USP15-USP7 axis and _UBE2T_ differential expression may predicts pathogenesis and poor prognosis in Myelodysplastic syndrome

Abstract

To evaluate the expression profile of the *UBE2T*, *UBE2O*, *USP7* and *USP15* genes in relation to the pathogenesis and clinical-laboratory and prognostic stratification of the Brazilian Myelodysplastic Syndrome (MDS). Initially, an *in-silico* Pan-Cancer evaluation was performed using the Gene Expression Profiling Interactive Analysis (GEPIA) database to verify the differential expression profile of these 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 seventy-two patients diagnosed with MDS and four 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. From the Pan-Cancer *in-silico* 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 Acute Myeloid Leukemia (AML). No data on the expression of these genes were identified in the GEPIA for MDS, only to Acute Myeloid Leukemia (AML). Only *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 Brazilian MDS patients, 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 ($p=0.0321$). The *USP7* and *USP15* genes were positive and strongly correlated in MDS ($r=0.82$; $r2=0.67$; $p<0.0001$). 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.

Key-words: Ubiquitination; Deubiquitination; Gene expression; Myelodysplastic syndrome.