Peripheral blood mononuclear cell gene expression and plasma protein profiles are differentially affected by glucose and lipid tolerance tests

UCD Conway Institute and Institute of Food and Health, School of Public Health and Population Science, University College Dublin, Belfield, Dublin 4, Ireland

Peripheral blood mononuclear cells (PBMC) are an easily accessed tissue type that show differential gene expression following nutritional stimulus in vivo\(^1\). This study addressed the hypothesis that the PBMC transcriptomic signature and the associated metabolic phenotype would be differentially regulated by lipid vs. carbohydrate nutritional challenges\(^2\).

An oral lipid tolerance test (OLTT) and a glucose tolerance test (OGTT) were completed in a ‘lean’ cohort of ten individuals selected from a representative sample of 200 healthy Irish adults aged 18–60 years (age: 24.6 ± 3.84 years, BMI: 24.5 ± 2.2 kg.m\(^{-2}\)). Fasting and postprandial peak plasma and PBMC samples were taken at 1 and 4 h post-OGTT and -OLTT, respectively. RNA was hybridised to Affymetrix Human Gene ST 1.0 arrays. Microarray data were normalised using RMA and R/BioConductor determined differentially expressed genes. The metabolic profile of volunteers was characterised including plasma TAG, NEFA, glucose, insulin and inflammatory profiles were determined.

A total of 2292 genes were differentially expressed following OLTT. No single genes were significantly differentially expressed following OGTT. The genes showing greatest changes in expression post-OLTT include CENPK, CLC, OCLN, TMEM176A, FOLR3, ANKRD22, VNN1 and PGA5 (all log Fc > ±1.3). Key genes involved in lipid metabolism (LPL, LRP1, PLIN3) and inflammation (IKBKG, NLRP3) were increased following the OLTT, but not OGTT. The KEGG pathway showing greatest enrichment, Fc gamma R-mediated phagocytosis, also contains genes related to inflammation. Most notably, the ERK-activated cPLA2 gene is present, which modulates arachidonic acid (AA) and EPA release from DAG. Given the central role of AA/EPA, this may affect downstream eicosanoid, prostaglandin, leukotriene or resolvin production.

The transcriptomic signature will be related to the metabolic phenotype, which included an increase in plasma glucose following the OGTT (\(P<0.0001\)), elevated plasma TAG post-OLTT (\(P = 0.0354\)) and lower NEFA concentration following both OGTT (\(P<0.0001\)) and OLTT (\(P = 0.001\)). Interestingly the increase in inflammatory gene expression was associated with greater postprandial plasma IL-6 (\(P = 0.0091\)) and EGF (\(P = 0.0053\)) and a decrease in IFNG (\(P = 0.104\)) concentrations post-OLTT, with no such changes post-OGTT.

In conclusion, the OLTT induced a pro-inflammatory state in the PBMC transcriptome and plasma protein markers implicated in insulin resistance, the Metabolic Syndrome and T2DM, with no such response following OGTT.

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