

Cervical cancer is due to high incidence the third most commonly diagnosed gynecological cancer in the Czech republic. More than 50% of these tumors are diagnosed in advanced stage (st. IIB and higher) and therapy is more difficult than in lower stage tumors. The standard treatment method for locally advanced cervical cancers is combined oncological therapy including external beam radiotherapy, brachytherapy and concomitant chemotherapy. This treatment provides good tumor control, but there is also a risk of late complications in irradiated area. Severe late complications affect 10-15% of patients. It is still not possible to predict late complications and therefore detection of valid predictive factors for high tissue radiosensitivity could help to identify patients with increased risk before therapy. Knowledge of such predictive factors would also help to individualize the treatment.

New molecular biological methods brought new findings about cancerogenesis, cell cycle regulation and cellular reaction to the radiation damage. It was hypothesized, that mutation of genes involved in DNA damage repair or cell proliferation are one of causes of high tissue radiosensitivity.

The aim of our study was to evaluate relations between *ATM* and *TGFβ1* polymorphisms and late tissue toxicity in patients treated for cervical carcinoma by chemoradiotherapy at the Department of Oncology and Radiotherapy of Faculty Hospital Hradec Králové. The second purpose was validation of methods for gene polymorphisms analysis.

The study included 55 patients with locally advanced cervical cancer (FIGO IIB and higher) treated by chemoradiotherapy. Two test tubes of anticoagulated blood were collected from each patient. DNA was extracted from leucocytes and after that the presence of tested polymorphisms was investigated at the Institute of Clinical Biochemistry and Diagnostics of Faculty Hospital Hradec Králové. Statistical analysis was performed at the Institute of Biostatistics and Analyses, Masaryk University Brno.

We didn't prove association between single polymorphisms of candidate genes *ATM* and *TGFβ1* and late toxicity after chemoradiotherapy. On the other hand we established significant association between compound homozygous haplotype of gene *TGFβ1* – Triple homozygot (- 509C>T, 1552delAGG a L10P) and late complications grade III-IV (p=0,021) and grade I-IV (p=0,012). Our project also contributed to improvement of methods for investigation of genetic markers.

According to our study and new publications compound haplotypes or genotypes seem to be more useful for explanation of relation between late tissue toxicity and genetic factors than single polymorphisms of candidate genes.