Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

FANCD2 (Fanconi anemia, complementation group D2)

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Published in Atlas Database: June 2002

Online updated version: http://AtlasGeneticsOncology.org/Genes/FAD.html
DOI: 10.4267/2042/37893

This article is an update of: Huret JL. FAD (Fanconi anaemia group D). Atlas Genet Cytogenet Oncol Haematol.1998;2(3):83.

Identity

Other names: FAD; FAD2; FACD; FANCD

HGNC (Hugo): FANCD2

Location: 3p25-26

Local order: not far from XPC, in 3p25.

Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

44 exons; 4356 bp open reading frame; the first exon is non-coding.

Protein

Description

1452 amino acids; 155 kDa (FANCD2-S isoform, for short), and 162 kDa (FANCD2-L isoform, for long) by ubiquitin addition.

Expression

Weak.

Localisation

Nucleus.

Function

The FA complex is comprised of: FANCA, 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 (i.e. FANCD2-L), 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 (FANCD2-S).
FANCD2co-localizes with BRCA1 in DNA damaged-induced loci and in the synaptonemal complex of meotic chromosomes as well.

Homology

Significant homologies can be found with proteins from various species.

Implicated in

Fanconi anaemia (FA)

FANCD2 is implicated in the FA complementation group D, a heterogeneous group, with at least 2 genes: FANCD2, and a yet undiscovered FANCD1. FA complementation group D represents about 1% of FA

cases. In FA complementation group D patients, the FA complex is normal, in contrast with results found in group A, B (with a yet unknown gene), C, E, F, and G patients.

Disease

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

Prognosis

Fanconi anaemia's prognosis is poor; mean survival is 20 years: patients die of bone marrow failure (infections, haemorrhages), leukaemia, or solid cancer.
It has recently been shown that significant phenotypic differences were found between the various complementation groups. Patients from the rare groups FA-D, FA-E, and FA-F had somatic abnormalities more frequently.

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).

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This article should be referenced as such:

Huret JL. FANCD2 (Fanconi anemia, complementation group D2). Atlas Genet Cytogenet Oncol Haematol. 2002; 6(4):275-276.