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Gene Section
Mini Review

CLTC (clathrin heavy polypeptide)

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Identity

Other names: clathrin heavy chain; KIAAOO34; CLH-17

HGNC (Hugo): CLTC

Location: 17q23

Note
Must not be confused with CLTCL1 (clathrin heavy polypeptide-like 1).

DNA/RNA

Transcription

32 exons, 6111 bp mRNA.

Protein

Description

Clathrin is the major protein constituent of the coat that surrounds organelles (cytoplasmic vesicles) to mediate selective protein transport. Clathrin coats are involved in receptor-mediated endocytosis and intracellular trafficking and recycling of receptors, which accounts for its characteristic punctate cytoplasmic and perinuclear cellular distribution. Structurally, clathrin is a triskelion (three-legged) shaped protein complex that is composed of a trimer of heavy chains (CLTC) each bound to a single light chain. CLTC is a 1675 amino acid residue protein encoded by a gene consisting of 32 exons. Its known domains include a N-terminal

globular domain (residues 1-494) that interacts with adaptor proteins (AP-1, AP-2, b-arrestin), a light chain-binding region (residues 1074-1552), and a trimerization domain (residues 1550-1600) near the C-terminus.

Localisation

Cytoplasmic vesicles.

Function

Mediate endocytosis of transmembrane receptors.

Implicated in

Anaplasic large cell lymphoma (ALCL) with t(2;17)(p23;q23) --> ALK - CLTC

Disease
ALCL are high grade non Hodgkin lymphomas; ALK+ ALCL are ALCL where ALK is involved in a fusion gene; ALK+ ALCL represent 50 to 60 % of ALCL cases (they are CD30+, ALK+); belong to the "cytoplasmic ALK+" subset.

Prognosis
Although presenting as a high grade tumour, a 80% five yr survival is associated with this anomaly.

Hybrid/Mutated gene
5' CLTC - 3' ALK

Abnormal protein
NH2 CLTC - COOH ALK

Inflammatory myofibroblastic tumors with t(2;17)(p23;q23)

Note
In these tumors, the fusion point in CLTC is identical, being at amino acid 1634 (corresponding to the 3' end of exon 31 of CLTC), such that almost all of CLTC is included in the fusion protein, including its

trimerization domain. As a fusion partner, CLTC has been postulated to provide CLTC-ALK with deregulated expression driven by its constitutively activated promoter and constitutive oligomerization of the chimeric protein via the CLTC multimerization domains normally used for clathrin coat assembly. Since ALK is a tyrosine kinase that is activated by cross-phosphorylation following ligand binding, CLTC-ALK-induced oligomerization may result in a constitutively activated ALK tyrosine kinase domain. In this sense, CLTC is likely to function in CLTC-ALK as other prototypical «dimerizing translocation partners" in fusions involving tyrosine kinase genes.

Disease
Rare soft tissue tumour found in children and young adults.

Prognosis
Good prognosis.

Hybrid/Mutated gene
5' CLTC - 3' ALK.

Xp11 renal translocation carcinoma with t(X;17)(p11;q23)

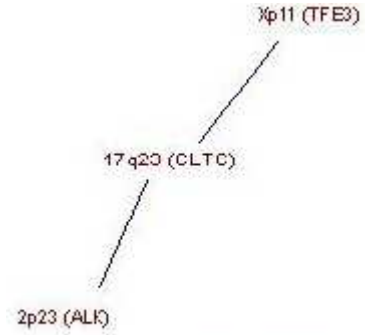
Note
In the CLTC-TFE3 fusion, the fusion point on CLTC is at amino acid 932 (corresponding to the end of exon 17), thereby excluding the CLTC trimerization domain from the predicted fusion protein. As in other TFE3 gene fusions, the nuclear localization and DNA binding domains of TFE3 are retained in CLTC-TFE3. Based on these features and existing data on other TFE3 fusion proteins, CLTC-TFE3 may act as an aberrant transcription factor, with the CLTC promoter driving constitutive expression.

Disease
Rare renal carcinoma (single case report).

Prognosis
Unknown prognosis.

Hybrid/Mutated gene
5' CLTC 3'TFE3.

Breakpoints



CLTC and partners. Editor 06/2005.

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