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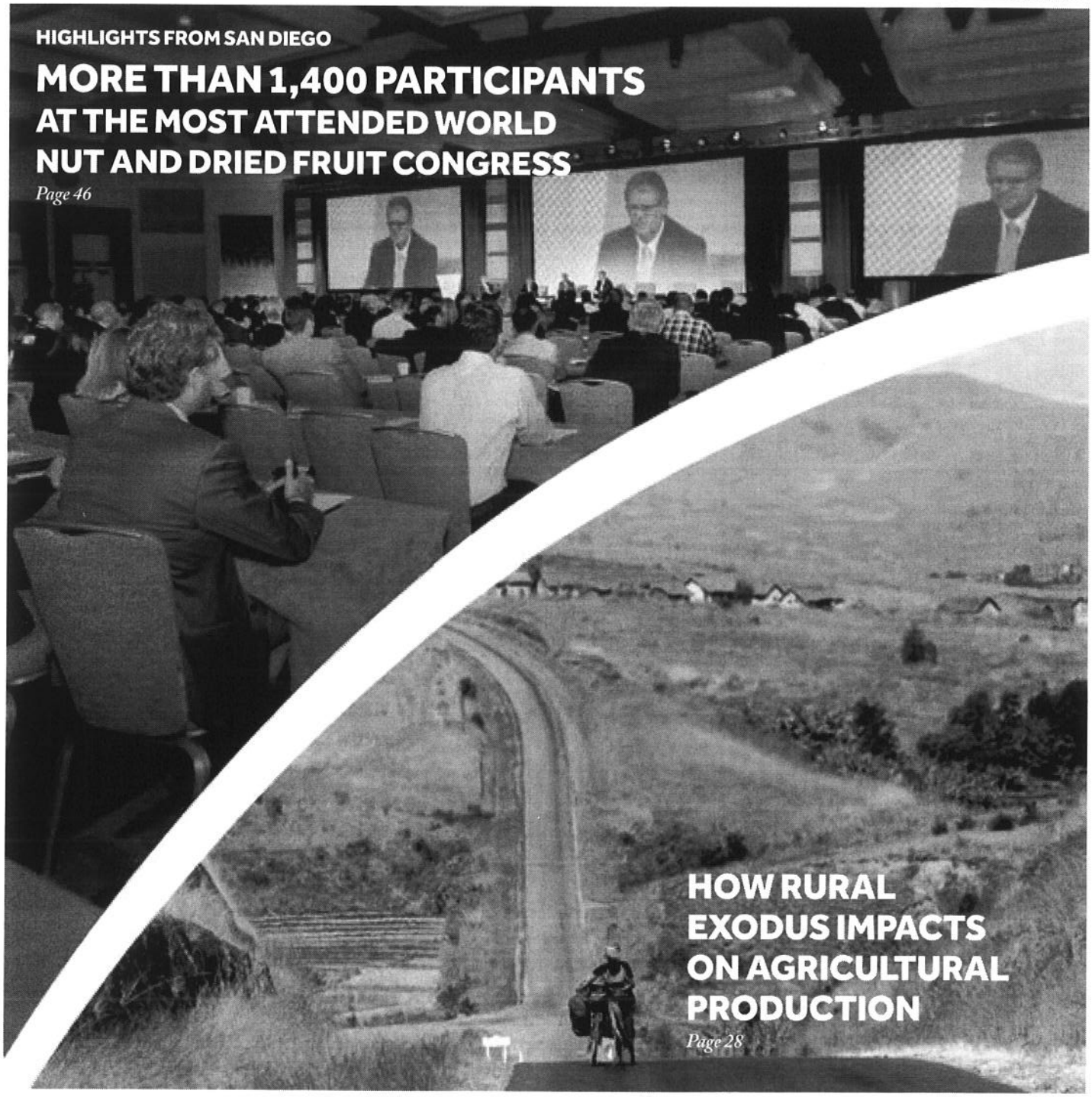

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MARINE AND VEGETABLE OMEGA-3 FATTY ACIDS ACT SYNERGISTICALLY AND ARE PARTNERS: UPDATES FROM THE PREDIMED STUDY

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Results from PREDIMED support and reinforce the beneficial properties of omega-3 and alpha-linolenic acid, suggesting that marine and vegetable omega-3 fatty acids act synergistically and are partners rather than competitors in reducing death risk.

