

ABSTRACT

Obesity is a risk factor for development of cardiovascular disease, diabetes type 2 and some cancers. Newly detected genetic risk factor for body weight is the *FTO* gene ("fat mass and obesity associated").

The aim of this thesis was determine 1) whether the presence of risk alleles correlate with BMI in Czech population and to determine 2) whether there is an association between variants in the *FTO* gene and risk of myocardial infarction/ acute coronary syndrome (MI/ ACS), 3) renal failure (ESRD), or 4) incidence of colorectal cancer (CRC). We analyzed polymorphisms rs17817449 (first intron) and rs17818902 (3rd intron) using by PCR-RFLP and then also RT PCR. We found an association of the first intron variant (but not the 3rd one) and BMI in Czech control population. We have detected an association of 1st intron SNP and BMI changes during the intervention study in obese children, but not in obese females. We found a correlation between the risk allele and increased risk of ACS (OR 1.49) in patients with MI. In patients with ESRD was detected association between the risk allele and the risk of disease (OR 1.37). We didn't confirmed the association between rs17817449 and the development of CRC. Representative selected groups of the Czech populations "MONICA" and "HAPPIE" were used as controls.

One possibility could be the potential impact of polymorphism on the relative telomere length (RTL). We detected in a study of pre- and postmenopausal women from Prague (3PMFs) that carriers of at least one risk allele have shorter rTL.

The exact mechanism of the *FTO* effect on disease determination is not yet known, however, the *FTO* exhibit a DNA demethylase activity. The difference between global DNA methylation status of individuals with different genotypes for rs17817449 in healthy control population were analyzed.