Abstract

Neuroblastoma is the most common extracranial solid tumor that occurs during infancy. Despite the great progress has been made in contemporary clinic medicine some forms of neuroblastoma disease are still found very difficult to treat . This work focuses on the effects of histone deacetylase inhibitors (HDAC) in the neuroblastoma cell lines. It is known that HDAC inhibitors may contribute to recurrence of the tumor cells by affecting the chromatin structure and thus increase the expression of critical tumor suppressor genes. These genes activate apoptotic pathways that may even be independent of caspases. We observed the efficiency of used HDAC inhibitors as under standard conditions an in hypoxia (1 % O_2). Inadequate amount of oxygen supply is one of the characteristic features of tumors and it also may contribute to chemoresistance. With the hypoxia-induced chemoresistance of tumor cells, the influence of HIF-1α is expected. Some HDAC inhibitors reduce the amount of HIF-1α in hypoxia and thus HIF transcription factor activity. Thus, the first part of this study is concerned with the acquisition of suitable experimental arrangement for the monitoring of induction of cellular death in human neuroblastoma cell lines SK-N-AS and UKF-NB-3. Secondly, this paper provides the evaluation of the influence of culture conditions (standard; hypoxic, 1% O_2) on the induction of cell death by cisplatin, valproic acid, trichostatin A and sodium butyrate in these cell lines. In the following experiments it was found, that cellular death induced by valproic acid under the given conditions can occur independently of the activated caspases. However, it was not absolutely proved that this apoptosis is induced by AIF translocation to the cell nucleus.

(In Czech)