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Gene Section
Review

OOEP (Oocyte expressed protein)

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Abstract

Oocyte expressed protein, alias OOEP, is a component of the subcortical maternal complex (SCMC) that play its roles in oocytes and in early stages of embryogenesis. In this review it is done an insight on its DNA, its RNA, its protein encoded and on the diseases where OOEP is involved.

Keywords
OOEP; Oocyte expressed protein; subcortical maternal complex, SCMC, embryogenesis, zygote

Identity

Other names: C6orf156, Em:AC019205.2, KHDC2, FLOPED, HOEP19, KH homology domain containing 2, KH homology domain-containing protein 2, KH Homology Domain Containing 2, oocyte and embryo protein 19, oocyte expressed protein homolog (dog), oocyte- and embryo-specific protein 19, MOEP19, OEP19

HGNC (Hugo): OOEP

Location: 6q13

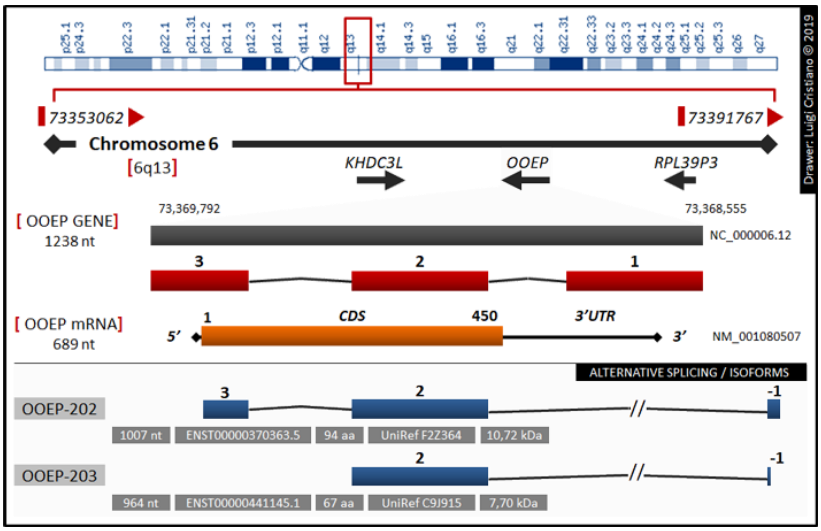

Figure. 1. OOEP gene, transcript and splicing variants/isoforms. The figure shows the locus on chromosome 6 of the OOEP gene, its transcript and its alternative splicing/isoforms (blue). The primary transcript is OOEP-201 mRNA (orange), but also EEF1G-202/203 variants seem be able to codify a protein (reworked from https://www.ncbi.nlm.nih.gov/gene/1937; http://grch37.ensembl.org; www.genecards.org)

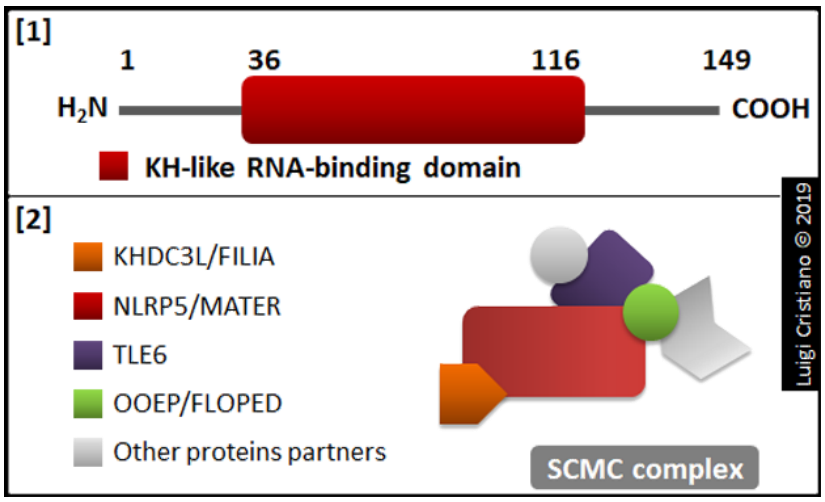

Figure.2 OOEP protein structure. (1) Primary structure of OOEP with emphasis on its main domain; (2) protein-protein interactions in the SCMC complex (reworked from Babbere et al., 2016).

