Abstract

Myelodysplastic syndrome (MDS) is a heterogeneous group of diseases characterized by ineffective hematopoiesis which is caused by damage of differentiation of pluripotent haematopoietic stem cells. *TP53* gene mutations are identified approximately in 10% of MDS and represent a negative prognostic factor. Altered *TP53* gene expression may have similar effect as the mutation. Mutations or deregulated expression of this gene have an impact on many cellular processes including apoptosis, DNA repair, cell growth and angiogenesis.

In this work, the expression mRNA levels of genes involved in p53 signalling pathway were studied in $CD34^+$ pluripotent haematopoietic cells from bone marrow of patients with low-risk MDS.

MDS patients showed increased expression of genes involved in apoptosis induction, regulation of cell cycle and DNA repair (*BAX, BBC3, CCNE1, CDC25A, CDKN1A, FAS, GADD45A*) as compared to healthy subjects. The patients with *TP53* mutation had decreased expression of apoptotic genes (*BAX, PIDD, TRAF2*) and increased gene expression of apoptotic inhibitor (*BCL2A1*), indicating a reduced activity of apoptotic pathways and that way the pathological cell clone may gain a growth advantage. Deregulation of 21 genes (*BAX, BBC3, EGR1, KAT2B, MDM2* etc.) was observed in patients with del (5q) compared to those without the deletion. The univariate analysis showed that, in addition to the *TP53* mutation, the change in *BTG2, CCNH, CDK4* and *E2F3* gene expression also affected the overall survival of MDS patients. In summary, the results show that low-risk MDS patients have an overall deregulated p53 signalling pathway even without significant change in *TP53* gene expression and, moreover, not only the mutation alone may affect overall survival of the patients.

Key words: myelodysplastic syndrome, *TP53* gene, mutation, del(5q), gene expression