Atlas of Genetics and Cytogenetics in Oncology and Haematology

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# Leukaemia Section

## Short Communication

# t(3;11)(p11;p15) NUP98/POU1F1

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## Abstract

Review on t(3;11)(p11;p15), with data on clinics, and the genes involved.

**KEYWORDS**
Chromosome 3; Chromosome 11; NUP98; POU1F1; Acute myeloid leukemia; Therapy-related leukemia.

## Clinics and pathology

### *Disease*

**Acute myeloid leukemia (AML)**

### *Epidemiology*

Two cases to date. In the first case, a 57-year-old female was initially diagnosed with a breast adenocarcinoma and she developed therapy-related AML-M4 fourteen years later (Lisboa et al., 2013). In the second case, a 19-year-old white male was diagnosed with de novo AML-M4 (Walker et al., 2013).

### *Prognosis*

The first patient was treated with chemotherapy (cytarabine, daunorubicin, and cyclosporin) and a complete response was achieved. The patient showed evidence of relapse ten months later and died within five months after relapse (Lisboa et al., 2013). The second patient had complete remission (CR) after induction treatment with cytarabine and daunorubicin. The post-CR therapy included high-dose cytarabine, cytoxan, and etoposide. The patient had a disease-free survival of 92+ months and an overall survival of 92.9+ months (Walker et al., 2013).

## Genes involved and proteins

### *NUP98 (nucleoporin 98)*

**Location**
11p15

**Protein**
A 98 kDa nucleoporin. It is a component of the nuclear pore complexes (NPCs) and participates in many cellular processes, including nuclear import, nuclear export, mitotic progression, and regulation of gene expression (Gough et al., 2011). NUP98 protein contains N-terminal Gly-Leu-Phe-Gly (GLGF) repeat domains and a C-terminal RNA binding domain. Translocations between this gene and many other partner genes have been observed in leukemias. Rearrangements typically result in fusion proteins with the N-terminal GLGF domain of this gene to the C-terminus of the partner gene and they seem to be associated with poor prognosis (Struski et al., 2017; Kearney, L 2002).

### *POU1F1 (POU class 1 homeobox 1)*

**Location**

3p11

**Protein**

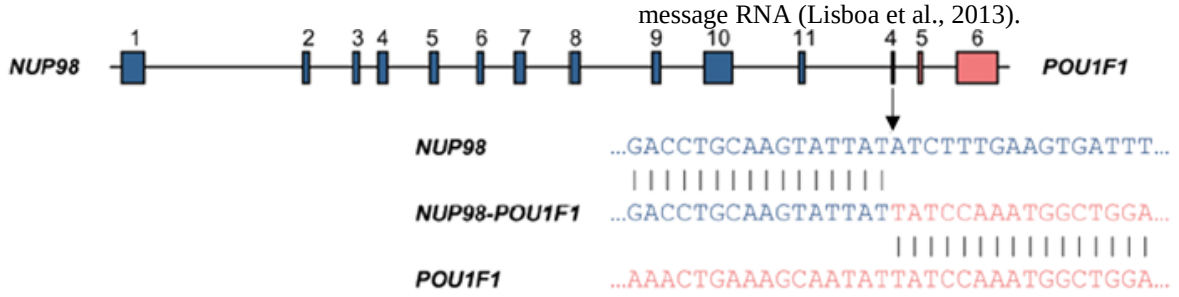
POU1F1, also known as PIT1, is a member of the POU family of transcription factors. It regulates expression of several genes involved in pituitary development and hormone expression (Ingraham et al., 1998) and also plays a role in cell proliferation and differentiation (Costoya et al., 1998; Pellegrini et al., 2006). Deregulation of POU1F1 is implicated in pituitary adenoma, combined pituitary hormone deficiency, breast carcinoma, and acute myeloid leukemia (Franc et al., 2014; Gao et al., 2016). POU1F1 protein contains an N-terminal transactivation domain and a C-terminal DNA binding domain including a homeodomain (Franc et al., 2014).

# Result of the chromosomal anomaly

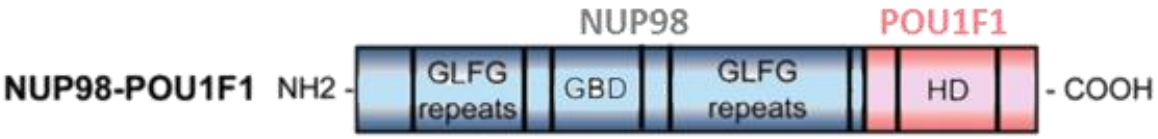
## *Hybrid gene*

**Description**

Description: 5' NUP98 - 3' POU1F1 was produced in the case reported by Lisboa et al. in 2013. The breakpoints were 7490 bp downstream of NUP98 exon 11 and 129 bp downstream of the start of POU1F1 exon 4 (Figure A). The POU1F1 exon 4 was not included in the mature NUP98/POU1F1 message RNA (Lisboa et al., 2013).




## *Fusion protein*




Schematic representation of the NUP98-POU1F1 fusion protein (Modified from Lisboa et el., 2013).

**Description**

The NUP98/POU1F1 fusion protein contains the GLFG repeats of NUP98 and the homeodomian of POU1F1 (Figure B).

**Oncogenesis**

It is expected that the expression of NUP98/POU1F1 fusion gene is under the control of NUP98 promoter, leading to POU1F1 overexpressioin which results in increased proliferation of leukemia cells. It is hypothesized that the FLT3-ITD mutation collaborates with NUP98/POU1F1 in malignant transformation (Lisboa et el., 2013).

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