c.268G>A substitution in *NTHL1* gene in Polish polyposis patients

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Polyposis of gastrointestinal tract are high risk factor of colorectal cancer development. Despite of high risk of colorectal cancer the risk of extracolonic feature is pretty high. Polyposis are the features of the risk syndromes such us FAP, PJS, JPS, SPS. In significant percentage of cases the genetic causes of disease is unknown. Recent reports indicated biallelic mutations in the *NTHL1* gene, which is involved in baseexcision repair (BER), as predisposing to an elevated risk of colorectal cancer (CRC). We aimed to evaluate the significance of the p.Q82* truncating variant in predisposition to intestinal polyposis by assessing its frequency in Polish polyposis patients. We genotyped 644 Polish polyposis patients and 634 controls and we found the p.Q82* variant in four polyposis patients; in three, it was homozygous (OR=6.90, P value=0.202). We also looked closer at the disease course in patients carrying NTHL1 mutations. Two homozygous patients also presented other neoplasia. In the family case, we noticed the earlier presence of polyps in proband and early hepatoblastoma in his brother. We cannot univocally confirm the relationship of p.Q82* with increased risk of CRC. However, homozygous p.Q82* was 10-fold more frequent in patients without other mutations identified, which makes reasonable NTHL1 gene screening in this group. We conclude that in the case of polyposis patients, without polyposis causing mutation detected, the NTHL1 gene screening should be recommended.