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**Title: The role of iron concentration and alterations in genes associated with iron metabolism in cancer.**

**Keywords:** level of iron, gene, metabolism, ferritin, transferrin, cancer

**Introduction:** Iron plays an important role in many metabolic processes, is included in the delivery of oxygen to cells and redox processes. Deficiency and excess of iron can lead to multiple organ failures. The latest studies show that the iron can significantly influence the risk of cancer development and progression. Scientists reported association between high serum iron level and the risk of colon, liver, stomach and breast cancers. The low iron level was detected in patients with colorectal, breast, bladder and lung cancers. However, there are also studies in which authors did not find any correlation between iron levels and the risk of cancer. The discrepancies between studies might be explained in part by the influence of other factors e.g. genetic variants in proteins involved in iron metabolism and redox processes.

**Aim:** The aim of the study was to analyze correlation between of the serum Fe level, Fe parameters and variations in genes coding proteins involved in iron metabolism with occurrence of lung, prostate, colorectal and breast cancers.

#### **Materials and methods:**

The study group consisted of 850 cancer patients, including breast (300), lung (200), prostate (200) and colon (150), and equal number of healthy controls matched to cases by sex, year of birth (+/- 3 years), cancer family history among I<sup>o</sup> relatives, smoking (+/- 10%) and adnexectomy status in group with breast cancer.

From all individuals were collected serum samples and analyzed iron concentration and iron metabolism parameters (UIBC, concentration and transferrin saturation and serum ferritin). Serum samples from cancer patients were collected at the time of cancer diagnosis, before treatment. In addition, seven variants in seven genes (rs1799945 in *HFE*, rs3817672 in *TFRI*, rs10421768 in *HAMP*, rs1049296 in *TF*, rs4880 in *SOD2*, rs1001179 in *CAT*, rs1050450 in *GPX1*) associated with iron metabolism and redox processes were genotyped.

#### **Results:**

Results have shown an association of Fe level with lung, prostate and colon cancers. Fe level >1497µg/l and ferritin >301.27 were significantly associated with >2 -fold higher probability of lung cancer diagnosis, whereas Fe concentration in range 1113.51-1471.76µg/l was associated with >2-fold lower probability of prostate cancer diagnosis. In group of colon cancer probability of cancer diagnosis was significantly decreasing with increased Fe level >637.78µg/l.

Analysis of genotypes revealed and association of TT genotype in rs1049296 in *TF* gene with prostate cancer risk and GG genotype in rs10421768 in *HAMP* with lung cancer risk.

#### **Conclusions:**

Results suggest that Fe level potentially may be a diagnostic marker for lung, prostate and colon cancers. Variation in *TF* and *HAMP* genes may be significantly associated with prostate cancer and lung cancer risk, respectively.

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