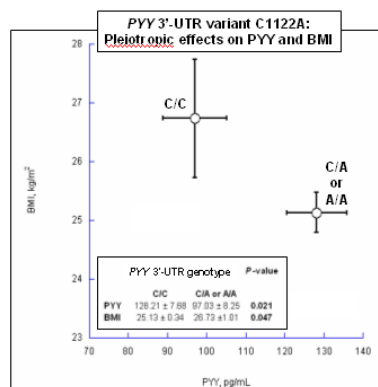


PEPTIDE YY 3'-UTR POLYMORPHISM REGULATES PLASMA PYY LEVEL AND ASSOCIATES WITH METABOLIC SYNDROME TRAITS.

Pei-an Betty Shih, Lei Wang, Gen Wen, Caroline Nievergelt, Manjula Mahata, Srikrishna Khandrika, Bruce A. Hamilton, Sushil K. Mahata, Daniel T. O'Connor. Division of Nephrology, University of California, San Diego.

Obesity is a significant contributor to hypertension and subsequent cardio-renal diseases risk, therefore the investigation of genetic background that predisposes individuals to obesity is important for prevention of downstream cardio-renal disease. Circulating Peptide YY (PYY) is known for its appetite and energy expenditure regulating



properties; linkage and association studies have also suggested the *PYY* gene contributes to susceptibility for obesity, abdominal fat, and Type 2 diabetes. To explore whether common SNPs at the human *PYY* gene influence plasma PYY, body weight and other cardio-renal disease risk factors, we systematically resequenced *PYY* gene, and genotyped 3 potentially functional common SNPs in a

twin study sample to determine individual SNP and haplotype associations. We also experimentally validated the marker-on-trait associations using *in cella* *PYY* 3'-UTR/reporter analysis in rat PC12 chromaffin cell line. We have demonstrated that plasma PYY is highly heritable, and provided evidence of pleiotropy for plasma PYY with body mass index (BMI). In addition to PYY and BMI, *PYY* 3'-UTR SNP also significantly associates with total cholesterol, ApoB, and leptin. In summary, *PYY* genetic variation confers susceptibility not only to obesity, but may also contribute to development of metabolic syndrome and increase risk for subsequent cardio-renal disease.