EXPLORATION OF BINDING MODES BETWEEN p300 AND CHETOMIN BY Zn EJECTION USING COMPUTATIONAL METHODS

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Abstract: The analysis of the interaction between the zinc-finger transcription factor p300 and a class of small molecules called epipolythiodioxopiperazines (ETPs) is examined. These compounds appear to unfold p300, which is significant for cancer because if p300 is unfolded it disrupts the HIF pathway; consequently tumor cells’ ability to function under hypoxic conditions becomes limited. Density Functional Theory (DFT) and Docking methods were used to determine structural characteristics, binding modes, and a possible mechanism of action between Chetomin and p300. Our calculations reveal the tetrahedral geometry remains intact after p300 binds with Chetomin, an approximate barrier energy exists of 5 kcal/mol for the binding of Chetomin to p300 and orbital interactions illustrate that stabilization of the p300-Chetomin complex prior to Zinc Ejection is the result of back donation of Zinc electrons to the empty d-orbitals of the Sulfur atoms in Chetomin.

Keywords: p300, Chetomin, HIF, DFT, docking

Acknowledgements: 2010 Summer CRTA-NIH-NCI