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

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Abstract

Review on the translocation t(6;11)(q13;q12) EEF1G/OOEP involving EEF1G (alias, eukaryotic translation elongation factor 1 gamma) gene and OOEP (alias, oocyte expressed protein) gene. The novel fusion gene was detected in acute lymphoblastic leukemia/lymphoblastic lymphoma patients but the presence of the correspondent protein is still unknown.

Keywords
Chromosome 6; chromosome 11; EEF1G; eukaryotic translation elongation factor 1 gamma; EF1G, GIG35, PRO1608, EEF1γ, EEF1Bγ, EEF-1B gamma, EF-1-gamma, elongation factor 1-gamma, translation elongation factor EEF-1 gamma chain, pancreatic tumor-related protein; OOEP, oocyte expressed protein, chromosome 6 open reading frame 156, C6orf156, FLOPED, KH homology domain-containing protein 2, KHDC2, oocyte- and embryo-specific protein 19, MOEP19, t(6;11)(q13;q12), acute lymphoblastic leukemia/lymphoblastic lymphoma

Clinics and pathology

Disease
Acute lymphoblastic leukemia/lymphoblastic lymphoma

Note
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 aggressive 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, instead located on chromosome 11. This leads to the know but not still well-characterized translocation t(6;11)(q13;q12) EEF1G/OOEP.

Prognosis
There is no evidence of impact of the EEF1G/OOEP fusion gene on the tumor behavior and also its contribute in the prognosis of acute lymphoblastic leukemia/lymphoblastic lymphoma is still unknown.

Genes involved and proteins

EEF1G
Location 11q12.3
Alias: Eukaryotic translation elongation factor 1 gamma, EF1G, GIG35, PRO1608, EEF1γ, EEF1Bγ, EEF-1B Gamma, EF-1-Gamma, Elongation Factor 1-Gamma, Translation Elongation Factor EEF-1 Gamma Chain, Pancreatic Tumor-Related Protein

Eukaryotic translation elongation factor 1 gamma is a protein that plays a main function in the elongation step of translation process but also covers numerous moonlighting roles.
Figure 1. Schematic representation of the EEF1G gene, OOEP gene and the novel eEF1G-OOEP fusion gene. In the upper side of the picture there are the genomic sequence of EEF1G and OOEP genes, while in the middle side is reported the chimeric fusion gene 5'EEF1G / 3'OOEP. The genomic sequence for EEF1G/ OOEP reported by Atak and colleagues (Atak et al., 2013) was analyzed with BlastN. The red portion is derived by EEF1G while the blue piece is derived by OOEP. Violet fraction is the overlapping between the two sequences. Finally, on the bottom side of the image there is the mRNA of EEF1G/ OOEP with the predicted coding sequence (CDS) and UTRs (http://insilico.ehu.es-translate/index2.php).

It is expressed ubiquitously in human tissues and often it is found over-expressed in human cancer samples and cancer cell lines.

**DNA/RNA**

**EEF1G** (Eukaryotic Translation Elongation Factor 1 Gamma) is a protein coding gene with 10 exons and a length of 14388 bp (RefSeq NC_000011.10). Its transcript is 1446 bp long (RefSeq NM_001404.5) but was observed five splice variants and nine pseudogenes probably originated by retrotransposition.

**Protein**

eEF1G is formed by 437 amino acids (RefSeq NP_001395.1), it has a molecular weight of 50.12 kDa and it is a multi-domain protein which consist of three main domains: from the amino to carboxyl half terminal there are a glutathione S-transferase (GST)-like N-terminus domain (NT-eEF1G), a glutathione S-transferase (GST)-like C-terminus domain (CT-eEF1G) and a conserved C-terminal domain (CD-eEF1G) (Achilonu et al., 2014).

eEF1G is a subunit of the eukaryotic elongation factor-1 complex named eEF1H that result by the aggregation of different proteins that play a central role in peptide elongation during eukaryotic protein biosynthesis. The physiological role of eEF1G is still not well defined, however eEF1G seems to be necessary for guarantee the stability to entire eEF1H complex and to stimulate the activity of the eEF1B2 subunit during the elongation step of translation (Mansilla et al., 2002). However, are known that it has multiple non-canonical roles (moonlighting roles) inside the cell such as the interaction with cytoskeleton and binding with various mRNA and several proteins, comprise membrane-bound receptors (Coumans et al., 2014; Corbi et al., 2010; Cho et al., 2003).

**OOEP**

**Location** 6q13

Alias: oocyte expressed protein, chromosome 6 open reading frame 156, C6orf156, FLOPED, KH homology domain-containing protein 2, KHDC2, oocyte- and embryo-specific protein 19, MOEP19.

