



cima

CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

ONCOLOGY DIVISION



Mechanisms of overexpression of the EVI1 gene (3q26) and its role in acute myeloid leukemia

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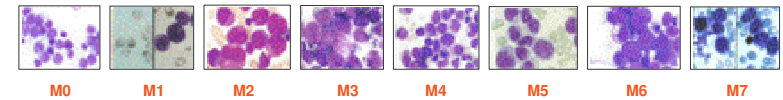
III REUNIÓN ANUAL RTICC

Red Temática de Investigación Cooperativa en Cáncer
Instituto de Salud Carlos III (ISCIII)
Ministerio de Ciencia e Innovación (MICINN)

20
09

AML is a heterogeneous malignancy

FAB classification: Morphology



M0 M1 M2 M3 M4 M5 M6 M7



complex network of
cytogenetic aberrations and molecular mutations

World Health Organization (WHO)

AML with recurrent genetic abnormalities

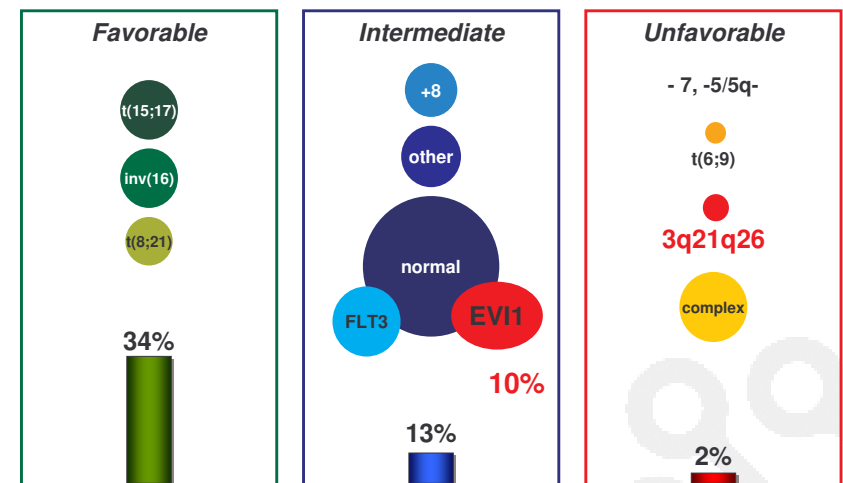
- t(8;21); RUNX1-RUNX1T1
- inv(16)/t(16;16); CBFB-MYH11
- t(15;17); PML-RARA
- t(9;11); MLL
- t(6;9); DEK-NUP214
- inv(3)(q21q26)/t(3;3)(q21;q26); RPN1-EVI1**
- t(1;22); RBM15-MKL1
- AML with mutated NPM1
- AML with mutated CEBPA

AML with multilineage dysplasia

AML therapy related

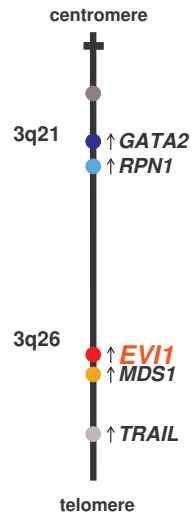
AML, not otherwise categorized

Cytogenetic findings: predict prognosis



Survival at 5 years

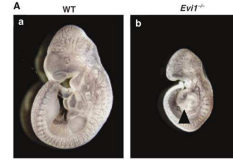
COMPLEX MECHANISM



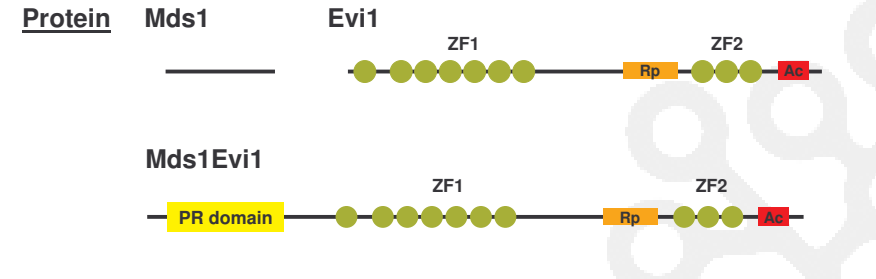
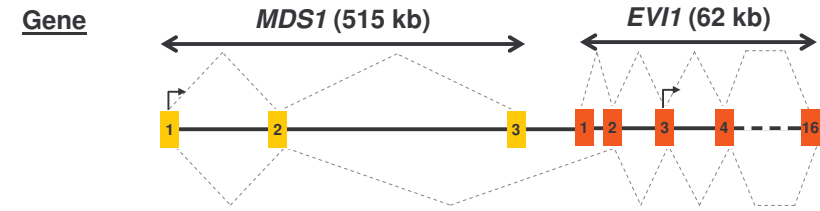
EVI1 (3q26.2)

