Glutathione S-Transferase (GST) M1, but Not GSTT1, Genotype Influences Plasma Proteomic Profiles in Caucasian and East Asian Young Adults

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Glutathione S-transferase (GST) M1 and T1 are major detoxifying enzymes that have been associated with a number of chronic diseases, but their effect on various physiological pathways remains unclear. We investigated the association between the common GSTM1 and GSTT1 genotypes and multiple disease-related high-abundance proteins of the plasma proteome in young Caucasian ($n = 476$) and East Asian ($n = 352$) adults. Overnight fasting blood samples were collected, and 54 high-abundance plasma proteins from several physiological pathways were quantified by mass spectrometry-based multiple reaction monitoring (LC-MRM/MS). Subjects were genotyped for GSTM1 and GSTT1 deletion polymorphisms. Principal component analysis was used to identify proteomic profiles, and differences in individual protein concentrations between genotypes were assessed by ANCOVA. Among Caucasians, 19 proteins differed between GSTM1 genotypes ($P < 0.05$), with all protein concentrations being higher among the null genotypes. However, only complement C3 reached the Bonferroni-corrected significance threshold for multiple testing ($P < 0.0009$). Among East Asians, three proteins differed between GSTM1 genotypes ($P < 0.05$) with higher concentrations among the null genotypes, but none reached the Bonferroni level of significance. Protein concentrations did not differ between GSTT1 genotypes in either ethnicity. These findings suggest that GSTM1 may have novel physiological effects related to immunity and cardiometabolic disease.

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