RAS MUTATIONS AND POLYMORPHISM 81T/C IN SPORADIC MEDULLARY THYROID CARCINOMA

Sykorova, Vlasta[1]; Dvorakova, Sarka[1]; Vaclavikova, Eliska[1]; Halkova, Tereza[1]; Ryska, Ales[2]; Kodet, Roman[3]; Kodetova, Daniela[3]; Betka, Jan[5]; Duskova, Jaroslava[6]; Vlcek, Petr[4]; Novak, Zdenek[7]; Bendlova, Bela[1]

[1]Institute of Endocrinology, Dept. of Molecular Endocrinology, Prague, Czech Republic; [2]Charles University Faculty of Medicine and University Hospital, The Fingerland Department of Pathology, Hradec Kralove, Czech Republic, Czech Republic; [3]2nd Faculty of Medicine and Faculty Hospital Motol, Department of Pathology and Molecular Medicine, Prague, Czech Republic; [5]1st Faculty of Medicine and Faculty Hospital Motol, Charles University, Department of Otorhinolaryngology and Head and Neck Surgery, Prague, Czech Republic;[6]1st Medical Faculty, Charles University, Institute of Pathology, Prague, Czech Republic; [4]2nd Faculty of Medicine, Charles University, Department of Nuclear Medicine and Endocrinology, Prague, Czech Republic; [7]Institute of Endocrinology, Department of Clinical Endocrinology, Prague, Czech Republic

Background/Purpose: The role of *RAS* mutations in the pathogenesis of sporadic medullary thyroid carcinoma (MTC) and polymorphism 81T/C in *H-RAS* gene in thyroid cancer has been recently suggested. The aim of our study was to determine the rate of *RAS* mutations and polymorphism 81T/C in a large cohort of sporadic MTC.

Methods: Our cohort consisted of 388 sporadic MTC (340 peripheral blood samples and 48 MTC tissues). All samples were genotyped for polymorphism 81T/C using TaqMan probes. The frequence of the polymorphism was correlated with 186 healthy controls. The presence of somatic mutations in *H-*, *K-* and *N-RAS* genes in 48 MTC tissue samples (21 *RET*-positive and 27 *RET*-negative) was determined by direct sequencing.

Results: The mutation in codon 13 of the *H-RAS* gene was detected in three patients and the mutation in codon 61 in five patients. In the *K-RAS* gene the mutation in codon 61 in one patient was detected. No mutation in *N-RAS* gene was found. All detected *RAS* mutations were found only in *RET*-negative MTC (33.3%). Any difference neither in frequencies of polymorphism 81T/C between patients and controls (36.97% vs. 36.29%) nor its relation to clinical-pathological features was revealed.

Discussion & Conclusion: Although we did not prove any influence of polymorphism 81T/C in *H-RAS* gene, it seems that mutations in *RAS* genes play an important role in the development of sporadic *RET*-negative MTC.

Supported by IGA MH CR NT 13901-4 and MH CZ 00023761.