**OliveNet™ Journal Club**

**Expert review of literature related to olives and olive oil**

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**Title**

Gene pathways associated with mitochondrial function. Oxidative stress and telomere length are differentially expressed in the liver of rats fed lifelong on virgin olive oil, sunflower or fish oils

**Author(s)**

Varela-Lopez et al

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**Keywords**

Virgin olive oil, sunflower oil, fish oil, aging, telomere length, liver function, mitochondrial function, gene pathways, microarray

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**Summary**

This is a unique study in which the effects on the liver of rats fed lifelong on three different dietary fat sources (virgin olive oil, sunflower oil, or fish oil), were examined. Although the liver is generally thought to respond well to aging, it was chosen for investigation as it well that dietary patterns affect the aging of this organ since it has key metabolic functions (2). Indeed, the prevalence of nonalcoholic fatty liver disease, which may encompass simple nonalcoholic hepatic steatosis and may progress to more serious fibrosis, cirrhosis, certain cases, hepatocellular carcinoma, is age-related (3, 4). The current study builds on previous work indicating that there is a strong association between macronutrient manipulation and dietary fat source and oxidative stress in the liver through changes in composition of the mitochondrial membrane resulting in altered function of the mitochondrial electron chain transport system and changes in mitochondrial DNA (5, 6). Therefore, in this study the effects of three different (common) dietary fat sources: virgin olive oil (high in monounsaturated fatty acids), sunflower oil (rich in n6 polyunsaturated fatty acids, and fish oil (high in n3 polyunsaturated fatty acids), were investigated. In this experiment rats in each group (12 per group), were fed a regular diet supplemented with either virgin olive oil, sunflower oil, or fish oil from weaning until either six months (young), or 24 months (old). The livers were then analysed at six and 24 months to compare the organs in young and old animals.

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**Key points and implications**

The authors investigated a number of parameters ranging from simple weight and histopathological analyses to more involved molecular studies including microarray-based gene expression studies. The findings, as reported by the authors, are summarized as follows: 1) the weight of the livers at 24 months were higher for the fish oil group compared to the virgin olive oil and sunflower oil groups, 2) the liver mitochondrial fatty
acid profile reflected the type of dietary fat; oleic acid was highest in the virgin olive oil group, linoleic acid highest in the sunflower oil group, and docohexaenoic acid highest in the fish oil group, 3) at 24 months significantly higher levels of fibrosis were observed by histopathology in the sunflower oil group, 4) the sunflower oil group displayed higher mitochondrial area and perimeter and lower mitochondrial density, 5) compared to young animals, higher expression of Tfam protein levels (associated with aging), were observed for the sunflower oil groups whereas, at 24 months the fish oil displayed lower expression level of Tfam compared to the virgin olive oil and sunflower groups, 6) at 24 months lowest levels of protein carbonyls (oxidative modification) were shown with virgin olive oil, 7) at 24 months lowest activity of mitochondrial transport electron chain complex 1 activity was observed with fish oil, 8) higher oxygen consumption ratio (indicator mitochondrial respiratory activity) in the virgin olive oil and sunflower oil groups compared with analogous groups of young animals, 9) at 24 months telomere length was greatest in the fish oil group, and 10) a comparison between analogous young and old groups indicated that gene expression changes were apparent in the fish oil (higher expression of seven genes in old rats, related to mitochondrial dysfunction (3), oxidative stress (2 including Keap1, a key component of the well-known Nrf2 antioxidant pathway), cell cycle (2), and telomere length (1, Xrcc1, important for genome stability)), and virgin olive oil (higher expression of eight genes in old rats, related to mitochondrial dysfunction (2), oxidative stress (4 including Keap 1), and telomere length (2, Xrcc1 and Xrcc6)). Overall the findings highlight the importance of dietary fat intake and effects on liver aging, with virgin olive oil and fish oil aiding age-related adaption through changes in gene expression. As indicated by the authors, when considering all of the data, virgin olive oil is appears to be the fat of choice for preserving liver function with age. Given the potential significance of this study with regards to dietary recommendations, it would be very beneficial to see this type of work extended to other organs and in vivo model systems.

Related publications
1. A. Varela-Lopez et al., Gene pathways associated with mitochondrial function, oxidative stress and telomere length are differentially expressed in the liver of rats fed lifelong on virgin olive, sunflower or fish oils. The Journal of nutritional biochemistry 52, 36-44 (2017).