STUDY OF METHYLATION MACHINERY IN PEDIATRIC MYELODYSPLASTIC SYNDROME: WHAT IS WRONG AND ASSOCIATED WITH LEUKEMIC TRANSFORMATION?

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INTRODUCTION

DNA methylation is considered a guardian of the fate of hematopoietic stem cells, as it acts to maintain the balance of these cells, their capacity for self-renewal and differentiation in the hematopoietic cell lines. The enzymes that control the methylation equilibrium as DNMTs, TET2, and APOBEC are called methylation machinery (Figure 1). These enzymes may play an important role in hematological neoplasms such as myelodysplastic syndrome (MDS). Pediatric MDS is a rare disease, so little is known about the molecular basis of MDS in pediatric patients. The aim of this study was to analyze the expression of *DNMTs*, *TET2* and *APOBEC3B* genes in pediatric primary MDS and their associations with MDS subtypes, cytogenetics and evolution of MDS toward AML.

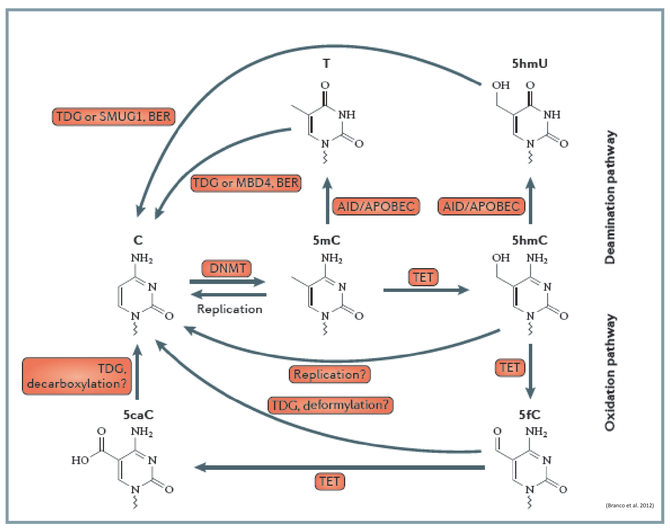


Figure 1: Equilibrium of DNA methylation: the methylation machinery

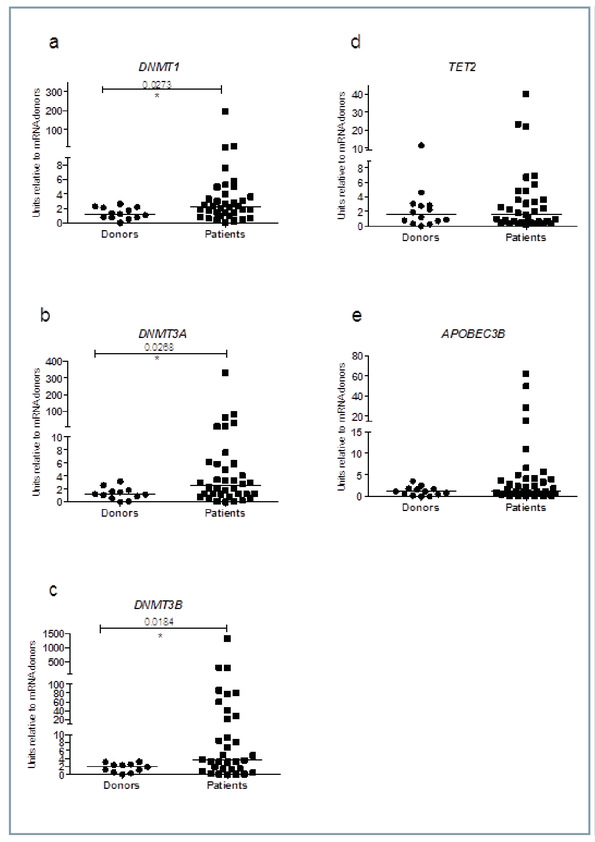


Figure 2: Comparison of relative expression levels of *DNMTs, TET2* and *APOBEC3B* genes among pediatric MDS patients and donors.