Ecotropic viral integration site 1

Critical role in development and leukemogenesis



EVI1: complex locus



EVI1 overexpression

3q21q26 rearrangements

inv(3)(q21q26)



t(3;3)(q21;q26)



Clinical features

erythroid and megakaryocytic dysplasia

elevated platelet count

minimal response to chemotherapy and poor prognosis

OBJETIVOS

1. Impacto pronóstico de la sobreexpresión de EVI1 en leucemia mieloide aguda
2. Mecanismos de sobreexpresión del gen EVI1
3. Papel de Evi1 como factor de transcripción

Material

Human Tissue Panel

21 normal tissues

Human Cell Lines

16 myeloid cell lines

Patient Samples

80 cases with 3q rearrangements

476 AML cases at diagnosis

Hospital La Fe
Valencia

Centro de Investigación Cáncer (CIC)
Salamanca

Hospital de la Santa Creu i Sant Pau
Barcelona

Hospital Negrín
Las Palmas, Canarias



EV11 overexpression in AML (No. 476)

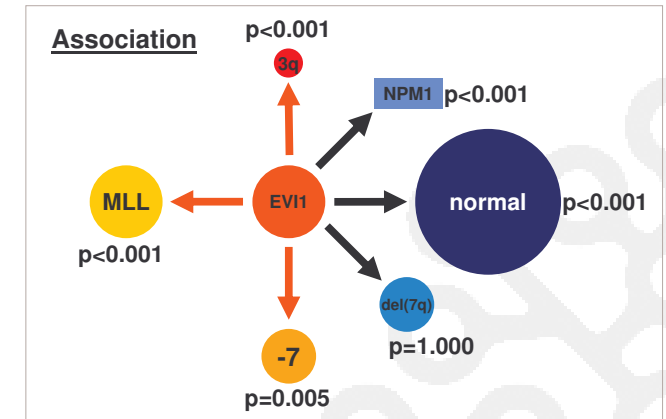
Prevalence

good: 4%

intermediate: 13%

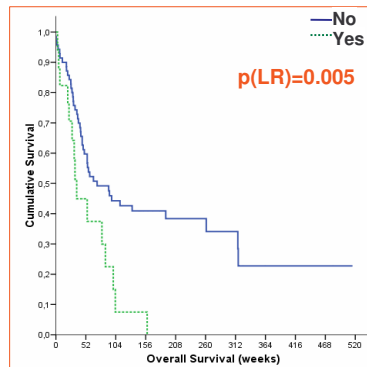
poor: 37%

p<0.001

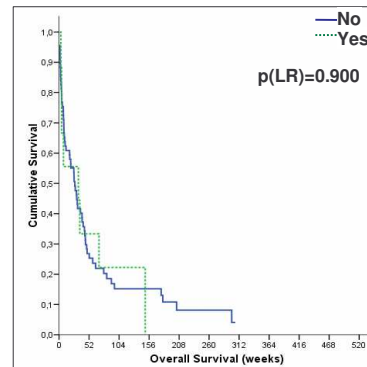


younger patients with EV11-1C overexpression had significantly worse overall survival

