

Detection of 8-hydroxy-2'deoxyadenosine and 8-hydroxy-2'deoxyguanosine by Avidin

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By using x-ray crystallography, isothermal titration calorimetry and fluorescence spectroscopy this study shows that avidin binds the oxidised nucleosides 8-hydroxy-2'deoxyadenosine and 2'deoxyguanosine.

Oxidised bases are endogenously present in the nuclear and mitochondrial DNA of most tissue types. An increase in the cellular concentration of these oxidised bases is an important marker for degenerative diseases such as Alzheimer's disease, aging and for carcinogenesis. Free radical attack, predominately by the $\cdot\text{OH}$ radical, is one of the main causes of oxidative DNA damage.

Avidin is a basic, glycosylated protein found in egg white. Its biological role remains unclear although bacterial growth inhibition and a role in reproduction have been proposed. It is known that avidin binds biotin (vitamin H) with very high affinity (10^{15}M^{-1}). Avidin forms a tetramer with each monomer formed from an 8-stranded anti-parallel β -barrel. With biotin bound, the loop between strands $\beta 3$ and $\beta 4$ is in an ordered conformation. However in the absence of biotin (or, as found in this study, the presence of 2'deoxyguanosine or 8-hydroxy-2'deoxyguanosine) this loop is disordered in the crystal structure. This study shows that 8-hydroxy-2'deoxyadenosine and 2'deoxyguanosine bind in the same hydrophobic pocket as biotin but with an affinity in the μM range. The lower affinity of this interaction correlates with the $\beta 3/\beta 4$ loop remaining disordered in the crystal structure.

It is hoped that these studies will lead to a robust and reliable assay system for the detection of oxidised bases in DNA

Keywords: avidin, 8-hydroxy-2'deoxyadenosine, 8-hydroxy-2'deoxyguanosine