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Gene Section
Short Communication

YPEL3 (yippee-like 3 (Drosophila))

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Abstract

Short communication on YPEL3, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

HGNC (Hugo): YPEL3

Location: 16p11.2

Local order: From telomere to centromere: MAPK3-GDPD3-LOC101928595-**YPEL3**-TBX6-PPP4C-ALDOA-FAM57B-C16orf92-DOC2A.

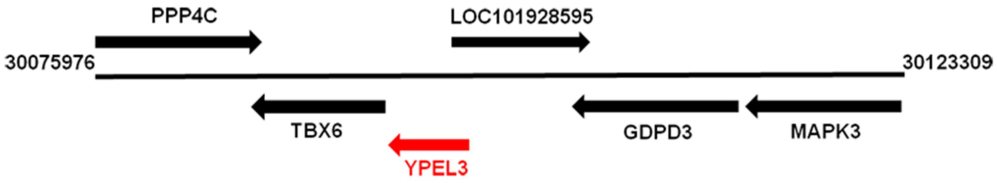
DNA/RNA

Description

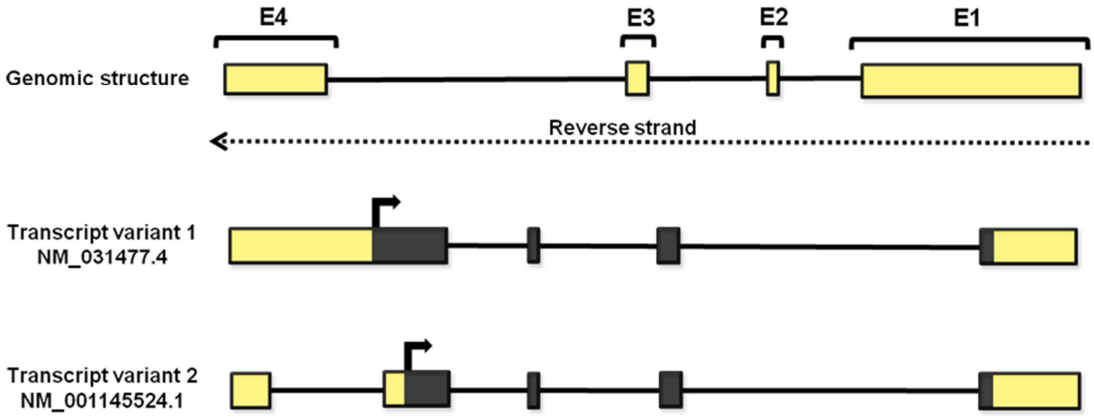
YPEL3 has 4 exons.

Transcription

YPEL3 has 2 transcript variants, resulting from the differential processing of the exon 1.
Transcript variant 1: 1588 bp mRNA (NCBI RefSeq NM_031477.4).
Transcript variant 2: 940 bp mRNA (NCBI RefSeq NM_001145524.1).



Local order of YPEL3 is shown together with leading and subsequent genes on chromosome 16.



Boxes show exons; filled boxes correspond to coding exons, empty boxes indicate noncoding exons. Lines connecting the boxes represent introns. Arrows indicate the translation initiation codon.

Protein

Note
Two transcript variants encode two protein isoforms differing at their amino-termini.
Protein yippee-like 3 isoform 1; 157 aa protein (NCBI RefSeq NP_113665.3).
Protein yippee-like 3 isoform 2; 119 aa protein (NCBI RefSeq NP_001138996.1).

Expression

In human, YPEL3 is expressed in the brain, heart, kidney, lung, pancreas, placenta, skeletal muscle, colon, ovary, leukocyte, prostate, small intestine, spleen, testis, thymus, bone marrow, leukocyte, tonsil, fetal brain, fetal heart, fetal kidney, fetal liver, fetal lung, fetal skeletal muscle, fetal spleen and fetal thymus (Hosono et al., 2004).

Localisation

Immunofluorescence staining with an antibody recognizing Ypel1, 2, 3 and 4 proteins suggests that Ypel1-4 are nuclear proteins. In interphase cells, Ypel1-4 are localized in nucleoli and the centrosome. In the mitotic phase, Ypel1-4 become localized on or close to the mitotic apparatus rather than in the centrosome (Hosono et al., 2004).

