*Proceedings of the Nutrition Society* (2011), **70 (OCE3)**, E59 doi:10.1017/S0029665111000991

*Joint Irish Section and American Society for Nutrition Meeting, 15–17 June 2011, 70th anniversary: 'Vitamins in early development and healthy ageing: impact on infectious and chronic disease'*

# Metabolic, inflammatory and transcriptomic markers are differentially regulated by carbohydrate *v.* lipid nutritional challenges

C. M. O. Grada, M. J. Morine, C. Morris, E. Dillon, M. Ryan, M. Walsh, L. Brennan, M. J. Gibney and H. M. Roche

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

Dietary lipids and carbohydrates have key relevance to metabolic health. Postprandial lipid challenges modulate transcriptomic activity in PBMC[1]. This study addressed the hypothesis that the metabolic phenotype and associated PBMC transcriptomic signature would be differentially regulated by lipid *v.* carbohydrate nutritional challenges.

An oral lipid tolerance test (OLTT) and oral glucose tolerance test (OGTT) were completed in a lean, young male cohort of nine individuals selected from a representative sample of 200 healthy Irish adults aged 18–60 years (age: 25, SD 3.84 years, BMI: 23.45, SD 2.3). Plasma was collected at fasting and multiple postprandial time points. Fasting and postprandial peak 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. A Bayesian algorithm[2] was used to adjust for patient effect. The metabolic profile of volunteers was characterised including plasma TAG, glucose, insulin and c-Peptide. Inflammatory profiles were determined.

There was a marked difference in metabolic marker response between challenges that included an increase in plasma glucose following the OGTT ($P<0.0001$), elevated plasma TAG post-OLTT ($P<0.0001$) and lower NEFA concentration following both OGTT ($P = 0.0031$) and OLTT ($P = 0.0002$). Both insulin and c-peptide area under the curve (AUC) were greater following OGTT compared with OLTT. Interestingly the increase in inflammatory gene expression was associated with greater postprandial plasma IL-6 and EGF along with a relative decrease in IFNG concentrations post-OLTT compared with OGTT.

A total of 705 genes were differentially expressed following OLTT. One hundred and forty-eight genes were differentially expressed following OGTT. Genes of particular biological relevance showing differential expression following OLTT related to metabolic health include socs1, irs2 and ifng. Following OGTT, Toll-like receptor signalling pathway gene expression was reduced, including jun, junb, fos, fosb, il8 and mip-1α.

In conclusion, the OLTT-induced plasma protein markers implicated in insulin resistance, the metabolic syndrome and T2DM along with a corresponding pro-inflammatory state in the PBMC transcriptome. In contrast, OGTT showed a reduction in inflammatory gene transcription within PBMC.

This work was conducted as part of a clinical trial (NCT01172951), funded under the Food for Health Research Initiative (NDP 2007–2013; 07FHRIUCD1) by the Department of Agriculture, Fisheries and Food, the Health Research Board and the Department of Health and Children. HMR is supported by Science Foundation Ireland Principal Investigator Programme (06/IM.1/B105).

1. Bouwens M, Grootte Bromhaar M, Jansen J *et al*. (2010) *Am J Clin Nutr* **91**, 208–217.
2. Johnson WE, Li C & Rabinovic A. (2007) *Biostatistics* **8**, 118–127.