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ROLE OF THE EXPRESSION OF *UBE2T*, *UBE2O*, *USP7* AND *USP15* GENES IN THE PATHOBIOLOGY OF MYELODYSPLASTIC SYNDROME

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Introduction

Myelodysplastic Syndrome (MDS) comprises a group of clonal hematological disorders closely associated with the presence of genomic instability in hematopoietic progenitor stem cells, commonly characterized by the presence of chromosomal alterations. The ubiquitin-proteasome system is an important proteolytic system with a role in the regulation of several cellular functions such as intracellular protein breakdown, cell cycle control, apoptosis and DNA repair. The role of the ubiquitination (*UBE2T* and *UBE2O*) and deubiquitination (*USP7* and *USP15*) genes is unknown regarding the pathobiology of MDS.

Methods

Initially, an *in silico* Pan-Cancer evaluation was performed using the *Gene Expression Profling Interactive Analysis* (GEPIA) database in order to verify the differential expression profile of the *UBE2T, UBE2O, USP7* and *USP15* genes, as well as their role in survival of patients diagnosed with onco-hematological diseases, with a focus on MDS. Subsequently, it was followed by the validation of the gene expression findings of these targets in bone marrow samples from 72 patients diagnosed with MDS and 04 healthy individuals to control group, matched by sex, age and cytogenetic result, based on qPCR analyses. Gene expression data were evaluated in the case versus control association and in relation to clinical, laboratory and cytogenetic data of MDS patients. The research was submitted and approved by the Human Ethics Research Committee (PROPESQ-UFC - #35871620.9.0000.5054 / HGF/SUS - #35871620.9.3001.5040).

Results

From the Pan-Cancer screening in 30 different types of cancers in the GEPIA database, we identified the differential expression profile of the *UBE2T, UBE2O, USP7* and *USP15* genes only in types of onco-hematological diseases, the Lymphoid Neoplasm Diffuse Lymphoma of large B cells (DLBC) and Acute Myeloid Leukemia (AML). No data on the expression of these genes were identified in the GEPIA for MDS. In DLBC, the genes *UBE2T, UBE2O* and *USP7* showed a significantly increased expression compared to controls. In addition, it was identified that the *UBE2T* gene had a reduced expression in patients with AML compared to controls. No differences were identified regarding the expression of these genes and survival in patients with DLBC and AML.

In the evaluation of the expression of these genes in MDS, we identified that only the *USP15* gene had a reduced expression in relation to healthy individuals (p=0.03). Regarding the clinical and laboratory variables of MDS, an increase in the expression of the *UBE2T* gene was identified in patients with chromosomal abnormalities compared to patients with normal karyotype (p=0.032).The *USP7* and USP15 genes were positive and strongly correlated in MDS (r=0.82; r2=0.67; p<0.0001).

Results

Figure 1 - Gene expression of *UBE2T*, *UBE2O*, *USP7* and *USP15* in MDS patients compared to controls.

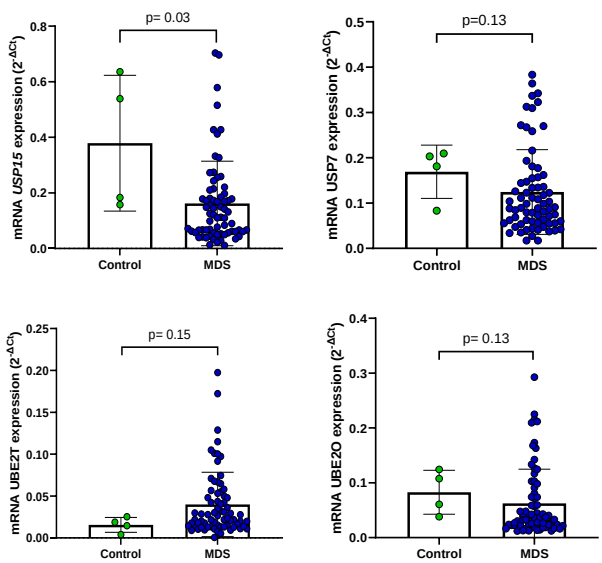


Figure 2 - Correlation analysis between *USP7* and *USP15* gene expression.

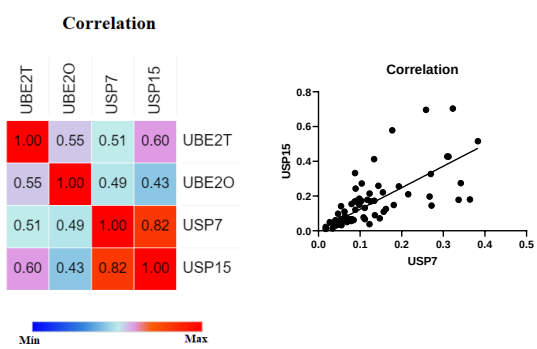
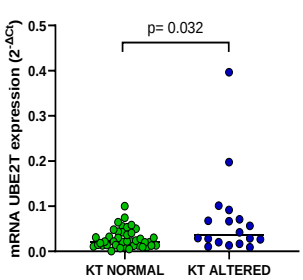


Figure 3 - *UBE2T* gene expression in MDS patients in relation to the karyotype variable.



Conclusions

Our results highlight that the differential gene expression of *USP15-USP7* axis and *UBE2T* may play an important role in the control of genomic instability establishing one of the most striking characteristics in MDS, the chromossomal abnormalities.

Contact

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