A Computational Study of the Role of Zinc Finger Structures in DNA Repair[1]

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Xeroderma Pigmentosum Group A (XPA) is an essential protein for Nucleotide Excision Repair (NER), whose active site is a zinc finger domain. The zinc dication in this domain can be substituted by carcinogenic metals that inactivate the protein. XPA's role in NER has been disputed in the scientific world, with some believing that it has the capability of DNA repair by itself. XPA's capacity to repair DNA by either absorption of charge or charge pathway disruption was analyzed computationally. Using high-level *ab initio* calculations including solvation effects, computations were run on small systems that model the zinc finger in XPA, for purposes of time and practicality while keeping relatively high accuracy.

According to our calculations, XPA most likely does not absorb charge from DNA damage sites with its intact zinc finger structure. If XPA has a direct role in DNA repair, its most likely function is that of charge pathway disruption. Additionally, our calculations agree with experimental results, which indicate that cadmium substitution leads to a change in oxidation state. Our computations also suggest possible conformational changes in the protein itself, which may play a role in XPA's inactivation.

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