P12: METABOLOMICS ASSOCIATED WITH GWAS(MGWAS) RELATED TO THE BASAL METABOLIC RATE(BMR) IN OVERWEIGHT/OBESE KOREAN WOMEN.

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Backgrounds: In previous GWAS work in obese/overweight 77 Korean women, five new loci associated with BMR and BMI, including NRG3, OR8U8, BCL2L2-PABPN1, PABPN1, and SLC22A17 were identified. This study aimed to identify key metabolites and metabolic pathways controlled by significant genes (mGWAS).
Methods: Through the ultra performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS), the data were analyzed using partial least-squares discriminate analysis (PLS-DA) score plots. Possible metabolic pathways related to lean and obesity were detected by metabolites associated with GWAS.
Results: Waist, Lean body mass, body fat mass were strongly affected by BMI rather than BMR. However, plasma TG and TC were significantly higher in obesity with Low BMR than in lean with High BMR. The levels of metabolites such as lyso-phosphatidylcholines (LPC) with saturated fatty acids (C14:0, C16:0), branched-chain amino acids (BCAA; Leu, Ile, Val), aromatic amino acids (AAA; Phe, Trp, Tyr), uric acid (UA) and arginine were increased, but LPCs with unsaturated fatty acids (C18:1, C18:2, C20:3, C20:4, C20:5) and medium chain acyl-carnitine (AcyCN) were decreased in obesity classified by either BMI or BMR. Targeting to NRG3, BCL2L2 PABPN1 and SLC22A17 genes from GWAS, the metabolites (mGWAS) were positively associated with UA, succinic acid, arginine, uridine and aspartic acid. UA and arginine were common metabolites from both the general metabolomics and targeted obese genes classified BMI and BMR.
Conclusion: The metabolites associated with the disturbance of beta -oxidation, lipid, BCAA and AAA catabolism, urea cycle and purine/pyrimidine metabolism play the important roles in the obesity classified by either BMI or BMR in middle age of Korean women. This research enables us to better understand obesity and increases the predictability of the obesity related risk by mGWAS.