GENOMIC PROFILE OF *RUNX1-ETV6*$^{+}$ PAEDIATRIC B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKAEMIA

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INTRODUCTION

- B-cell precursor acute lymphoblastic leukaemias (BCP-ALL) are characterized by recurrent translocations, with t(12;21)(p13;q22) being the most common. This translocation generates the *ETV6-RUNX1(ER)* and the reciprocal *RUNX1-ETV6 (RE)* gene fusions in 100% and 76% of cases, respectively.
- Studies have shown that *RE* high expression confers worse prognosis. Moreover, other genetic changes have been described as important risk stratification markers.
- We aimed to characterize the genomic profile of patients harboring *RUNX1-ETV6*.

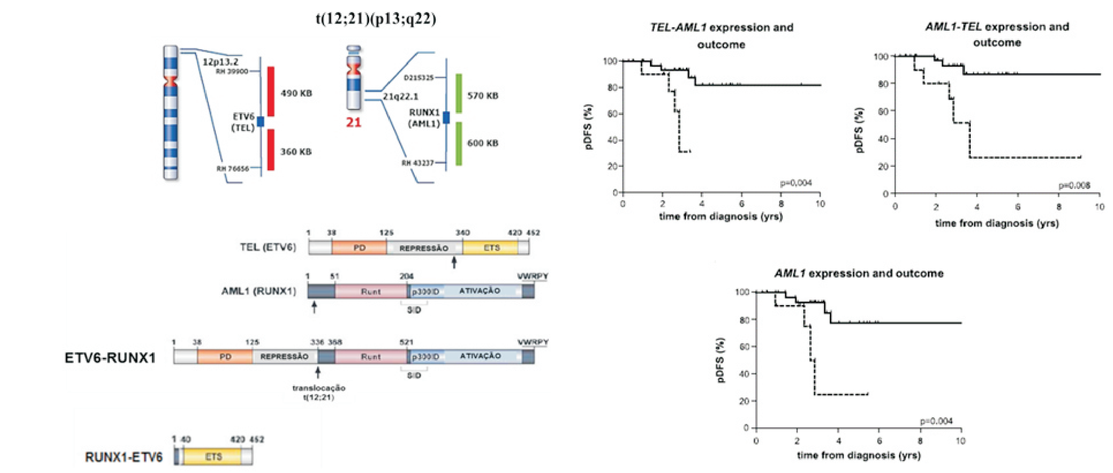


Figure 1. A. Schematic representation of *ETV6* and *RUNX1* fusion**. B.** Disease free survival of BCP-ALL according to *ETV6-RUNX1* and *RUNX1-ETV6* expression.

METHODS AND RESULTS

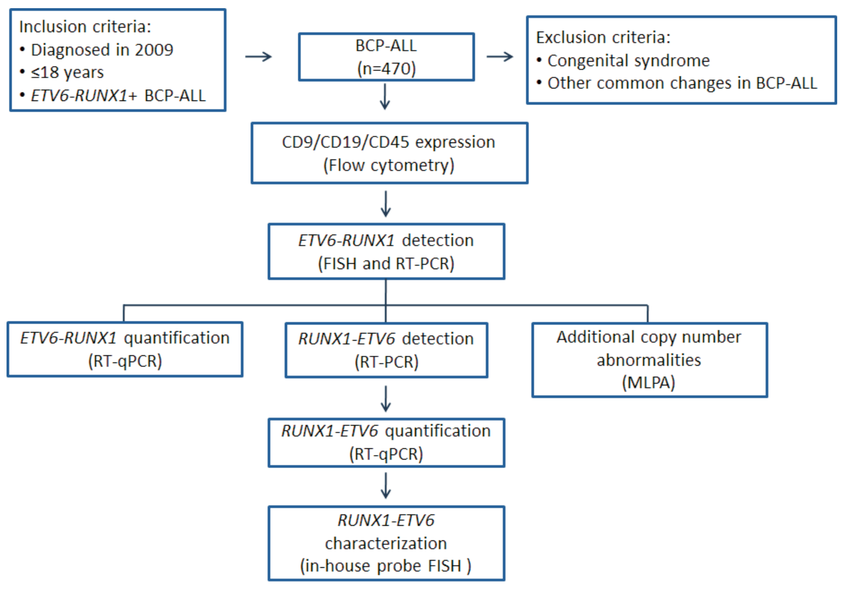


Table 1. Demographic and laboratory characteristics of the patients in relation to the presence of the direct and reciprocal transcript found by RT-PCR

