ABSTRACT

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Title of diploma thesis: Genetic polymorphism in the NBS1 gene for diagnosis and treatment of patients with cervical carcinoma

The aim of this diploma thesis is to find optimal methods for screening of mutation 657del5 and estimate frequency of heterozygotes and homozygotes for the mutation 657del5 in population of the Czech republic.

In the first section of the theoretical part is comprehensively pointed out the effect of factors affecting the integrity of genetic information and the formation of mutations in DNA. On the contrary, the second section devotes to the ability of cells to respond to this damage. In detail, the thesis devotes to the NBS1 gene and its product nibrin. In the complex MRE11/Rad50/NBN nibrin is an important member of the mechanisms of repair of double strand breaks NHEJ (non-homologous end joining) and HR (homologous recombination).

The thesis is focused on nibrin and its functions, but also to mutations that prevent these functions and causes genetic disease Nijmegen breakage syndrome. Nibrin is translated from the sequence of the NBS1 gene. Gene NBS1 appears in population with several various mutations, which are spreaded worldwide. But in the thesis is discussed higher frequency of mutation 657del5 in population of Central and Eastern Europe.

657del5 mutation was investigated by two methods – the fragmentation analysis and real-time PCR in the experimental part of the work. Selection of the best method was based on sensitivity, the usability for the screening and the time and cost of requirements. As the most optimal method was selected real-time PCR. This method was used for screening of mutation 657del5 in group of 177 persons from the Czech republic. Frequencies of heterozygotes and homozygotes was fix on 1,1 % and 0 %. The frequency of mutant allele 657del5 was calculated at 0,6 %. The results of screeaning showed the population frequency of heterozygous individuals is 1:88.