FANCC (Fanconi anaemia complementation group C)

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Identity

Other names: FAC
HGNC (Hugo): FANCC
Location: 9q22.3
Local order: next to PTCH and XPAC

DNA/RNA

Description
14 exons; spans 80 kb.

Transcription
mRNA of 2.3, 3.2, and 4.6 kb (alternative splicing in 5', variable 3' untranslated region, exon 13 skipping).

Protein

Description
558 amino acids; 63 kDa.

Expression
Wide, in particular in the bones; high expression in proliferating cells, low in differentiated cells.

Localisation
Cytoplasmic (mostly) and nuclear.

Function
Part of the FA complex with FANCA, FANCE, FANCF, and FANCG; this complex is only found in the nucleus.
FANCA and FANCG form a complex in the cytoplasm, through a N-term FANCA (including the nuclear localization signal) - FANCG interaction; FANCC join the complex; phosphorylation of FANCA would induce its translocation into the nucleus. This FA complex translocates into the nucleus, where FANCE and FANCF are present; FANCE and FANCF join the complex. The FA complex subsequently interacts with FANCD2 by monoubiquitination of FANCD2 during S phase or following DNA damage. Activated (ubiquinated) FANCD2, downstream in the FA pathway, will then interact with other proteins involved in DNA repair, possibly BRCA1; after DNA repair, FANCD2 return to the non-ubiquinated form. FANCC may have multifunctional roles, in addition to its involvement in the FA pathway. FANCC binds to cdc2 (mitotic cyclin-dependent kinase), STAT1, GRP94 (a chaperon protein), NADPH, and a number of other proteins; involved in DNA repair and in suppressing interferon gamma induced cellular apoptosis.
Homology

No known homology.

Mutations

Germinal

Most mutations are found in exon 1, intron 4, and exon 14.

Implicated in

Fanconi anaemia (FA)

FACC is implicated in the FA complementation group C; it represents about 15% of FA cases.

Disease

Fanconi anaemia is a chromosome instability syndrome/cancer prone disease (at risk of leukaemia).

Prognosis

Fanconi anaemia's prognosis is poor; mean survival is 16 years: patients die of bone marrow failure (infections, haemorrhages), leukaemia, or androgen therapy related liver tumours.

It has recently been shown that significant phenotypic differences were found between the various complementation groups. FA group C patients had less somatic abnormalities. However, there is a certain clinical heterogeneity.

Cytogenetics

Spontaneous, chromatid/chromosome breaks; increased rate of breaks compared to control, when induced by breaking agent.

References


This article should be referenced as such: