Decreased BNIP3L expression independently predicts a worse prognosis in myelodysplastic syndromes

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Deregulation of apoptosis contributes to myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) progression. BNIP3 and BNIP3L are pro-apoptotic proteins deregulated in several neoplasms. However, their expression has never been evaluated in myeloid malignancies. We evaluated the expression of *BNIP3* and *BNIP3L* in MDS and AML patients and correlated with clinical features. Gene expression was analyzed by qPCR in bone marrow samples from patients with MDS (n=65), AML with myelodysplasia-related changes (AML-MRC) (n=11), *de novo* AML (n=63) and healthy donors (n=26). Appropriated statistical analysis was performed and the data is showed as median [max-min]. BNIP3 transcripts were reduced in MDS [1.88 (0.03 - 32.60)] cells compared with normal cells [5.16 (0.67 - 33.85)], p=0.004, but did not differ between healthy donors and AML patients. *BNIP3L* transcripts were reduced in AML-MRC and *de novo* AML compared with normal cells [0.83 (0.19 - 4.91) and 0.84 (0.20 - 6.15) vs. 2.56 (0.65 - 6.56), p=0.004, p<0.0001, respectively]. *BNIP3L* expression was not altered in MDS patients. However, the high-risk MDS group [1.20 (0.69 - 2.24)] showed decreased *BNIP3L* expression in comparison to healthy donors (p<0.05). Interestingly, *BNIP3L* expression was reduced in four out of five patients who progressed according to WHO classification (p<0.05). Multivariate analyses indicated that low *BNIP3L* expression was an independent prognostic factor for worse patient event-free survival (EFS) and overall survival (OS) (all p<0.05). Our results suggest that BNIP3 is most likely to participate in the imbalance of apoptosis found in MDS cells, whereas BNIP3L may be involved in the decreased apoptosis of high-risk MDS and AML. Downregulation of BNIP3L appears to be an important event in MDS and

AML progression and modulation of this gene may be an interesting approach to fight these malignancies in the future.