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File: ■ Virgin Olive Oil (*Olea europaea*)
■ Gene Expression
■ Metabolic Syndrome

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RE: Consumption of Virgin Olive Oil Represses the in vivo Expression of Pro-Inflammatory Genes in Patients with Metabolic Syndrome

Camargo A, Ruano J, Fernandez JM, et al. Gene expression changes in mononuclear cells from patients with metabolic syndrome after acute intake of phenol-rich virgin olive oil. *BMC Genomics*. 2010;11:253. DOI: 10.1186/1471-2164-11-253.

Human, animal, and in vitro studies have shown that the acute intake of virgin olive oil (*Olea europaea*) with a high phenol content results in a greater reduction in pro-inflammatory, pro-oxidant, and pro-thrombotic markers than does consumption of virgin olive oil with a low phenol content. These studies showed that olive oil modified gene expression coding for proteins involved in cellular mechanisms related to oxidative stress resistance, lipid metabolism, and other mechanisms associated with atherosclerosis development. However, it is not known whether these changes in gene expression are attributable to oleic acid or to polar minor components of olive oil, possibly as a consequence of their antioxidant activity or through a direct interaction with receptors, enzymes, or transcription factors. Thus, the objective of the present randomized, double-blind, crossover study was to identify those genes that undergo changes in expression in peripheral blood mononuclear cells (PBMCs) in patients with metabolic syndrome.

Twenty subjects (9 men and 11 women) from the Lipids and Atherosclerosis Unit at the Hospital Universitario Reina Sofia (Cordoba, Spain) who met at least 3 of the criteria for a diagnosis of metabolic syndrome, but had no chronic diseases, participated in this study. The 5 criteria used for metabolic syndrome were central obesity, high blood pressure or antihypertensive therapy, high fasting glucose, hypertriglyceridemia, and a low level of high-density-lipoprotein cholesterol. After a 6-week washout period, during which the subjects were instructed to abstain from vitamin, soy supplement, and drug intake, they were randomly assigned to consume a virgin olive oil-based breakfast meal (40 mL virgin olive oil; CANOLIVA®; Antonio Cano e Hijos; Cordoba, Spain) with either a low (70 ppm) or a high (398 ppm) content of phenolic compounds together with 60 g of white bread. All subjects maintained a low-fat, carbohydrate-rich diet throughout the study to eliminate the potential effect of usual dietary habits. Crossover followed a 1-week washout period between breakfasts. A 24-hour avoidance of phenol-rich food

included a 12-hour fast just prior to each breakfast. Compliance was evaluated by reviewing dietary records and food-frequency questionnaires completed by the participants.

Venous blood samples were collected 0, 30, 60, 120, and 240 minutes after the consumption of the breakfast meal for the measurement of non-esterified fatty acids, triglycerides, high-density-lipoprotein cholesterol, glucose, and insulin. Areas under the curve (AUCs) for these variables were calculated and compared between the 2 interventions. PBMCs were isolated within 2 hours of blood collection for a gene expression microarray analysis. Total RNA was extracted from the PBMCs, purified, and then quantified. Each microarray analysis involved a comparison of total RNA from PBMCs obtained after intake of olive oil with a high phenol content with that after intake of olive oil with a low phenol content.

No significant differences in the AUCs for non-esterified fatty acids, triglycerides, high-density-lipoprotein cholesterol, glucose, or insulin were observed between the 2 interventions. A total of 98 genes were found to be differentially expressed in human PBMCs following use of phenol-rich olive oil ($P \leq 0.01$), 79 of which were underexpressed and 19 of which were overexpressed. The most underexpressed genes (1.95- to 2.74-fold) were as follows: *G0S2, EGR2, EGR1, FOSB, IL1B, NR4A2, EGR3, RASGEF1B, CXCL1,* and *PTGS2.* The most overexpressed genes (1.46- to 1.57-fold) were as follows: *CA1, RAP1GAP, GYPB, FN1,* and *SELENBP1.* A sex analysis showed that 32 genes were differentially expressed in both men and women; 218 genes were differentially expressed only in men, and 111 genes were differentially expressed only in women. Many of these genes are known to be linked to type 2 diabetes, obesity, and dyslipidemia or are involved in inflammatory processes mediated by transcription factor NF-κB, activator protein-1 transcription factor complex AP-1, cytokines, mitogen-activated protein kinases, or arachidonic acid pathways.

The results of this study indicate that the consumption of virgin olive oil rich in phenolic compounds repressed the in vivo expression of several pro-inflammatory genes, which consequently diminished the inflammatory profile of PBMCs. The authors conclude that the "results provide at least a partial molecular basis for [a] reduced risk of cardiovascular disease observed in Mediterranean countries, where virgin olive oil represents a main source of dietary fat." Further research is necessary to determine whether prolonged feeding maintains these effects. It remains undetermined whether one or several phenolic components are primarily responsible for these benefits, or if the entire phenolic fraction has synergistic effects.

—Brenda Milot, ELS

Enclosure: Referenced article is an Open Access article via BioMed Central.