Gene	Gene name	RefSeq	Locus	Location	Start	End	Lenght (nt)
AL499605.1-201	OOEP pseudogene	ENST00000604628.1	1p21.1	Chrom. 1	106544342	106544744	403
AL355333.1	OOEP pseudogene	ENSG00000270234	10p14	Chrom. 10	8724010	8724288	279

Table.1 OOEP pseudogenes (reworked from https://www.ncbi.nlm.nih.gov/gene/1937)

DNA/RNA

Description

OOEP, alias oocyte expressed protein, is a protein coding gene that starts at 73,368,555 nt and ends at 73,369,792nnt from qter and with a length of 1238 bp.
The current reference sequence is NC_000006.12 and contain 3 exons.
It is proximal to KHDC3L (KH domain containing 3 like, subcortical maternal complex member) gene and to RPL39P3 (ribosomal protein L39 pseudogene 3) gene. Around the genomic locus of OOEP take place different promoter or enhancer transcriptional elements.
Two strong elements are closer to the sequence of OOEP gene and are located at +0.3 kb and at -27.3 kb respectively.

Transcription

OOEP transcript is 689 bp long with a reference sequence reported in GeneBank as NM_001080507. It lacks the 5' UTR, the CDS is extended from 1 to 450 nt and the 3' UTR is extended in the remaining part of the sequence, i.e. from 451 to 689 nt.
Splice variants for OOEP was observed: the main reference variant is OOEP (OOEP-201) and the others are OOEP-202 and OOEP-203 (Figure.1). OOEP-202, 1007 nt long, is formed by a fragment of exon 3, by the entire exon 2, it lacks the first exon and gains a forth distant element. OOEP-203, 964 nt long, lacks exons 3 and 1, maintains the entire exon2 and gains another distant element. All three transcript variants encode a protein.

Pseudogene

For OOEP are known some pseudogenes that are classified as processed pseudogenes and are listed in Table 1.

Protein

Description

The canonical sequence for OOEP protein (RefSeq NP_001073976) counts 149 amino acids and has a molecular weight of 17.17 kDa and a theoretical pI of 6.59. Contains a KH-domain, a typical domain of the type I superfamily of RNA binding proteins (Herr et al., 2008), that could mediate RNA transcript regulation during the oogenesis and early embryogenesis stages.
There are known other two isoforms produced by alternative splicing: the isoform OOEP-202 (UniRef, F2Z364) is formed by 94 residues and has a molecular weight of 10.72 kDa, while the isoform OOEP-203 (UniRef, C9J915) counts 67 amino acids and has 7.70 kDa of molecular weight.

Expression

OOEP, as the others factors of the subcortical maternal complex (SCMC), is uniquely expressed in mammalian oocytes and in early embryo (Bebbere et al., 2016). However, some authors found mouse OOEP transcripts also in ovary and thymus, although the protein could not be detected. This may suggest that the transcript remains untranslated (Herr et al.,

2008) and perhaps plays a regulatory function. The human OOEP mRNA was found in pituitary gland (Herr et al., 2008; Carninci and Hayashizaki, 1999), placenta (https://www.ncbi.nlm.nih.gov/gene) and testis, where it was overexpressed (https://www.gtexportal.org/home/gene/ENSG00000203907; https://genevisible.com/tissues/HS/UniProt/A6NGQ2).
It was also found in traces in ovary, endometrium, prostate, salivary gland, adrenal, appendix, brain, digestive system and related organs (esophagus, stomach, duodenum, small intestine, colon, gall bladder, liver, pancreas), lung, fat cells, heart, spleen, thyroid and urinary bladder (from https://www.ncbi. nlm.nih.gov/gene).

Localisation

OOEP is located in the cytoplasm.

Function

OOEP is a component of the subcortical maternal complex (SCMC) that includes at least other three proteins, i.e. KHDC3L (also known as KH domain containing protein 3, FILIA), NLRP5 (also called Maternal Antigen That Embryo Requires, MATER) and TLE6 (also known as Transducin-Like Enhancer of Split 6).
These proteins are expressed by maternal effect genes (MEGs) exclusively in oocytes and early embryos and are physically bound together in the SCMC complex.
Also only a mutation on one of them, such as TLE6, induces instability of the complex and may be a cause of human female infertility and earliest human embryonic lethality (Bebbere et al., 2016; Alazami et al., 2015; Zhu et al., 2015; Bebbere et al., 2014).
OOEP plays an essential role for zygote progression beyond the first embryonic cell divisions (Bebbere et al., 2014) and it is hypotized that it could play a role in the formation/stabilization of the oocyte cytoskeleton, called oocyte cytoplasmic lattices (CPLs) and also it could be involved in the organization and regulation of the translational machinery through the interaction between SCMC complex with other protein and/or protein complexes (Bebbere et al., 2016; Tashiro et al., 2010).
In addition, OOEP could be involved in RNA degradation during oocyte maturation and in the early stages of embryogenesis (Wang et al., 2012) and it could be directly or indirectly involved in the binding of the mRNAs and in their correct subcellular localization (Bebbere et al., 2016). In mouse oocytes was found that OOEP may participate in the regulation of genome stability (He et al., 2018), but it is not confirmed in humans yet.

