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Research Area (E) Cancer and rare immune-mediated disease therapy and regulation

Assosiation of MALAT1 gene polymorphism rs3200401 and genitory cancers in Ukrainian population

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Introduction. One of the most abundant and widely conserved lncRNA is metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) also known as nuclear-enriched abundant transcript 2 (NEAT2).Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) was originally indicated as metastasis prognostic factor in patients with early-stage non-small cell lung cancer (NSCLC), but later studies identified its abundant expression in normal tissues (e.g. heart, lung, kidney, pancreas, liver, brain). However, the associations between *MALAT1* genetic polymorphisms with different types of cancers are less studied although there is an increasing amount of evidence in this regard.

In present study we have analyzed the association between *MALAT1* rs3200401 SNP and prostate adenocarcinoma (PA), clear cell renal cell carcinoma (CCRCC) and transitional cell bladder cancer (TCBC) emergence as well as their metastasis potential among Ukrainian patients. DNA extraction was performed from whole venous blood of 526 subjects (426 patients with genitourinary oncological processes and 100 control individuals). The allelic discrimination in *MALAT1* (rs3200401) SNP was done by RT-PCR.

Results. The results of association analysis between MALAT1 rs3200401 genotypes and cancer emergence was found in the crude recessive (Pc = 0.005; ORc = 0.268, 95% CI = 0.108-0.666) and crude additive (Pc = 0.003; ORc = 0.246, 95% CI = 0.098-0.62 – for TT genotype) models for general cancer group. After adjustment for age, sex and smoking the association was preserved both in recessive (Pa = 0.007; ORa = 0.275, 95% CI = 0.107-0.707) and additive (Pa = 0.005; ORa = 0.251, 95% CI = 0.096-0.655 – for TT genotype) models. Significant difference was also revealed in the crude recessive (Pc = 0.031; ORc = 0.101, 95% CI = 0.013-0.814) and crude additive (Pc = 0.026; ORc = 0.092, 95% CI = 0.011-0.75 – for TT genotype) models in CCRCC group. In contrast, after the adjustment for covariates the association was lost both in recessive (Pa = 0.064; ORa = 0.134, 95% CI = 0.016-1.121), and additive (Pa = 0.053; ORa = 0.122, 95% CI = 0.014-1.028 – for TT genotype) models of inheritance. Significant association was found in the crude dominant (Pc = 0.008; ORc = 0.475, 95% CI = 0.274-0.825), crude over-dominant (Pc = 0.046; ORc = 0.55, 95% CI = 0.306-0.989) and crude additive (Pc = 0.024; ORc = 0.504, 95% CI = 0.278-0.914 – for CT genotype) models in TCBC group. But after the using of multivariable logistic regression analysis with adjustment for age, sex and smoking the significant difference was obtained in the dominant (Pa = 0.018; ORa = 0.504, 95% CI = 0.286-0,889) and additive (Pa = 0.045; ORa = 0.534, 95% CI = 0.289-0,987 – for CT genotype) models, but not in the over-dominant (Pa = 0.077; ORa = 0.579, 95% CI = 0.316-1.06) model. It was also revealed significant protective effect for TT genotype both in crude recessive (Pc = 0.004; ORc = 0.161, 95% CI = 0,047-0,555) and crude additive (Pc = 0.005; ORc = 0.168, 95% CI = 0.048-0.589) models for PA. Moreover, after the adjustment for age and smoking the significant association was preserved in recessive (Pa = 0.005; ORa = 0.164, 95% CI = 0.047-0.577) as well as additive (Pa = 0.006; ORa = 0.17, 95% CI = 0.048-0.609 – for TT genotype) models.

Perspectives. In further studies we are going to explore the functional significance of this SNP and estimate the expression rate of *MALAT1* depending on rs3200401 genetic variant.