 15, 2009

Abasic sites and single base bulges are thermodynamically destabilizing DNA defects that can lead to cancerous transformations if left unrepaired by the cell. Here we discuss the binding properties with abasic sites and single base bulges of $Rh(bpy)_2(chrysi)^{3+}$, a complex previously shown to bind thermodynamically destabilized mismatch sites via metalloinsertion. Photocleavage experiments show that $Rh(bpy)_2(chrysi)^{3+}$ selectively binds abasic sites with affinities of $1-4 \times 10^6\ M^{-1}$; specific binding is independent of unpaired base identity but is somewhat contingent on sequence context. Single base bulges are also selectively bound and cleaved, but in this case, the association constants are significantly lower ($\sim 10^5\ M^{-1}$), and the binding is dependent on both unpaired base identity and bulge sequence context. A wide variety of evidence, including strand scission asymmetry, binding enantiospecificity, and MALDI-TOF cleavage fragment analysis, suggests that $Rh(bpy)_2(chrysi)^{3+}$ binds abasic sites, like mismatches, through insertion of the bulky chrysi ligand into the base pair stack from the minor groove side and ejection of the unpaired base. At single base bulge sites, a similar, though not identical, metalloinsertion mode is suggested. The recognition of abasic sites and single base bulges with bulky metalloinsertors holds promise for diagnostic and therapeutic applications.

Full text (subscription may be required):
http://dx.doi.org/10.1021/bi801885w