**ZNF259 rs964184 genetic variant is associated with metabolic syndrome in a Portuguese population**

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**Background:** Zinc finger protein (ZPR1) encoded by the ZNF259 gene has been associated with defects in transcription and cell cycle progression. Additionally, the promoter site of ZPR1 binds to peroxisome proliferator-activated receptor gamma (PPARG), which plays a crucial role in insulin sensitivity and obesity. It's not consensual in its association with Metabolic Syndrome (MetS).

**Aim:** To estimate the influence of the ZNF259 rs964184 variant in MetS appearance.

**Methods:** A case-control study was performed with 3134 subjects (mean age 52.8 ± 8.1 years, 76.4% male) recruited from the Research Unit database, a regional quality clinical registry of hospital admissions. 1756 were patients with MetS and 1378 controls without MetS. MetS was diagnosed according to the International Diabetes Federation (IDF) criteria. The ZNF259 rs964184 C>G was genotyped with the TaqMan PCR assay (Applied Biosystems 7300 Real-Time). The bivariate analysis evaluated the genotypic and allelic distribution in the two groups, with and without MetS. Multivariate Logistic Regression assessed the variables independently associated with MetS.

**Results:** There were significant differences in genotype and allele distributions for the ZNF259 C>G variant between patients with MetS and without MetS. Wild-type genotype CC was increased in the non-MetS group, whereas the risk GG was higher in patients with MetS (P = 0.008). Similarly, C allele frequencies were significantly higher in the non-MetS group, whereas the G allele was highly present in MetS population (P = 0.002). After multivariate logistic regression, GC genotype (OR = 1.23; 95% CI: 1.05 – 1.45; p = 0.011) and GG genotype (OR = 1.59; 95% CI: 1.01 – 2.50; p = 0.047) remained as independent risk factors for Metabolic Syndrome.

**Conclusions:** This study presents novel data and findings that may have important implications for assessing MetS risk in our population. For the first time in a Portuguese population, we demonstrated that ZNF259 genetic changes are significantly associated with more than 60% increased probability of having Metabolic Syndrome.