**TAS2R38 VARIATION AND BITTER TASTE PERCEPTION:**

**ANALYSIS OF GENDER, AGE AND LIFESTYLE INTERACTIONS**

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**Background and Objectives**: In the new era of Precision Medicine, Cardiovascular Precision nutrition aims to prevent and manage cardiovascular risk factors and diseases by tailoring dietary interventions or recommendations to the individual's genetic background and other individualized characteristics. Taste is one important factor in determining food consumption, obesity risk and other cardiovascular phenotypes. The variability in the perception of bitter taste is highly determined by genetics. Common polymorphisms in the TAS2R28 gene have been associated with bitter taste in several studies. However the potential modulations by gender, age and lifestyle factors have been scarcely investigated. Our aim was to analyze the association between the A49P (rs713598) polymorphism and bitter taste perception, as well as the interactions between the polymorphism and gender, age and smoking.

**Methods**: We carried out a cross-sectional study in 1265 participants (median age 41 years; 484 males and 781 females) in the OBENUTIC study, a case-control study in a Mediterranean population. Cases (n=289) were obese subjects and controls non-obese subjects recruited from the general population. All were administered a direct tasting of concentrations of 5.6 mM of phenylthiocarbamide (PTC), a TAS2R38 agonist. The intensity of taste perception to PTC was noted on a 0 to 5 scale. The rs713598 polymorphism was determined.

**Results:** After adjustment for gender, age, obesity and smoking (n=284 smokers), the TAS2R38-A49P (rs713598) polymorphism was strongly associated with bitter taste perception (0.52+/-0.1 in AA-non tasters; 2.5+/-0.1 in AP and 2.9+/-0.1 in PP; P=9.4x10E-127). Age (P=5x10E-9), gender male (P=3x10E-5) and smoking (P=0.039) were associated with lower bitter taste perception. We obtained a statistically significant interaction between the polymorphism and age (P-int=0.002), but not for gender (P-int=0.103) or smoking (P-int=0.203).

**Conclusions**: The TAS2R38-A49P (rs713598) polymorphism is strongly associated with bitter taste sensitivity. However this association was heterogeneous by age.