**OOEP (Oocyte expressed protein)**

Luigi Cristiano

Aesthetic and medical biotechnologies research unit, Prestige, Terranuova Bracciolini, Italy; prestige.infoemed@gmail.com

Published in Atlas Database: March 2019

Online updated version: http://AtlasGeneticsOncology.org/Genes/OOEPID71121ch6q13.html

Printable original version: http://documents.revues.inist.fr/bitstream/handle/2042/70677/03-2019-OOEPID71121ch6q13.pdf

DOI: 10.4267/2042/70677

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence. © 2020 Atlas of Genetics and Cytogenetics in Oncology and Haematology

**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)
**OOEP** (Oocyte expressed protein)

Cristiano L

Atlas Genet Cytogenet Oncol Haematol. 2020; 24(3)

**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 | ENST0000064628.1 | 1p21.1     | Chrom. 1    | 106544342   | 10654744    | 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 73,369,792 nt 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 exon 2 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 pl of 6.59. Contains a KH-domain, a typical domain of the type I superfamly 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.,
and perhaps plays a regulatory function. The human OOEP mRNA was found in pituitary gland (Herr et al., 2008; Carminci 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 (Bebebre et al., 2016; Alazami et al., 2015; Zhu et al., 2015; Bebebere et al., 2014). OOEP plays an essential role for zygote progression beyond the first embryonic cell divisions (Bebebere et al., 2014) and it is hypothized that it could play a role in the formation/stabilization of the oocyte cytoskeleton, called oocyte cytoplasmatic 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 (Bebebere 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 (Bebebere 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               |

**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, OOEPEIF3A, 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’ EEFFIG / 3’ OOEP derived by the genomic translocation and fusion of a part of OOEP gene, situated on chromosome 6, with a portion of EEFFIG gene, located on chromosome 11. This leads to the know but not still well-characterized translocation (6;11)(q13;q12) EEFFIG/ 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 embryo 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.proteinnatlas.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.proteinnatlas.org/ENSG00000203907-OOEP/pathology).

**References**

Alazami AM, Awad SM, Coskun S, Al-Hassan S, Hijazi H, Abdulwahab FM, Poizat C, Akiruya FS. TLE6 mutation causes the earliest known human embryonic lethality. Genome Biol. 2015 Nov 5;16:240

Atak ZK, Gianfelici V, Hulselmans G, De Keersmaecker K, Devasia AG, Geerdens E, Mentens N, Chiaretti S, Durinck K, Uyttebroeck A, Vandenberghe P, Wlodarska I, Cloos J, Foá R, Speleman F, Coels J, Aerts S. Comprehensive analysis of transcriptome variation uncovers known and novel driver events in T-cell acute lymphoblastic leukemia. PLoS Genet. 2013;9(12):e1003997

Bebbere D, Ariu F, Bogliolo L, Masala L, Murrone O, Fattorini M, Falchi L, Ledda S. Expression of maternally derived KHDC3, NLRPS5, OOEP and TLE6 is associated with oocyte developmental competence in the ovine species. BMC Dev Biol. 2014 Nov 25;14:40

Bebbere D, Masala L, Albertini DF, Ledda S. The subcortical maternal complex: multiple functions for one biological structure? J Assist Reprod Genet. 2016 Nov;33(11):1431-1438

Carrinci P, Hayashizaki Y. High-efficiency full-length cDNA cloning. Methods Enzymol. 1999;303:303-19-44

He DJ, Wang L, Zhang ZB, Guo K, Li L, Xie X, Cui QH, Zheng P. Maternal gene Ooep may participate in homologous recombination-mediated DNA double-strand break repair in mouse oocytes Zool Res 2018 Nov 13;39(6):387-395

Herr JC, Cherthin O, Digilio L, Jha KN, Vemuganti S, Flickinger CJ. Distribution of RNA binding protein MOEP19 in the oocyte cortex and early embryo indicates pre-patterning related to blastomere polarity and trophoderm specification Dev Biol 2008 Feb 15;314(2):300-316

Jiang L, Huang J, Higgs BW, Hu Z, Xiao Z, Yao X, Conley S, Zhong H, Liu Z, Brohawn P, Shen D, Wu S, Ge X, Jiang Y, Zhao Y, Lou Y, Morehouse C, Zhu W, Sebastian Y, Czapiga M, Oganesyan V, Fu H, Niu Y, Zhang W, Streicher K, Tice D, Zhao H, Zhu M, Xu L, Herbst R, Su X, Gu Y, Li S, Huang L, Gu J, Han B, Jallal B, Shen H, Yao Y. Genomic Landscape Survey Identities SRSF1 as a Key Oncodriver in Small Cell Lung Cancer PLoS Genet 2016 Apr 19;12(4):e1005895

Li S, Dong Y, Wang K, Wang Z, Zhang X. Transcriptomic analyses reveal the underlying pro-malignant functions of PTHR1 for osteosarcoma via activation of Wnt and angiogenesis pathways J Orthop Surg Res 2017 Nov 9;12(1):168

Lu Y, Li J, Cheng J, Lubahn DB. Messenger RNA profile analysis decipher new Esrrb responsive genes in prostate cancer cells BMC Mol Biol 2015 Dec 1;16:21

Penrose HM, Cable C, Heller S, Ungerleider N, Nakhoul H, Baddo M, Hartono AB, Lee SB, Burov ME, Flemington EF, Crawford SE, Savkovic SD. Loss of Forkhead Box G3 Facilitates Inflammatory Colon Cancer: Transcriptome Profiling of the Immune Landscape and Novel Targets Cell Mol Gastroenterol Hepatol 2019;7(2):391-408

Tashiro F, Kanai-Azuma M, Miyazaki S, Kato M, Tanaka T, Toyoda S, Yamato E, Kawakami H, Miyazaki T, Miyazaki J. Maternal-effect gene Ces5/Ooep/Moep19/Floped is essential for oocyte cytoplasmic lattice formation and embryonic development at the maternal-zygotic stage transition Genes Cells 2010 Aug;15(8):813-28

Veskimäe K, Scaravilli M, Niininen W, Karvonen H, Jaatinen S, Nykter M, Visakorpi T, Mäenpää J, Ungureanu D, Staff S.
Expression Analysis of Platinum Sensitive and Resistant Epithelial Ovarian Cancer Patient Samples Reveals New Candidates for Targeted Therapies Transl Oncol 2018 Oct;11(5):1160-1170

Wang J, Xu M, Zhu K, Li L, Liu X. The N-terminus of FILIA forms an atypical KH domain with a unique extension involved in interaction with RNA PLoS One 2012;7(1):e30209

Zhang P, Dixon M, Zucchelli M, Hamblinki F, Levkov L, Hovatta O, Kere J. Expression analysis of the NLRP gene family suggests a role in human preimplantation development PLoS One 2008 Jul 23;3(7):e2755

Zhu K, Yan L, Zhang X, Lu X, Wang T, Yan J, Liu X, Qiao J, Li L. Identification of a human subcortical maternal complex Mol Hum Reprod 2015 Apr;21(4):320-9

This article should be referenced as such:

Cristiano L. OOEP (Oocyte expressed protein). Atlas Genet Cytogenet Oncol Haematol. 2020; 24(3):112-116.