Variables	*ETV6-RUNX1*		*P* value
	RUNX1-ETV6^{-} n (%)	*RUNX1-ETV6*$^{+}$ n (%)*	
Age (months)			*P* = 0.236
0-12	2 (8.3)	-	
13-120	20 (83.4)	41 (89.1)	
>120	2 (8.3)	4 (8.6)	
Sex			*P* = 0.122
Female	9 (37.5)	18 (39.1)	
Male	15 (62.5)	28 (60.9)	
BCP-ALL subtype			*P* = 0.631
pro-B	1 (4.1)	0	
Common	21 (87.6)	39 (88.6)	
pre-B	2 (8.3)	5 (11.3)	
WBC (x10^{9}/L)			*P* = 0.603
<50.000	19 (79.1)	39 (84.7)	
>50.000	5 (20.9)	7 (15.3)	
CD9 expression			*P* = 0.001
≤ 64%	14 (58.3)	10 (21.7)	
> 64%	9 (37.5)	36 (78.3)	
Total	24 (34.3)	46 (65.7)	

* RT-PCR for detection of *RUNX1-ETV6* was performed in 70 cases.
WBC, white blood cell count

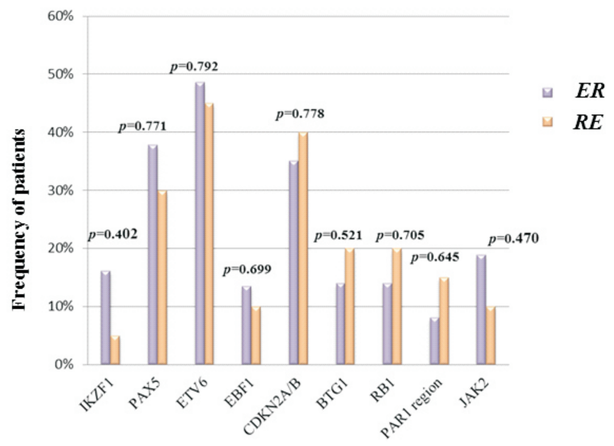


Figure 2. Frequency of deletions evaluated by MLPA in patients according to the presence of direct and reciprocal transcript.

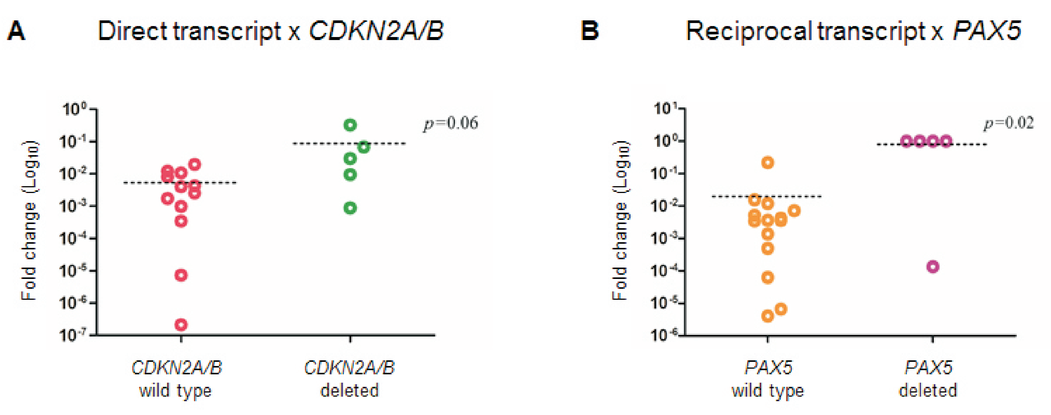


Figure 3. Evaluation of direct and reciprocal transcripts by RT-qPCR according to *CDKN2A/B* and *PAX5* status

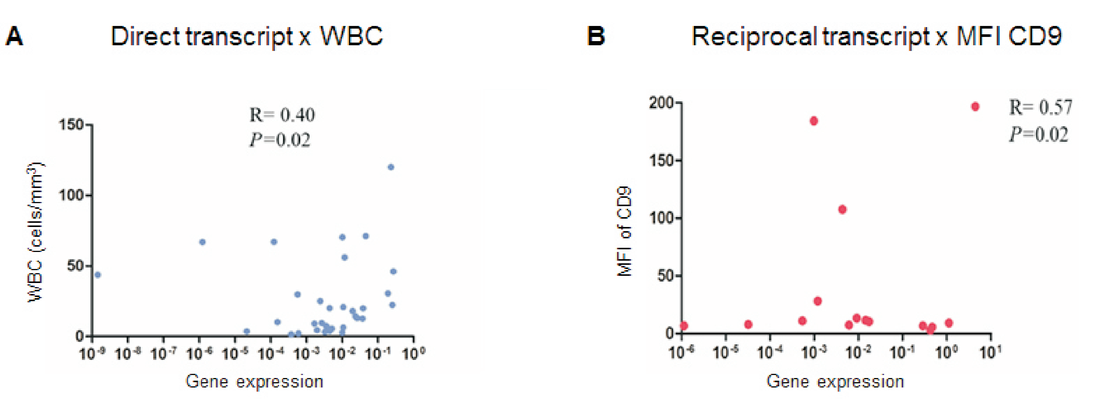


Figure 4. Correlation analysis between gene expression of the direct and reciprocal transcript and laboratorial characteristics (age, white blood cell count, percentage od CD9 and MFI of CD9). Only significantly statistical analysis were ilustred.

