ISSN 0972-3757
International Journal of
HUMAN GENETICS

PRINT: ISSN 0972-3757 ONLINE: 2456-6360
Int J Hum Genet, 12(3): 151-156 (2012)
DOI: 10.31901/24566330.2012/12.03.04

ATP-ase as a Potential Drug Target for Cancer, Tumor Growth and Cellular Functions

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KEYWORDS ATP-ase. Heat Shock Proteins. Nucleotide Binding Domains. Hsp 70 and Hsp 90, Cell Proliferation. Cell functions

ABSTRACT ATP-ases are a group of enzymes that utilizes ATP hydrolysis, and the subsequent release of energy, to achieve a cellular function. The cellular functions involving ATP-ases are plentiful and diverse including initiation of DNA replication, DNA repair and remodeling, protein folding and chaperoning, protein degradation, intracellular transport, and ion transport. A large number of these enzymes represent attractive drug targets, and drugs targeting ATP-ases, such as proton pump inhibitors. Two families of molecular chaperones, heat shock protein 90 and heat shock protein 70, possess N-terminal nucleotide binding domains (NBD) and require ATP-ase activity for their functions. NBD is charged and highly polar in nature and there is no crystal structure yet published. These two families of ATP-ases represent significant therapeutic targets for the treatment of cancer. The ATP-ase activity of Hsp90, in addition to its various co-chaperones, is essential for maintaining the conformational maturation and stability of key signaling molecules involved in cell proliferation, survival, and transformation. The mechanism by which Hsp90 functions is complex, requiring the sequential binding and dissociation of various co-chaperones as well as the hydrolysis of ATP to drive the chaperone cycle. Inhibition of ATP-ase activity at nucleotide binding site of the Hsp90 leads to prevent tumor growth. Till now, only two antibiotics (ansamycin and geldanamycin) were discovered for inhibiting ATP-ase enzymes. This article discuss about types of ATP-ases, interaction with chaperons and various ATP-ase inhibitors at NBD, chaperones inhibitors and also the possibilities for discovering more antibiotics to inhibit cell proliferations and cellular functions.