**DNA/RNA**

OOEP gene is composed by 3 exons (RefSeq NC_000006.12) and its transcript is 689 nt long (RefSeq NM_001080507).

**Protein**

Oocyte expressed protein, alias OOEP, is a component of the subcortical maternal complex (SCMC) that plays its roles in oocytes and in early stages of embryogenesis (Bebbere et al., 2016).

**Result of the chromosomal anomaly**

**Hybrid gene**

The result of chromosomal anomaly is the novel fusion gene 5’ EEF1G / 3’ OOEP. Atak and
colleagues (Atak et al., 2013) found its DNA in T-cell acute lymphoblastic leukemia (T-ALL), but there are no data or evidence about its mRNA and its protein. So, in this review, with the use of various tools and software will be predicted the possible transcript and also the probable protein. However, the data collected are hypothesis and have to be experimental verified.

**Description**

The fusion gene 5’ EEF1G / 3’ OOEP was found in T-cell acute lymphoblastic leukemia (T-ALL) (Atak et al., 2013) and it derives by the genomic translocation t(6;11)(q13;q12) EEF1G/OOEP, i.e. by fusion of a part of OOEP gene, situated on chromosome 6, with a portion of EEF1G gene, instead located on chromosome 11.

In particular, the fusion interests part of exon 8 and exon 7 of EEF1G that result fused with a portion of the second intron sequence, i.e. intron 2-3, of the OOEP-202, an alternative splicing form of OOEP that contains also the ribosomal protein L39 pseudogene 3, alias RPL39P3 (https://www.ensembl.org).

By the analysis of the sequences reported in Ensembl appears that the portion of the OOEP gene that is fused with EEF1G is really a portion of RPL39P3 pseudogene.

**Transcript**

There is no evidence about the mRNA of the EEF1G/OOEP fusion gene. However, with bioinformatic tools it is possible to predict its sequence and characterizing it. It seems to be formed by both the non-coding 5’UTR and 3’UTR and a coding sequence (CDS). The CDS is among 221 and 374 nt with a length of 154 nt and it is apparently protein-coding. It was chosen the longer codifying sequence of the 5’->3’ strand in that the sequence offers more reading possibilities (https://www.ncbi.nlm.nih.gov/orffinder/).

**Fusion protein**

**Description**

There is no evidence about the protein of the EEF1G/OOEP fusion gene. However, with INSILICO and ORFFINDER tools (http://insilico.ehu.es/translate/index2.php; https://www.ncbi.nlm.nih.gov/orffinder/) is possible to predict the protein sequence of the EEF1G/OOEP mRNA.

The protein counts 51 amino acids with a molecular mass of 6.41 kDa and a theoretical pI of 12.55 (https://web.expasy.org/cgi-bin/protparam/protparam). Surprisingly a perfect sequence homology with ribosomal L39 protein (RPL39) is noted by BlastP analysis and can be found the ribosomal L39 putative domain (https://blast.ncbi.nlm.nih.gov/Blast.cgi). The post-translational modifications are unknown.

**Expression / Localisation**

There is no evidence not only of the protein but also of its localization. However, the predicted subcellular localization for the protein is cytoplasm (http://linux1.softberry.com/cgi-bin/programs/proloc/protcampln.pl).

![Figure 2](https://example.com)
Oncogenesis

It is unclear the role in oncogenesis of the translocation t(6;11)(q13;q12) EEF1G/OOEP and there is no evidence about its effective transcription and/or translation. Perhaps the EEF1G/OOEP fusion gene plays a regulatory role or it is instead effectively translated into a functional protein, that by bioinformatic analysis seems to be RPL39-like protein and that deriving from RPL39P3 pseudogene. It was demonstrated that RPL39 plays a role in metaplastic breast cancer where shows an oncogenic activity through the increase of the inducible nitric oxide synthase (NOS2). Moreover, it was evidenced that a high RPL39 and iNOS expression are associated with a reduction in patient overall survival (Dave et al., 2017), so the abnormal translocation t(6;11)(q13;q12) EEF1G/OOEP could be linked with an increase of RPL39 levels in acute lymphoblastic leukemia/lymphoblastic lymphoma cancer cells by the translation of its pseudogene RPL39P3. In addition, some authors found high expression of RPL39P3 in human colon cancer LIM1863 cell line (Chen et al., 2016). However, these are only hypothesis and the truly oncogenic potential of EEF1G/OOEP in proliferation and cancer aggressiveness needs to be better elucidated.

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