

Gene Section

Mini Review

HSPD1 (heat shock 60kDa protein 1)

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Published in Atlas Database: February 2007

Online updated version: <http://AtlasGeneticsOncology.org/Genes/HSPD1ID40888ch2q33.html>

DOI: 10.4267/2042/38438

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Identity

Hugo: HSPD1

Other names: HSP60; HSP65; HuCHA60; Chaperonin 60kDa (CPN60); GROEL; SPG13

Location: 2q33.1

DNA/RNA

Description

The HSP60 gene contains 12 exons and 11 introns and was predicted to span over approximately 13 kb of the genomic DNA. The first exon is non-coding region.

Transcription

Two transcript variants encoding the same protein have been identified for HSP60 gene. This variant which was named HSP60s1 and HSP60s2 (s for short) comparing it to the much longer regular HSP60 gene.

Pseudogene

Twelve pseudogenes located on chromosome 3, 4, 5, 6, 8 and 12 have been associated with HSP60.

Protein

Description

The HSP60 consists of 573 amino acids corresponding to a molecular weight of 61.05 kDa. The HSP60 proteins are ubiquitous abundant proteins of eubacterial genomes and also known as the Chaperonin. The Chaperonins divided into 2 subfamilies:

Type I (HSP60/GROEL) and type II (TCP-1 ring complex).

Type I are present in prokaryotes (eubacteria) and organelles (mitochondria and chloroplast).

Type II are presents in archabacteria and in the eukaryotic cytosol.

HSP60 family have the ring-shape oligomeric protein complex with a large central cavity, and composed of 14 proteins which organized into two 7-protein ring that are stacked on each other like double donut. This structure is reversible dissociate in the presence of Mg²⁺ and ATP, ATPase activity, and have role in folding and assembly of oligomeric protein structures.

Expression

HSP60 expression is ubiquitous in the pre-natal, different organ system, immune system, blood, epithelial tissue and cells.

Localisation

Mainly in the mitochondria, but growing body of evidence showed that there are also extra-mitochondrial such as in the cell surface, peroxisomes and the endoplasmic reticulum.

Function

Assisting mitochondrial protein folding, unfolding, and degradation.

HSP60 also have anti-apoptosis and pro-apoptosis roles.

Homology

Up to now more than 150 homologues of HSP60 sequences with pair-wise similarity extending from 40-100% at the amino acid level. Among them: in rat (*Rattus norvegicus*), pufferfish (*Fugu rubripes*), zebrafish (*Danio rerio*), the nematode *Caenorhabditis elegans* and the mouse (*Mus musculus*).

Mutations

Germinal

Not known in *Homo sapiens*.

Somatic

Hereditary spastic paraplegia (SPG13) is associated with a mutation in the HSP60 gene: The amino acid 72 Valine is changed to Isoleucine.

In Sudden Death Infant Syndrome (SIDS), there are two mutations reported in the coding region of HSP60: N158S and G573A.

Implicated in

Various carcinomas

Disease

HSP60 reported to be over-expressed in exo-cervix cancer, colorectal cancer and prostate carcinoma. But down-regulate its expression in bladder cancer and lung carcinoma.

Prognosis

Controversy; worse prognosis in bladder cancer and acute myeloid leukemia. Others shows favorable prognosis, such as in ovarian cancer, osteo sarcoma and esophageal cancer.

Oncogenesis

The discrepancy of HSP60 expression and/or prognosis during carcinogenesis might be due to its pro- and anti-apoptotic roles in the cancer cells. The cytosolic and organellar forms of HSP60 might explain the anti- and pro-apoptotic roles.

Diseases linked to deficiency of HSP60

Disease

There is a few reports on HSP60 deficiency in human. Studies reported a patient with systemic mitochondrial encephalopathy, which had lower HSP60 concentration than normal person.

Another HSP60 deficient patient presented with congenital lactic acidemia.

In short chain acyl-CoA dehydrogenase, SCAD.

HSP deficiency also reported in fibroblast derived from a patient with a fatal systemic mitochondrial disease leading to deficiency of multiple mitochondrial enzyme and mitochondrial abnormality.

Autoimmune diseases

Note: First clinical trials using HSP60 (peptide 277) has been tested in type-2 diabetes.

Disease

HSP60 have been implicated in T cell activation and cause inflammatory reaction. It involved in the pathogenesis of a number of autoimmune diseases in inflammatory conditions such as type-1 diabetes, juvenile chronic arthritis, atherosclerosis, Cohn disease, autoimmunity in women, rheumatoid arthritis, systemic lupus erythematoses, Sjogren syndrome and mix connective tissue diseases.

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This article should be referenced as such:

Faried A, Faried LS. HSPD1 (heat shock 60kDa protein 1). *Atlas Genet Cytogenet Oncol Haematol.*2007;11(3):194-196.
