ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

DIPARTIMENTO
DI FARMACIA
E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno **4 Marzo 2024**
alle ore **15.00**

Prof. David Huffman

Professor of Chemistry from the Western Michigan University
(ospite Prof. Stefano Ciurli)

terrà un seminario dal titolo:

The State of Copper in the Cell

Area tematica: Neuroscience; Nutrition and health;
Metal metabolism/Bioinorganic Chemistry

in presenza:
Aula A, Farmacologia, Via Irnerio 48, Bologna BO

e/o in streaming:
https://teams.microsoft.com/l/meetup-join/19%3aN09c0NIyEssBnF7ObCyDOQwkgDWm1qdd9f7F2nJV9fw1%40thread.tacv2/1631519544944?context=%7b%22Tid%22%3a%22e99647dc-1b08-454a-bf8c-699181b389ab%22%2c%22Oid%22%3a%225a941351-ef41-4aa4-8771-fa50a6d62ca1%22%7d

Colleghi e studenti sono cordialmente invitati

ABSTRACT

Wilson protein (WLNP) is a P1b-type ATPase crucial for pumping Cu(I) into the Golgi or alternately, out of the cell. The six approximately 70-80 amino acid (aa) metal-binding domains (MBDs) in the first 650 aa (N-terminus) of this 1,465 aa protein bind Cu(I) avidly. The first four MBDs are proposed to capture Cu(I) initially, then deliver it to MBDs 5 and 6. Strikingly, when MBD4 is expressed by itself, it is highly resistant to both chemical and thermal denaturation: 50 % of its structure is retained in 5.9 M guanidine hydrochloride (GuHCl) and it has a melting temperature of 78 ˚C. In contrast, when MBDs1-3 are expressed together as a single protein, 50 % of its structure is retained at 2.3 M GuHCl and the melting temperature is 58˚C. Furthermore, the unusual stability of MBD4 is preserved when it is expressed in a protein construct that contains all four MBDs (MBDs1-4). Steady state and time-resolved fluorescence was used to study the effect of disease-causing mutations in MBD5-6. In the picosecond time regime, both Y532H and V536A relaxed much faster than native protein. This highlights the importance role of residues near the interfacial region between domains 5 and 6. Generally, our results suggest a lack of cooperativity between MBDs. The MBDs operate as cellular ligands for Cu(I), but other cellular components that could participate as biological ligands for Cu(I) or Cu(II) will be discussed.

BIOGRAPHICAL SKETCHES

David Huffman grew up in a small farming community in central Illinois and attended college in Greenville, South Carolina. After college he managed a package plant for biological wastewater treatment. A volunteer lecture in a high school class led to an enjoyable year teaching science, math, and history courses. The ease of this experience led him to begin a master's degree in Inorganic Chemistry at Illinois State University under the direction of Dr. Douglax X. West, performing EPR and measuring magnetic moments of metal thiosemicarbazone complexes, later tested as antifungal and anticancer agents. For doctoral studies, he joined the laboratory of Dr. Kenneth S. Suslick at the University of Illinois at Urbana-Champaign, synthesizing new hindered metalloporphyrins and their peptide complexes, using novel 15-mer amphiphilic peptides. He then performed postdoctoral research with Dr. Thomas V. O'Halloran at Northwestern University, first studying copper resistant bacteria, then yeast and human metallochaperones and their molecular targets. Now at Western Michigan University he studies the function of copper transporting proteins.