Age<60 years



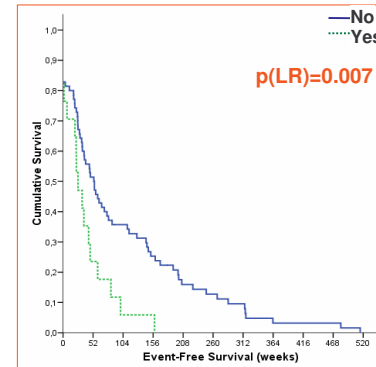
Age>60 years



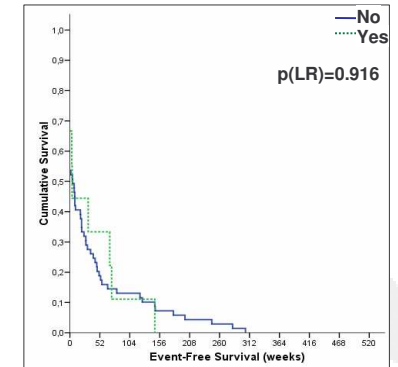
→ EV11 in diagnosis

younger patients with EV11-1C overexpression had significantly worse event free survival

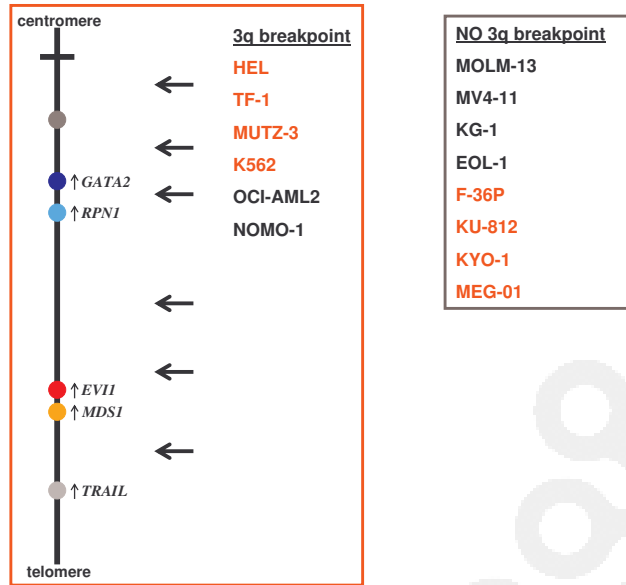
Age<60 years



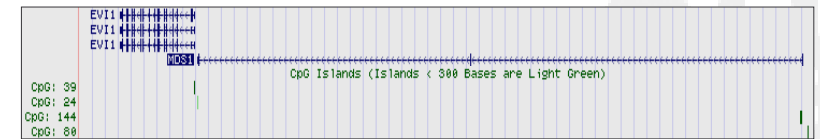
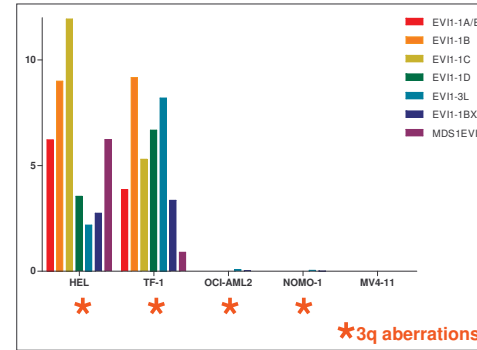
Age>60 years



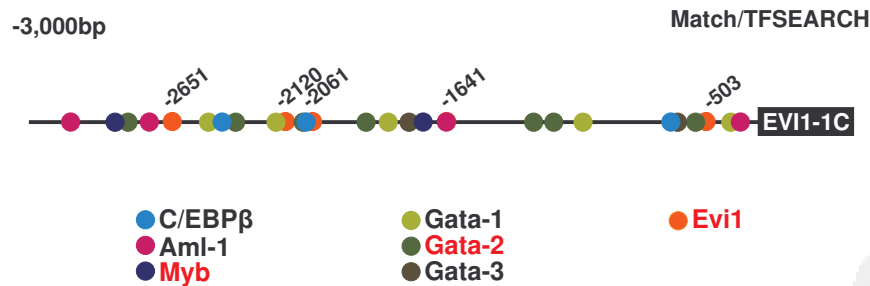
3q rearrangements and EVI1 overexpression



Analysis of the methylation status of EVI1 and MDS1EVI1 promoters



Identification of transcription factors within the proximal promoter region of EVI1



Estudio funcional del promotor de EVI1

