Abstract 2

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Presentation Preference:
- Paper Presentation

General Subject of Presentation: Stress and Natural Remedies

STRESS CHAPERONE MORTALIN IN MITOCHONDRIAL FUNCTIONS AND AGE-RELATED NEURODEGENERATION

Keywords: Mortalin, stress protein, old age disease

Mortalin/mthsp70/Grp75 is a hsp70 family of stress protein. It was first cloned in our laboratory in 1993 in a cybrid screening system. Over the years, it has emerged as a dynamic protein with several essential functions including chaperoning, intracellular trafficking, mitochondrial import of proteins, cell proliferation and control of ROS production. It is upregulated and contribute to a variety of human cancers. Consistent with this, cancer cells compromised for mortalin enter growth arrest or apoptosis, the two innate checkpoints to carcinogenesis. It is enriched in cancer cells and contributes to carcinogenesis by sequestrating the wild-type p53, a key tumor suppressor protein, in the cytoplasm resulting in the abrogation of its (i) transcriptional activation function and (ii) regulation on centrosome duplication. Most recently, we found that the mortalin-p53 interaction occurs in cancer cells that are stressed physiologically and are frequently associated with p53 mutations. Besides its role in cancer, mortalin is also an important protein for brain that utilizes high energy and hence heavily depends on mitochondrial functions. In a proteomic screening, mortalin was found to be decreased in Parkinson's disease and oxidized in Alzheimer's disease, depicting that the "functional lack of mortalin" is related to these diseases. Knockdown of mortalin homologue in worms (C. elegans) caused abnormalities in mitochondria, premature senescence and progeria like phenotype. Functional significance of mortalin in cancers and neurodegenerative disorders will be discussed.