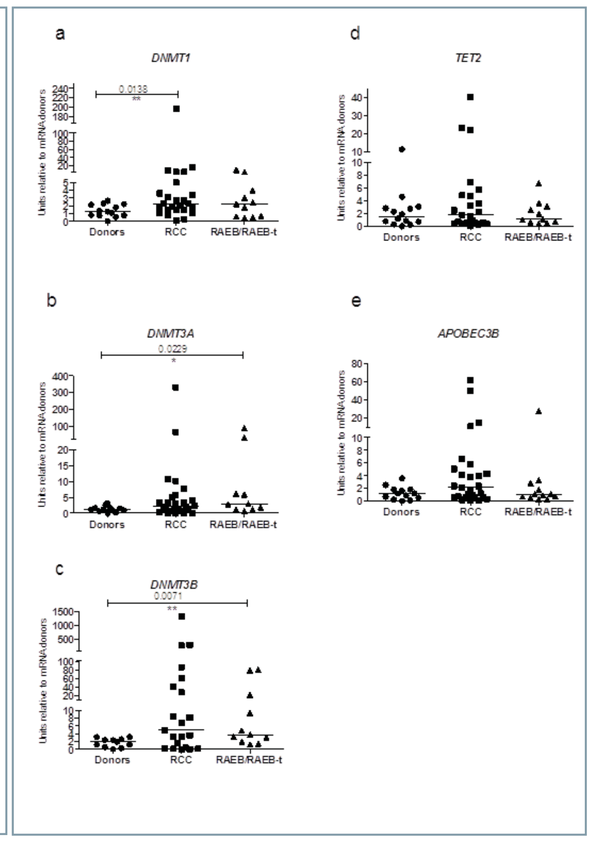
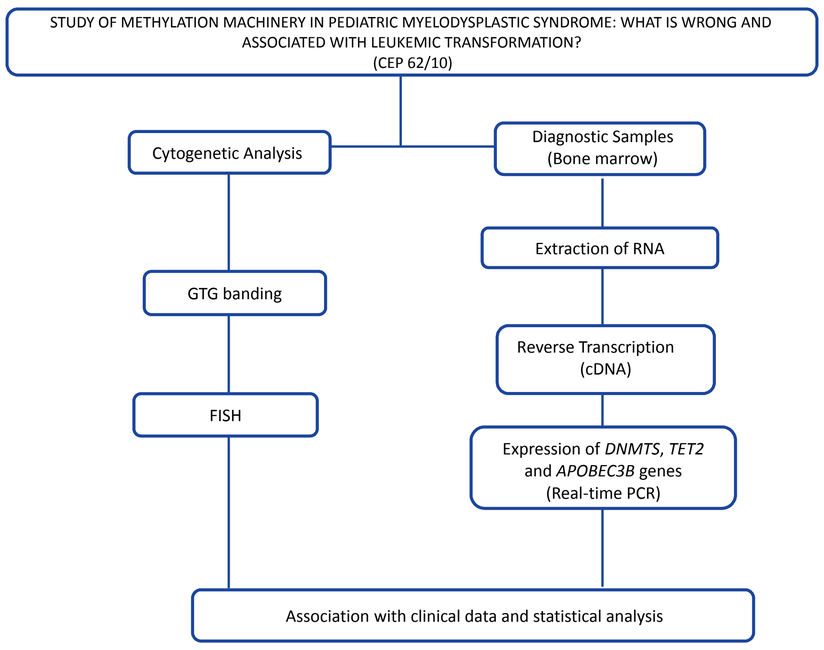


Figure 3: Comparative analysis of expression levels according the subtypes of pediatric MDS and donors.

