Monitoring of molecular changes in rhabdomyosarcomas (RMS) – abstract:

Introduction: Rhabdomyosarcomas (RMS) are most common soft-tissue sarcomas of childhood. They are subclassified into two major subtypes - embryonal RMS (E-RMS) and alveolar RMS (A-RMS). Both variants express MyoD1 gene. MyoD1 gene is often published as specific marker for RMS. MyoD1 belongs among myogenic regulatory factors (MRF). Loss of heterozygosity (LOH) seems to be potential molecular marker for RMS. LOH occurs frequently at 11p15 region, where also MyoD1 gene is located.
Purpose: We studied LOH frequency at the 11p15 region in A-RMS and E-RMS. Then we measured MyoD1 m-RNA level by quantitative real time PCR (RQ-RT-PCR) and judged MyoD1 specifity for RMS and its use in monitoring minimal diseminated desease (MDD). We compared results from LOH analysis with MyoD1 expression data to determine whether LOH influenced level of MyoD1 transcript or not.
Materials and methods: We examined 36 RMS and 8 non-RMS patients using LOH analysis. We used 3 microsatellite polymorphic markers (D11S921, D11S1307, D11S1888) from the MyoD1 region. We examined primary tumors and constitutional sample (peripheral blood or bone marrow aspirate) from the same patient using fragment analysis at genetic analyzer ABI PRISM 310. We monitored the level of MyoD1 m-RNA using absolute quantification at Light Cycler 2.0 Roche.
Results: In the study 12/14 (86%) informative E-RMS patients, 7/22 (32%) informative A-RMS patients and 3/8 (38%) informative non-RMS patients demonstrated LOH on at least one of the microsatellite loci at the 11p15 region. Results from quantitative expression study showed that level of MyoD1 m-RNA is a little higher in A-RMS then in E-RMS. We also reported here that MyoD1 mRNA is not specific for RMS, but can be amplified from samples of many other tumors and in normal muscle tissue. From correlation between LOH and level of MyoD1 m-RNA resulted that deletion in the 11p15 region didn't lead to decrease of MyoD1 mRNA expression.
Conclusion: Our study demonstrates, that MyoD1 gene is neither specific molecular marker for RMS diagnosis, nor it isn´t suitable for monitoring resection borders in vicinity of tumor (expression in muscle tissue). Its detection may be used for monitoring of MDD dynamics. LOH is very frequent in E-RMS, less frequent in A-RMS, but it occurs also in some non-RMS patients.

Key words: rhabdomyosarcomas (RMS), loss of heterozygosity (LOH), microsatellite, absolute quantification , MyoD1 gene, minimal disseminated desease (MDD),
Klíčová slova: rabdomyosarkomy (RMS), ztráta heterozygosity (LOH), mikrosatelit, absolutní kvantifikace, MyoD1 gen, minimální diseminovaná nemoc (MDN)