Change of expression of the Tel/Aml1 regulated genes by the effect of histon deacetylases inhibitors.

Background: Acute lymphoblastic leukaemia is one of the most frequent leukaemias in children. It has in most cases very good prognosis and about 80% patients will be cured by chemotherapy or stem cells transplantation. ALL is caused by various genetic aberrations, one of them, translocation 12;21 is the matter of interest in this work. By our hypothesis the fusion protein Tel/Aml1 causes changes in the regulation of several genes important for the maturation of B lymphocytes. The mechanism is supposed to be based on change of chromatin state due to recrution of complex of histon deacetylases.

The use of inhibitors of histon deacetylases, like Valproic acid, could lead to reinduction of expression of the repressed genes and thus to promotion of differentiation. If that hypothesis would prove to be correct, Valproic acid could be considered as the potential cure for this type of leukaemia.

Material and methods: we have identified 21 genes downregulated by Tel/Aml1 using array technology. 9 of them, CD40, ANTXR2, PDGFRB, WDR7, ACK1, HRMT1L1, PAK1, MGMT and ARD1, we tested by RT-PCR on cell lines REH and NALM6. We used two series of samples for every line, one influenced by VPA and the second as control, each serie had ten samples. We measured the amount of transcripts of the selected genes in these series and counted, if there was increase of expression in VPA samples in comparison with control. Statistical analysis was done by Mann-Whitney test.

Results and conclusion: in five of our genes we found increase of expression induced by VPA – CD40, ANTXR2, PDGFRB, WDR7 and ACK1. But only for WDR7 and ACK1 wasn't found increase of expression in NALM6 line. For the other four genes – HRMT1L1, PAK1, MGMT and ARD1 – we haven't detected any increase in expression in any of our two cell lines. Genes ACK1 and WDR7 are thus potential targets for further studies.

Klíčová slova: leukémie, TEL/AML1, HDAC, PCR, změna exprese, B lymfocyt
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