METHODS



RESULTS

Table 1: Patients characteristics

Patients	Number
MDS	39
Gender	
Male/female	23/16
Age (yr), median (range)	7 (1 -18)
Hasle (2003 - 2016)	
CRR	27
RAEB/RAEB-t	7/5
Number of Cytopenia	
0/1	2/17
2/3	9/11
BM blast (%)	
<5%	27
5-19%	9
20-29%	3
Cytogenetics	
Normal	21
Abnormal	17
without mitosis	1
Evolution of dieases	
No	28
Yes	11
RCC to RAEB/RAEB-t	3
RCC to ALL	1
RAEB/RAEB-t to AML	7

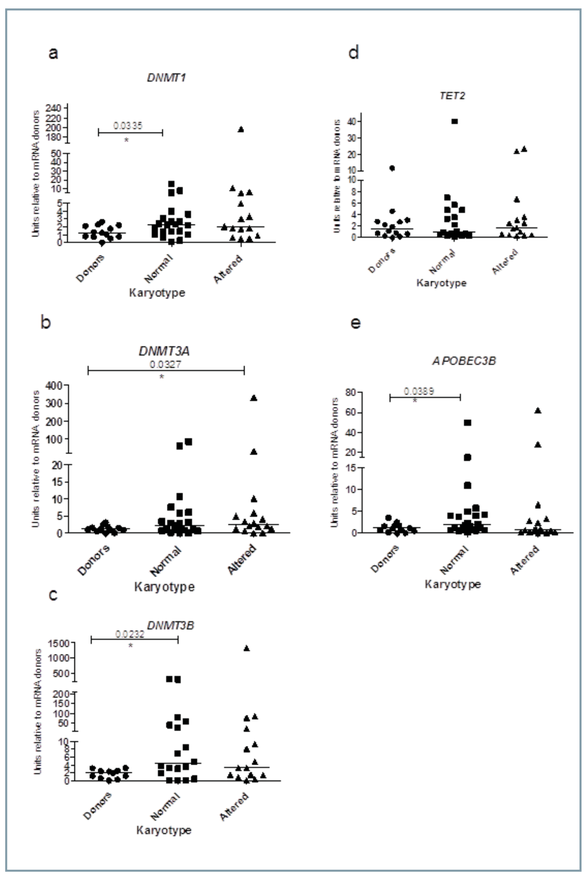


Figure 4: Analysis of relative expression levels of *DNMTs, TET2* and *APOBEC3B* genes with the cytogenetics presented in patients with pediatric MDS.

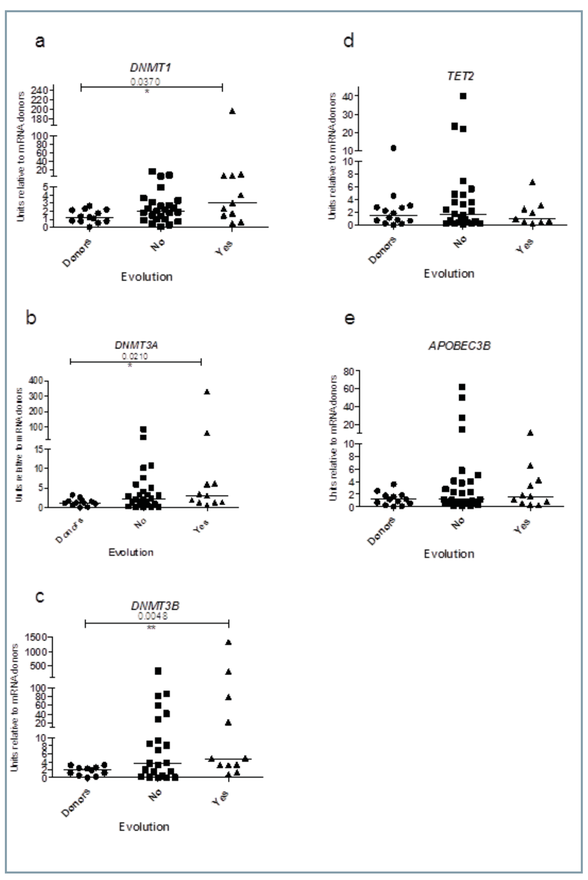


Figure 5: Analysis between relative expression levels of *DNMTs, TET2* and *APOBEC3B* genes with the evolution of MDS.

CONCLUSION

Our results suggest that the overexpression of DMNTs genes are associated with poor prognosis, being possible biomarkers of disease evolution from MDS to AML.

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