Structural importance of the additional metal binding site in HDAC1

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Histone deacetylases (HDACs) are a family of proteins whose main function is the removal of acetyl groups from lysine residues located on histone and non-histone substrates, which regulates gene transcription and other activities in cells. HDACs are composed by 18 isoforms grouped into four classes, three classes are zinc dependent, class I (HDAC1, 2, 3 and 8), II (HDAC4, 5, 6, 7, 9 and 1) and IV (HDAC11); and the other is NAD+-dependent (class III), so called "sirtuins"1. HDAC1 has been involved in cancer development, thus its inhibition has been emerges as promissory therapeutic strategy, and the acquisition of the structural knowledge could help in the rational drug design in order to achieve selective inhibitors2. HDAC1, possess two additional conserved metal binding sites (Site 1 and Site 2), also described in other isoform, suggesting a possible structural role that affects HDAC catalytical activity. In this work, we performed molecular dynamics (MD) simulation of HDAC1 in order to reveal structural details about these sites and how it affect the interactions with reported HDAC inhibitors. Our results suggest that these sites play an important structural role, since it impacts in the strucrual flexibility of HDCA1 refrelcted in parameters like RMSD and RMSF, it also affects the molecular recognition between he inhibitor and HDAC1.

Biography

Yudibeth Sixto-Lopez is PhD student from Escuela Superior de Medicina of the Instituto Politecnico Nacional, Mexico were she also did her Master. She performed an academic stay in University of Granada, Spain. She has published 6 papers in reputed journals.

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