Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Mini Review

KIF14 (kinesin family member 14)

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Identity

Hugo: KIF14
Other names: KIAA0042; HUMORFW; MGC142302
Location: 1q32.1
Local order: Genes flanking KIF14 at 1q32.1 are (centromeric to telomeric): ZNF281 (zinc finger protein 281), KIF14, DDX59 (DEAD (Asp-Glu-Ala-Asp) box polypeptide 59).

DNA/RNA

Description

Gene spans 68.5 kbp on the minus strand at 1q32.1.

Transcription

One known 6586 base transcript, 30 exons. The KIF14 promoter is bound by p130/ E2F4 under growth arrest conditions; further details of transcriptional regulation are currently lacking.

Protein

Description

KIF14 is a 186 kDa, 1648 aa protein, containing kinesin motor and forkhead-associated (FHA) domains. It is a member of the N-3 family of kinesins. High-throughput studies have identified phosphorylations on Tyr-196; Ser-1200 and Ser-1292, and ubiquitination on Lys-275.

Expression

KIF14 was cloned from an immature myeloid cell line, KG-1. By qRT-PCR, KIF14 is expressed at low levels in normal adult tissues and at higher levels in placenta and fetal tissues; highest expression is in fetal thymus and liver. KIF14 expression varies with the cell cycle, with highest expression at G2-M.

Localisation

In HeLa cells, KIF14 is localized to the cytoplasm during interphase, and becomes tightly localized to the midbody and central spindle during cytokinesis.

Function

KIF14 is a mitotic kinesin motor protein with ATPase activity. It interacts with protein regulator of cytokinesis 1 (PRC1) and is essential for localizing citron kinase to the mitotic spindle. KIF14 knockdown results in failure of cytokinesis, leading to multinucleation and/or apoptosis, but no chromosome segregation defects.

Homology

There are KIF14 orthologs in several mammalian species. The closest Drosophila melanogaster gene, with 40% amino acid identity, is nebbish/tiovivo, encoding Klp38B (kinesin-like protein 38B). Klp38B is a mitotic kinesin that binds to chromatin and microtubules in the formation of the bipolar spindle and attachment of chromosomes to the spindle, and/or acts in cytokinesis.

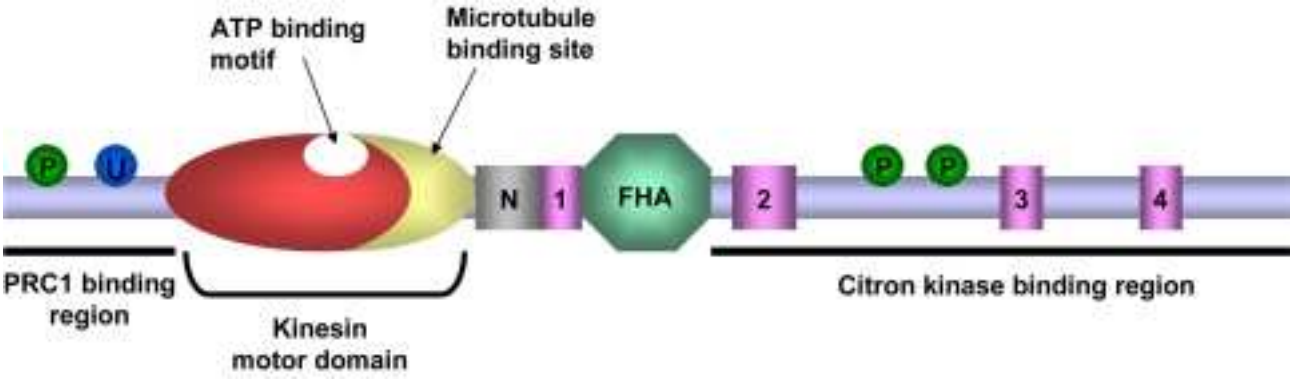
Mutations

Germinal

None yet identified.

Somatic

None yet identified.



Schematic representation of the KIF14 protein (not to scale). KIF14 contains two major effector domains. The first is a highly conserved 274 aa kinesin motor domain containing an ATP-binding site (aa 447-454) which is involved in microtubule-dependent ATPase activity, and a microtubule binding site (aa 455-628) involved in ATP-dependent protein transport. The second is a 67 aa forkhead-associated (FHA) domain (aa 825-891) which has similarity to the SMAD Mad Homology 2 (MH2) domain, and is involved in mediating protein-protein interactions with phosphoproteins, although no such interactions have been documented for KIF14. In addition to the highly conserved N-type neck region (N) adjacent to the motor domain, KIF14 also contains 4 other C-terminal regions predicted to form coiled-coil structures (1-4). Phosphorylation sites have been identified on Tyr-196, Ser-1200 and Ser-1292 (P), and a ubiquitination site identified on Lys-275 (U). The kinesin motor and FHA domains are flanked by a 354 aa N-terminal extension, and a 758 aa C-terminal stalk and tail region. The N-terminal extension is involved in the binding of PRC1 (protein-regulating cytokinesis 1), a protein crucial for the proper formation of the central spindle structure during cytokinesis. Citron kinase has been shown to interact with the C-terminal stalk and tail of KIF14, and this interaction is required for proper localization of KIF14 to the mitotic spindle.

Implicated in

Retinoblastoma

Prognosis

KIF14 mRNA and protein expression is greatly increased in tumors versus normal adult and fetal retina. mRNA expression is higher in older patients' tumors than younger.

Cytogenetics

KIF14 lies in a 'hotspot' of genomic gain at 1q31.3-1q32.1. Low-level genomic gain (3-5 copies) of the gene is observed in 50% of tumors. High-level amplification has been observed in one tumor (along with, but independent of, MYCN amplification).

Breast carcinoma

Prognosis

mRNA expression increases with grade, and is higher in ductal than lobular carcinoma, and in estrogen receptor (ER) negative over ER positive tumors. Expression correlates with proliferation, and overexpression is prognostic for poor overall and disease-free survival.

Cytogenetics

KIF14 lies in a 'hotspot' of genomic gain at 1q31.3-1q32.1. Low-level genomic gain of the gene is observed in 50% of breast cancer cell lines.

Non-small-cell lung carcinoma

Prognosis

mRNA expression decreases with differentiation, and is higher in squamous cell than adenocarcinoma. Overexpression is independently prognostic for poor disease-free survival, and prognostic for poor overall survival.

Oncogenesis

Knockdown of KIF14 decreases proliferation of H1299 NSCLC cells, and decreases their ability to form colonies in soft agar.

Hepatocellular carcinoma

Cytogenetics

Low-level gain of the KIF14 locus is seen in 58% tumors.

To be noted

Note: Numerous microarray studies indexed in Oncomine document overexpression of KIF14 in other cancers, including brain tumors, seminoma, prostate and tongue cancers.

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