Function

Studies show that the expression of YPEL3 gene is up-regulated during DNA damage, reflected as an increase in YPEL protein levels, likely through two functional p53 binding sites present on the YPEL3 gene promoter (Kelley et al., 2010).
When YPEL3 is expressed by a tetracycline inducible system at levels comparable to endogenous mRNA levels detected upon DNA damage, both MCF7 and U2OS cells showed fewer colonies compared to uninduced cells. YPEL3 expressing U2OS and MCF7 cells also showed an increase in cellular senescence as shown by increases β-galactosidase activity and the appearance of foci within the nuclei of senescent cells (SAHF) (Kelley et al., 2010).

Homology

In human, YPEL3 has 4 paralogs; YPEL1, YPEL2, YPEL4 and YPEL5. Ypel3 has 88.2% aminoacid sequence identity with Ypel1; 89.1% with Ypel2; 83.9% with Ypel4 and 43.8% with Ypel5 (Hosono et al., 2004).
Ypel3 is an ortholog of Drosophila Yippee protein and has 45.5% aminoacid sequence identity to Yippee. There are 100 YPEL family genes in 68 species including mammal, bird, amphibia, fish, protochordate, insect, nematode, coelenterate, echinoderm, protozoan, plant, and fungi. In this diverge range of organisms, YPEL family proteins show a high level of homology with many identical residues. Thus, a consensus sequence is deduced as follows: C-X_2-C-X_{19}-G-X_3-L-X_5-N-X_{13}-G-X_8-C-X_2-C-X_4-GWXY-X_{10}-K-X_6-E. In the consensus sequence, the number of non-consensus residues, designated as X, is identical for all species examined (Hosono et al., 2004).

Implicated in

Colon cancer

Note
YPEL3 is found to be down-regulated in 9 commercial colon tumor samples and in 22 patient colon adenocarcinoma (Tuttle et al., 2011).

Ovarian cancer

Note
A significant decrease in YPEL3 mRNA levels was detected in 9 commercial and 30 patient ovarian tumors. In Cp70 ovarian cells, hypermethylation of a CpG island immediately upstream of the YPEL3 promoter is suggested to be the basis for the observed down-regulation (Kelley et al., 2010).

Lung cancer

Note
YPEL3 mRNA is shown to be down-regulated in 8 of 9 commercial lung tumor samples (Tuttle et al., 2011).

Breast cancer

Note
YPEL3 is observed to be down-regulated in breast cancer cell models. Decrease in YPEL3 mRNA levels by siRNA causes an increase in the growth of estrogen receptor positive (ER+) MCF7 cells while YPEL3 over-expression decreases cell number. Moreover, YPEL3 mRNA as well as Ypel protein levels show an increase in MCF7 cells when 17β-estradiol (E2) is withdrawn. In contrast, the addition of E2 at a circulating level (1nM) decreases the expression of YPEL3. The down-regulation of YPEL3 by E2 can be reversed by the addition of selective estrogen receptor modulator, tamoxifen, TMX (Tuttle et al., 2012).
In addition to p53, E2-ER signaling plays a role in the regulation of YPEL3 gene expression based on the observations that the reduction of intracellular ERa levels in MCF7 cells by ERa knockdown increases the expression of YPEL3 gene (Tuttle et al., 2012).
Studies also showed that when grown in the absence of E2, MCF7 cells undergo cellular senescence, whereas the silencing of YPEL3 rescues cells from senescence. Further evidence that YPEL3 is involved in E2-ER mediated cellular senescence was obtained from studies showing that the treatment of MCF7 cells with TMX increases the expression of the YPEL3 gene and that TMX-induced cellular senescence is not observed when

YPEL3 is silenced. Importantly, cellular senescence induced by removal of E2 and/or over-expression of YPEL3 is independent of p53 expression.
Thus, it appears that YPEL3 plays a role in E2-ER signaling dependent cellular growth and senescence in MCF7 cells.
This in turn implies that Ypel3 is a tumor suppressor protein (Tuttle et al., 2012).

References

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