The Role of the NEET 2Fe-2S Proteins in Controlling the Fe/Fe-S and ROS Homeostasis in Health and Diseases

Abstract:

The seminar will be held in English

The human NEET proteins mitoNEET (mNT) and NAF-1 (encoded by cisd1 and cisd2 genes, respectively) were shown to be important players in the key cellular processes of apoptosis, autophagy, Fe/2Fe-2S and ROS homeostasis. These proteins shown to be important in neurological disorders (e.g. Parkinson and Alzheimer), have a novel ‘NEET fold’ and a unique 3Cyst:1His coordinating structure of their [2Fe-2S] clusters. In a recent studies (experimental and theoretical) we have shown the key role of the cluster coordinating histidine (H87 in mNT and H114 in NAF-1) and the importance of its deprotonated state in the stabilization of the [2Fe-2S] cluster of the NEET proteins; The latter ensure the NEET proteins’ proper fold and prevent the release of the clusters. Controlling the stabilization of the cluster is highly important to prevent Fe/2Fe-2S accumulation which leads to development of reactive oxygen species (ROS) that cause severe damage in cells and organs, e.g. brain. My lecture will describe the unique structure, cellular localization and function of the NEET proteins including the inner mitochondrial most ancient MiNT protein encoded by the cisd3 gene. It will also show the cellular and systemic effects of the absence of NAF-1 (CISD2) NEET protein in the neurological Wolfram Syndrome type 2 (WFS-2) disease, a monogenic autosomal recessive disorder, that is highly abundant in our region.

יום ד' 18.5.18, כיתה 300, 14:00 – 15:00