Myelodysplastic syndrome is a clonal hematopoietic stem cell disease. One mechanism contributing to the constellation of hypercellular marrow and peripheral blood cytopenia is a significant increase in programmed cell death (apoptosis) in hematopoietic cells. In MDS there is dysregulation of apoptosis due to the anomalies in pathways such as bcl-2, TNF-α, Fas-ligand, TRAIL, Caspase, NF-κB and p38 MAP kinase. In early disease stage there is an increase in apoptosis, however in advanced stages apoptosis decreases leading to an increase in leukemic transformation. p53 is a tumor suppressor gene and a key regulator of apoptosis. P53 mutations confer a poor prognosis in several hematologic malignancies. PUMA (p53 upregulated modulator of apoptosis) is also extremely effective in inducing apoptosis. PUMA is a critical mediator of p53-dependent and independent apoptosis.

The objectives of this study were i) To compare the expressions of p53 and PUMA in bone marrow hematopoietic cells of MDS patients with those of healthy subjects ii) to evaluate the prognostic effect of apoptosis regulators of p53 and PUMA on overall and event free survival of MDS patients, iii) to evaluate the relationship between p53 and PUMA.

Myelodysplastic syndrome patients compared to normal bone marrow samples were significantly higher in bone marrow of MDS patients as compared to normal bone marrow samples. In MDS samples, there was a moderate positive correlation between p53 and PUMA expressions. Although there was a mild correlation between PUMA expression and high scores in IPSS, WPSS and MPSS clinical scoring systems, such association was not identified for p53. Additionally, there was no association between p53 or PUMA expression levels and cytogenetic risk assessment, overall survival and event free survival.

Our results showed that p53 and PUMA expressions are significantly higher in bone marrow cells of MDS patients compared to healthy controls. This finding may be especially helpful in the diagnosis of hypocellular and normocellular MDS cases. The observation that PUMA expression increases during transformation while the expression of p53 is not significantly altered and disappearance of the correlation between p53 ve PUMA suggests that PUMA alterations might be a late event during the development of MDS or additional abnormalities occurring in high risk MDS may induce PUMA with p53 independent mechanisms. However, studies with higher number of cases comparing bone marrow samples from before and after transformation are needed for a more conclusive statement.

References: