

Summer Meeting hosted by the Irish Section, 16–19 July 2012, Translational nutrition: integrating research, practice and policy

## Dietary fat manipulation and not apolipoprotein E (epsilon) genotype has a significant impact on cytokine production – insights from the SATgene study

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It is recognised that polymorphisms in the apolipoprotein (*APOE* (epsilon) gene play an important role in cardiovascular disease (CVD) risk<sup>(1)</sup>. In addition to modestly higher plasma cholesterol, a pro-inflammatory phenotype has been reported in carriers of the *APOE4* allele<sup>(2)</sup>. Our aim was to explore the impact of chronic dietary fat manipulation on cytokines production according to *APOE* genotype.

Fifty two healthy participants (mean age 50 (SD 9) y and BMI 26.4 (SD 4.3) kg/m<sup>2</sup>) were prospectively recruited according to *APOE* genotype (*n* = 26 E3/E3 and *n* = 26 E3/E4), and assigned to three iso-energetic diets; low fat (LF, 24% energy (E) from fat, 8%E saturated fat (SFA)), high fat-high saturated fat (HSF, 38%E fat, 18%E SFA), and HSF with 3 g/d docosahexaenoic (HSF-DHA) diets, each for an 8-wk period in a sequential design. Fasting blood samples were collected at baseline and at the end of each of the intervention diets. Concentrations of interleukin (IL)-1β, IL-6, IL-8, IL-10 and tumour necrosis factor (TNF)-α were measured in cell free supernatants derived from whole blood culture assays stimulated for 24 h with either 0.05 or 1 μg/ml of bacterial lipopolysaccharide (LPS), using a cytokine multiplex antibody bead kit (Invitrogen)<sup>(3)</sup>. Cytokine production was corrected for the number of monocytes in the whole blood cultures.

Cytokine	Baseline (pg per 10 <sup>3</sup> monocytes)		LF diet (pg per 10 <sup>3</sup> monocytes)		HSF diet (pg per 10 <sup>3</sup> monocytes)		HSF-DHA diet (pg per 10 <sup>3</sup> monocytes)		P
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
IL-1β	9.46 <sup>a</sup>	0.75	11.5 <sup>a</sup>	0.98	11.1 <sup>a</sup>	0.86	10.1 <sup>a</sup>	1.09	NS
IL-6	48.9 <sup>a</sup>	3.96	62.5 <sup>a</sup>	7.40	55.7 <sup>a</sup>	4.47	52.5 <sup>a</sup>	5.53	NS
IL-8	380 <sup>a</sup>	46.5	454 <sup>a</sup>	38.6	419 <sup>a</sup>	44	348 <sup>a</sup>	34.7	NS
IL-10	1.14 <sup>b</sup>	0.13	1.41 <sup>a</sup>	0.14	1.21 <sup>ab</sup>	0.10	1.09 <sup>b</sup>	0.09	0.036
TNF-α	2.94 <sup>b</sup>	0.38	3.90 <sup>ab</sup>	0.47	4.60 <sup>a</sup>	0.51	4.99 <sup>a</sup>	0.69	0.012

Effect of dietary fat manipulation on cytokine production (pg per 10<sup>3</sup> monocytes) by 0.05 μg/ml LPS-stimulated whole blood cultures of fifty two healthy subjects. NS, not significant. <sup>a,b</sup>Mean values within a row with unlike superscript letters were significantly different (*P* ≤ 0.05).

No diet\*genotype interactions were found, although a significant diet interaction was observed for TNF-α and IL-10 production after stimulation with 0.05 μg/ml LPS (*P* = 0.012 and *P* = 0.036 respectively) and 1 μg/ml LPS (*P* = 0.006, *P* = 0.049). TNF-α concentrations were higher (*P* ≤ 0.05) after the HSF diet compared with the baseline, whereas IL-10 was higher (*P* ≤ 0.05) after the LF diet compared with the baseline and HSF-DHA diet. Our study data suggests a greater sensitivity of monocyte cytokine production to the quality and quantity of dietary fat, than *APOE* genotype in healthy participants.

1. Song YQ, Stampfer MJ & Liu SM (2004) *Ann Intern Med* **141**, 137–147.
2. Jofre-Monseny L, Minihane AM & Rimbach G (2008) *Mol Nutr Food Res* **52**, 131–145.
3. Chowdhury F, Williams A & Johnson P (2009) *J Immunol Methods* **340**, 55–64.