ABSTRACT

The myelodysplastic syndrome (MDS) is a group of hematopoietic clonal disorders resulting in the inefficient production of myeloid lineage blood cells, with the prevalence of patients older than 65 years. One of the possible treatment options for MDS is 5-azacytidine and 5-aza-2‘-deoxycytidine therapy. These compounds have been shown to cause the induction of cell-cycle arrest, cell differentiation and/or apoptosis. The *in vitro* experiments with 5-aza-2‘-deoxycytidine indicated that this compound causes the premature cellular senescence, a state of the irreversible cell-cycle arrest. We have asked, whether 5-azacytidine, as a molecule with similar structure, is capable of causing the same effect. This treatment strategy could be beneficial in case that the negative pro-inflammatory effect of senescent cells on their surroundings can be nullified. In this thesis we have shown that 5-azacytidine induces DNA damage response, which is described as a fundamental event for the onset of the cell senescence. We tested 5-azacytidine treated HeLa cells for several markers of the cell senescence – the increase of the β-galactosidase activity, the PML and PML nuclear bodies and the formation of persistent DNA damage signaling lesions – albeit all these markers were positive, it was the very low increase in values that lead us to the conclusion that 5-azacytidine does not cause the onset of senescence in HeLa cell line under the conditions comparable to the standard treatment protocol that has been used for the MDS patients. However, according to our results, 5-azacytidine does induce the increase in the secretion of interleukin IL6 and TGFβ. These results, if further confirmed on additional cell lines and *in vivo*, could provide valuable help for therapy modification.