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Single nucleotide polymorphisms in EGFR gene in NSCLC patients

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Lung cancer is a leading cause of mortality, taking pandemic proportions worldwide and Non-small-cell lung cancer (NSCLC) is the most frequent lung cancer type. Epidermal growth factor receptor (EGFR) was used as a potent biomarker for the development and implementation of NSCLC target therapy. Still, it was noticed that not all of the NSCLC patients responded equally to therapy, so it was proposed that polymorphisms might be one of potential cause of these differences affecting EGFR gene regulation. It was shown that single nucleotide polymorphisms (SNPs), namely -216G>T (rs712829) and -191C>A (rs712830) located in promoter region and 181946C>T (D994D) (rs2293347) in exon 25, could regulate activity of EGFR. This study was part of my PhD and one of purposes was to represent frequency of EGFR polymorphisms in population from Republic of Serbia and to identify potential risk factor for developing lung cancer phenotype. Tobacco smoking is cause of premature death and Republic of Serbia takes high place in annual mortality in Europe from lung cancer. We have genotyped those SNPs and to our knowledge that was the first time to show their genotype frequencies for NSCLC patients in Republic of Serbia. For this genotipisation procedure a sensitive, specific and optimized method was demanded. We used polymerase chain reaction-restriction length polymorphism (PCR-RFLP), that allows wide modifications, but its' optimisation might be time and cost consuming. All of obstacles were overcome and we have successfully optimized and performed PCR-RFLP, followed by direct sequencing, indeed. Based on this study, environmental factor like tobacco consumption and genetic susceptibility are potent risks for NSCLC patients in Republic of Serbia. Namely we have shown that GG genotype of EGFR polymorphisms -216G/T, was a risk factor for smokers to develop non small call lung cancer, so T allele might have protective role. Acknowledgement: The study was financially supported by the Ministry of Science, Republic of Serbia, 175056.



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