Gene Section
Mini Review

FANCA (Fanconi anaemia complementation group A)

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Identity

Other names: FACA; FAA; FA1
HGNC (Hugo): FANCA
Location: 16q24.3

DNA/RNA

Description
43 exons spanning 80 kb; 4365 bp open reading frame.

Transcription
5.5 kb mRNA

Protein

Description
1455 amino acids; 163 kDa; 2 nuclear localisation signals (NLS) consensus sequences in N-terminus and a leucine zipper in 1069-1090, none proven to functional as such; FANCA is normally phosphorylated.

Expression
Wide: brain, placenta, testis, tonsils (mRNA); in mice: protein expression predominant in lymphoid organs, testis, ovary.

Localisation
Both cytoplasmic and nuclear.

Function
Part of the FA complex with FANCC, 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 (involving 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.

Homology
No known homology or functional motifs.

Mutations

Germinal
Various nucleotide substitutions, deletions, or insertions have been described. Over 90% of the mutations are private, with about 30% being relatively large deletions. Founder mutations have been described in South Africa.
**Implicated in**

**Fanconi anaemia (FA)**

Fanconi anaemia is implicated in the FA complementation group A; it represents about 70% of FA cases.

**Disease**

Fanconi anaemia is a chromosome instability syndrome/cancer prone disease (at risk of leukemia and squamous cell carcinoma).

**Prognosis**

Fanconi anaemia’s prognosis is poor; mean survival is 20 years: patients die of bone marrow failure (infections, haemorrhages), leukemia, or solid cancer. It has recently been shown that significant phenotypic differences were found between the various complementation groups. In FA group A, patients homozygous for null mutations had an earlier onset of anemia and a higher incidence of leukemia than those with mutations producing an altered protein. Patients homozygous for null mutations in FANCA are high-risk groups with a poor hematologic outcome and should be considered as candidates both for frequent monitoring and early therapeutic intervention.

**Cytogenetics**

Spontaneously enhanced chromatid-type aberrations (breaks, gaps, interchanges; increased rate of breaks compared to control, when induced by specific clastogens known as DNA cross-linking agents (e.g. mitomycin C, diepoxybutane).

Wong JC, Alon N, Norga K, Kruyt FA, Youssoufian H, Buchwald M. Cloning and analysis of the mouse Fanconi anemia group A cDNA and an overlapping penta zinc finger cDNA. Genomics. 2000 Aug 1;67(3):273-83


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