Homology

OOEP is highly and abundant conserved in many species and its homology between the species is reported in Table.2

Organism	Species	Symbol	DNA Similarity (%)	PROT Similarity (%)
Human	H.sapiens	OOEP	100	100
Chimpanzee	P.troglodytes	OOEP	99.3	99.3
Macaco	M.mulatta	OOEP	96.0	95.3
Wolf	C.lupus	OOEP	78.7	71.8
Cattle	B.taurus	OOEP	77.4	68.6
Mouse	M.musculus	OOEP	68.2	54.6

Table.2 OOEP homology (reworked from https://www.ncbi.nlm.nih.gov/homologene?)

Mutations

The genomic alterations observed include the formation of novel fusion genes as EEF1G/OOEP (acute lymphoblastic leukemia/lymphoblastic lymphoma), EXOC2/OOEP (bladder transitional cell carcinoma), FAM19A2/OOEP (breast adenocarcinoma), KHDC1/OOEP, OOEP/ EIF3A, RERE/OOEP (prostate adenocarcinoma) and SENP6/OOEP (prostate adenocarcinoma) (http://atlasgeneticsoncology.org//Bands/6q13.html) , however there are no experimental data yet to understand the impact on cellular behaviour and so the implications in cancer of these fusion genes.

Implicated in

Top note
OOEP is a maternal-effect gene that is expressed in zygote and in early stages of embryo development. It is linked with female infertility, however there is some evidence of its involvement in cancers. We review the diseases in which OOEP gene showed overexpression, upregulation or aberrant fusion with other genes. Anyhow some authors found a downregulation of OOEP in ovarian cancer patient samples (Veskimäe et al., 2018), in colon cancer (Penrose et al., 2019) and in prostate cancer cells (Lu et al., 2015).

t(6;11)(q13;q12) EEF1G/OOEP

Disease
Acute lymphoblastic leukemia/lymphoblastic lymphoma (Atak et al, 2013)

Hybrid/Mutated gene
T-cell acute lymphoblastic leukemia (T-ALL) affects about 15% of pediatric patients and 25% of adult patients of total ALL cases. It is an agressive tumor characterized by the accumulation of multiple genomic mutations and chromosomal aberrations, such as frequently chromosomal translocations, that

bring to the formation of many in-frame fusion genes encoding the respective chimeric and oncogenic proteins (Atak et al., 2013). Among all these chromosomal aberrations it was found also the fusion gene 5' EEF1G / 3' OOEP deriving by the genomic translocation and fusion of a part of OOEP gene, situated on chromosome 6, with a portion of EEF1G gene, located on chromosome 11. This leads to the know but not still well-characterized translocation t(6;11)(q13;q12) EEF1G/OOEP.

Human female infertility/ early embryo lethality

Disease

Aberrant expression of SCMC members, such as OOEP, could compromise the fertility in women but also could be linked to abnormalities in preimplantation embryo development and in early lethality of the human embryos and so cover a significant role both in female inability to get pregnant and in failure of the development of implanted embryo after in vitro reproductive assistance procedures (Bebbere et al., 2016; Alazami et al., 2015; Zhu et al., 2015; Zhang et al., 2008).

To effort these considerations, an experiment in mouse demonstrated that a lack of OOEP gene (OOEP -/- knockout mice) causes complete infertility and disorganization/abnormalities in oocyte cytoplasmic lattices (CPLs). However, Ooep-null mice females grew to adulthood and showed no apparent abnormalities except the infertility (Tashiro et al., 2010).

Osteosarcoma

Some authors found OOEP gene upregulated in osteosarcoma cells (Li et al., 2017).

Small cell lung carcinoma

The expression of OOEP is increased in small cell lung carcinoma (Jiang et al., 2016).

Testis cancer

Some databases reported that the expression of OOEP is increased in testis cancer (https://www.proteinatlas.org/ENSG00000203907-OOEP/pathology; https://genevisible.com/cancers/HS/UniProt/A6NGQ2) but is not clear if also protein can be displayed.

Thyroid cancer

One database reported high levels for the presence of OOEP protein in thyroid cancer although its expression level in this cancer type was reported to be lower (https://www.proteinatlas.org/ENSG00000203907-OOEP/pathology).

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