Insulin-like factor 5 - a novel orexigenic hormone is dysregulated in obesity


Background:
Insulin-like peptide 5 (INS5) is a gut hormone produced by L-cells in the colorectal epithelium. The biological role of INS5 is poorly investigated and current knowledge about this hormone is limited by the fact that it is involved in the regulation of appetite, control of β-cell development and fertility in mice. Nothing is known about the function of this gut hormone in humans. In this study we have explored associations between serum levels of INS5 and multiple metabolic and hormonal variables in lean and obese men and women as well as effects of external interventions (e.g. food consumption, glucose loading test and bariatric surgery) on circulating levels of this newly discovered hormone.

Subjects and Methods:
INS5 levels were measured in serum samples by ELISA. 25 lean and obese females and 23 lean and obese males were included in the study. All cohorts were fully characterized with anthropometric, metabolic and hormonal parameters and correlations between INS5 concentrations and those parameters were evaluated. Furthermore we measured INS5 levels in 10 lean and obese individuals after an overnight fasting, after a meal and during an oral glucose tolerance test (OGTT). In addition 15 morbidly obese patients were tested before and after six months after they underwent weight loss intervention (bariatric surgery).

Results:
We found gender specific differences in basal INS5 serum levels in a cohort of healthy lean humans (n=48; males n=23, females n=25). In contrast no significant gender specific differences in basal serum INS5 levels in a cohort of obese humans (n=48; males n=23, females n=25) were observed (Figure 1).

Anthropometric, metabolic, inflammatory and hormonal parameters were measured before and sixth months after bariatric surgery. All parameters improved dramatically six months after the intervention (Table 2).

We found significant lower INS5 levels after weight loss which was induced by bariatric surgery. Furthermore we observed significant lower INS5 levels between patients that were obese with and without T2DM before and after the intervention (Figure 3).

Influence of nutrition and glucose on INS5 levels: A) INS5 serum levels were measured before and 30, 60, 90 and 120 minutes after a meal. There were no significant acute changes of INS5 after a meal. B) INS5 serum levels were measured before the glucose load and 30, 60, 90 and 120 minutes after. INS5 levels tend to decrease in obese males and females at 90 and 30 min, respectively (Figure 4).

Summary and Conclusion:
We found gender-specific differences in INS5 levels in lean individuals. Negative influence of insulin resistance and T2DM on INS5 in obese individuals may indicate a link between β-cell function and INS5 regulation. INS5 levels decreased after weight loss which might be due to an effect of adipose tissue on the biosynthesis of INS5 or changes in the metabolic and inflammatory profile after weight loss. Therefore, INS5 may become an interesting target for the development of new therapeutic agents to treat metabolic disorders.