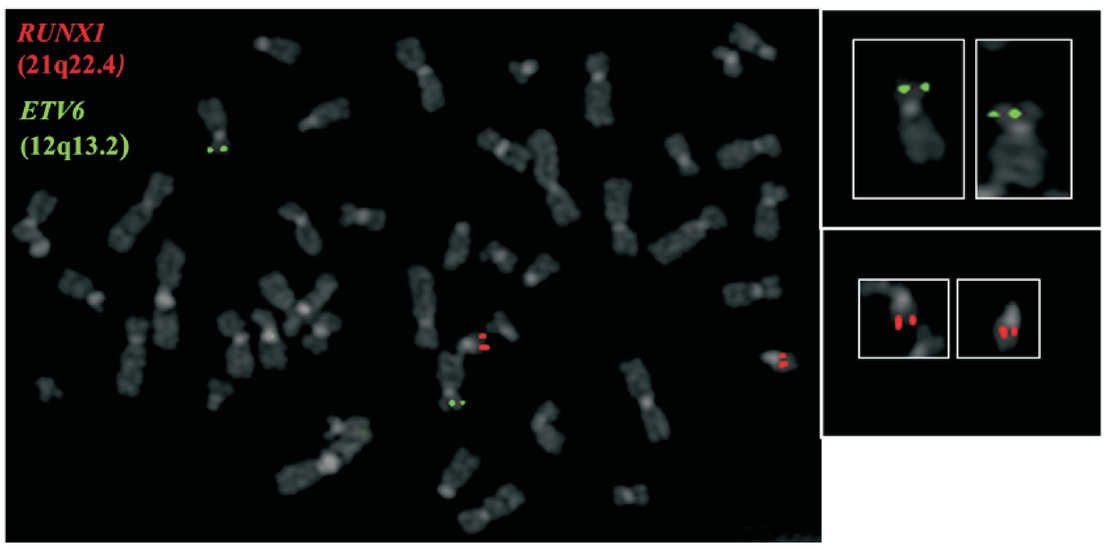
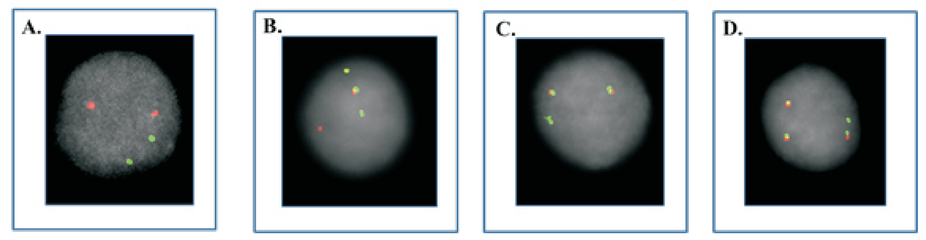


Figure 6. Location confirmation of in-house probes designed to reciprocal transcript detection by FISH .

- **FISH analysis using commercial probe**



- **FISH analysis using in-house probes**

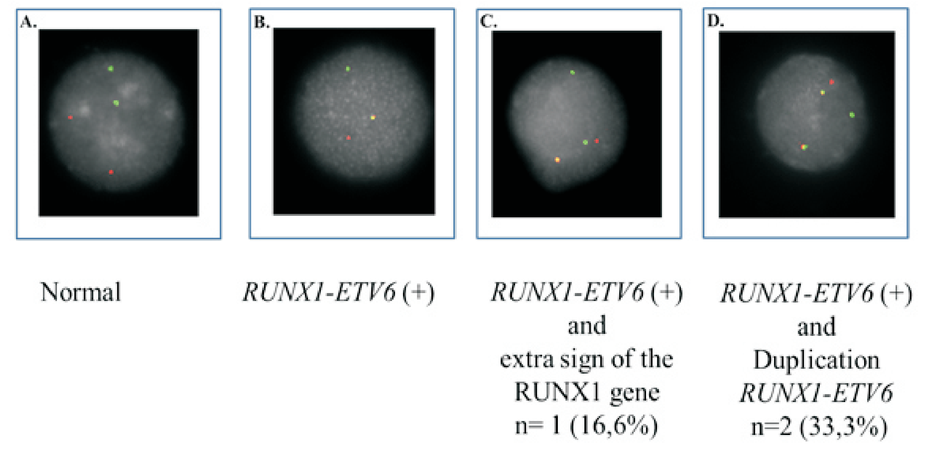


Figure 7. Detection of direct and reciprocal transcripts and additional changes by FISH

CONCLUSIONS

The correlation between RE expression and *PAX5* del is still unclear and is worthy of further investigation. In addition, all cases with RE duplication had a concomitant del of the non-rearranged *ETV6* allele, which suggests that this loss may contribute to the formation of the duplication. Our results suggest that patients with RE have a heterogeneous pattern and the characterization of this subgroup may provide new insights for risk stratification and treatment strategies.

Development agency: Ministério da Saúde, FAPERJ, CNPq

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