Atlas of Genetics and Cytogenetics in Oncology and Haematology

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# Gene Section
## Mini Review

# EIF3C (eukaryotic translation initiation factor 3, subunit C)

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## Identity

**Hugo:** EIF3C
**Other names:** EIF3S8; eIF3-p110; eIF3 subunit p110; p110
**Location:** 16p11.2
**Note:** eIF3c is one of 12 subunit proteins comprising the eukaryotic initiation factor 3 (eIF3) complex.

## DNA/RNA

### Description

The EIF3C gene is composed of 21 exons. No alternative splicing has been reported for eIF3c.
The EIF3C gene is located on chromosome 16p11.2 within an unstable region prone to duplication, and intact duplication of the entire EIF3C gene has been demonstrated in multiple tissue types. One mechanism of eIF3c overexpression, observed in various tumor types, may be gene duplication.

## Protein

### Description

The eIF3c protein is 913 amino acids in length. The eIF3c protein possesses the PCI (proteasome component region) domain within its C-terminal half (also referred to as PINT domain). Domain searching reveals that EIF3c also possesses a winged helix repressor DNA-binding domain overlapping with the PCI domain.

### Expression

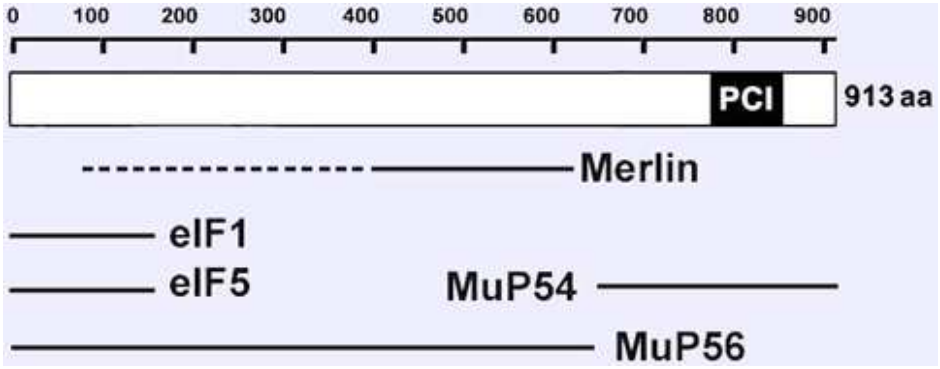
Ubiquitous.

### Localisation

eIF3c is cytoplasmic. There is some evidence of eIF3c occurring in the nucleus consistent with reports of intranuclear protein translation as well as regulation of protein translation by interaction with the COP9 signalosome.

### Function

The initiation of protein translation is a complex sequence of events mediated by the interaction of eIF3 with phosphorylated mTOR. Multiple interactions by eIF3 subsequently take place during the progression of protein translation initiation including the proper positioning of the preinitiation complex on the 40S ribosome mediated by eIF3. EIF3c has a significant role in binding to two AUG recognition factors, eIF1 and eIF5, and these interactions are required for proper AUG scanning by the preinitiation complex.
EIF3c is overexpressed in some tumors including seminomas and meningiomas. EIF3c can also interact with the neurofibromatosis 2 (NF2) tumor suppressor merlin (schwannomin) and merlin can inhibit eIF3c mediated cell proliferation. In meningiomas eIF3c expression was inversely related to merlin expression and was overexpressed in meningiomas that had lost merlin expression. EIF3c overexpression can also transform NIH/3T3 fibroblasts, indicated by decreased doubling times, increased clonogenicity, increased viability, facilitated S-phase entry, attenuated apoptosis, formation of transformed foci, and anchorage-independent growth.




Schematic of the 913 amino acid eIF3c protein with amino acid positions shown and locations of the PCI domain. Also indicated are the known minimal regions in eIF3c required for binding by interacting proteins. These include eIF complexes eIF1 and eIF5, the NF2 tumor suppressor merlin, and murine viral stress mediated inhibitors of protein translation MuP56 and MuP54. For merlin, the broken line indicates a region promoting stronger merlin binding when included. Note that eIF3c also binds the COP9 signalosome protein CSN7 in Arabidopsis, which may mediate inhibition of protein translation.

Murine EIF3c is also a target of inhibitory proteins induced by viral stress. Viral induced MuP56 and MuP54 bind eIF3c in different locations resulting in protein translation inhibition.
In Arabidopsis, eIF3c also interacts with the COP9 signalosome subunit CSN7 in the nucleus. COP9 binding is thought to be associated with downregulated protein translation. eIF3c possesses the PCI domain common among proteasome member proteins and also found in other eIF subunit proteins.

### *Homology*

eIF3c is the homolog to yeast NIP1 (37% identity).

## Mutations

**Note:** No eIF3c mutations have been reported.

## Implicated in

### *Various cancer*

**Oncogenesis**

eIF3c has been noted overexpressed in a subset of testicular tumors ( seminomas ). EIF3c has also been shown overexpressed in meningiomas that have lost expression of the neurofibromatosis 2 tumor suppressor merlin (approximately 50% of sporadic meningiomas).

## To be noted

**Note:** eIF3c is an oncoprotein overexpressed in tumors. As such eIF3c is a potential therapeutic target. eIF3c may be a particularly good therapeutic target for NF2 since all tumors that had lost merlin function had overexpressed eIF3c.

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