The role of the Zn^{2+} in the SAHA inhibition of the Histone deacetylase-like amidohydrolase (FB188 HDAH).

Carlos Kubli-Garfias[1], Cynthia Raquel Trejo-Muñoz[2], Ricardo Vázquez-Ramírez[1]

[1]Universidad Nacional Autónoma de México, Instituto de Investigaciones Biomédicas, Ciudad de México.
[2]Escuela Superior de Medicina, Instituto Politécnico Nacional, Ciudad de México.

The zinc-containing enzyme HDAC-like amidohydrolase (HDAH), identified in the *Bordetella alcaligenes* bacteria, strain FB188, is similar to enzymes that participate in epigenetic mechanisms such as histone modifications. The X-ray crystal structure of FB188 HDAH complexed with the antagonist SAHA (suberoylanilide hydroxamic acid) has been solved (PDB ID: 1ZZ1). The complex crystallizes as a tetramer in the asymmetric unit cell of the crystal yielding a suitable structure to analyze the dynamics of the inhibitory mechanism of SAHA on the enzyme. One invariable Zn^{2+}-SAHA-enzyme coordinate interaction region and one highly variable amide-phenyl group region were clearly observed. Applying computational chemistry techniques and quantum mechanics theory, several physicochemical properties were calculated to characterize the differences among the four monomers of the active site of the amidohydrolase. Notably, in the Zn^{2+}-enzyme coordinate interaction region a consistent network of eight H-bonds occurs among the hydroxamic acid moiety of SAHA and some neighbor polar residues of the catalytic site, making stable the polar environment. The Zinc-ion is surrounded in some extent by the H-bond network. The Zn^{2+} coordination forms an octahedral-symmetrical bi-tetrahedral geometry in the four monomers. The neat octahedral structure, makes the zinc-ion a strong center of union and stability of the enzyme-SAHA complex.