The presence of fats in our daily diet is essential to maintain a correct health status. However, among fats, saturated, unsaturated and their subtypes, have a differential role. Actually, the quality of dietary fat is well-recognized as being even more important than the total amount of fat for the prevention of cardiovascular diseases (CVD), including coronary heart disease (CHD) and overall death.[1] Generally, CVD risk can be reduced by decreasing the intake of trans-fat intake from partially hydrogenated vegetable oils. Moreover, it can also be diminished by reducing saturated fatty acids (SFAs) and replacing them with a combination of polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs).[1,2] In 2013, the main findings from the PREvención con Dieta MEDiterránea (PREDIMED) study, a randomized primary-prevention nutrition trial, in individuals at high CVD risk[3], showed that Mediterranean diets, which were high in MUFAs and PUFAs, as they were supplemented with extra-virgin olive oil or nuts (15g walnuts, 7.5g almonds and 7.5g hazelnuts), and low in SFAs and trans fat, were effective for the prevention of clinical events of CVD compared with a low-fat control diet.[3] In fact, last prospective subanalysis from PREDIMED trial expanded these results as researchers evaluated the role of fats on CVD. We showed that the intakes of MUFAs and PUFAs were associated with a lower risk of CVD and death, whereas SFA and trans-fat intakes were associated with a higher risk of CVD. Importantly, we also found that replacement of SFAs with MUFAs, and PUFAs or of trans-fat with MUFAs was inversely associated with CVD.[4]

Beyond the effects of SFA versus MUFA and PUFA, different studies suggest a cardioprotective role of some fatty acids (FA) belonging to the omega 3 (ω-3) category. These are essential fatty acids as the body cannot make them from other intermediators. Omega-3 fatty acids are an integral part of cell membranes throughout the body and affect the function of the cell receptors in these membranes. Moreover, they provide the basis for generating hormones that regulate a series of blood processes and cellular inflammation, and bind to receptors in cells that regulate genetic function.[5] According to these effects, ω-3 FA have been shown to help prevent coronary heart disease and stroke, and may play protective roles in cancer and other metabolic conditions.[6] There are three main subtypes of ω-3. Long ω-3 FA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), come mainly from fish, so they are sometimes called "marine ω-3". Alpha-linolenic acid (ALA) is shorter than EPA and DHA and it is the most common ω-3 fatty acid in most Western diets. It is found in vegetable oils and nuts (especially walnuts), flax seeds and flaxseed oil, leafy vegetables, and some animal fat, especially in grass-fed animals.

EPA and DHA have been widely studied and their intake has been associated with a lower risk of CHD.[7] However, the human body generally uses ALA for energy, and conversion into EPA and DHA is very limited. Despite of this, since few years, ALA is being a new focus of attention due to its putative preventive role on CVD,[8] but results are somewhat controversial according to the latest systematic review and meta-analysis conducted by Pan and collaborators.[9] In fact, the combinatory effects of ALA and EPA plus DHA, or the effects of ALA in the context of high EPA and DHA have not been assessed yet.

To evaluate it, Aleix and collaborators have recently studied the role of ALA in a background of high marine ω-3 FA (EPA and DHA) intake in the PREDIMED cohort. This work has been published in the prestigious *Journal of the American Heart Association*.[10] We investigated whether meeting the International Society for the Study of Fatty Acids and Lipids' recommendations for dietary ALA (at least 0.7% of total daily energy) and/or long ω-3 (≥500 mg/day) at baseline was related to different outcomes through the follow-up (approximately 5 years) in the PREDIMED trial. We showed that meeting the ALA recommendations was associated with a significant 28% lower risk of all-cause death and non-significantly to fatal CVD. On the other hand, meeting the long ω-3 fatty acid consumption recommendations was associated with a 39% lower risk of CVD and 46% of CHD. The association was found non-significant for all-cause

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The highest protection against all-cause death occurred in participants meeting both recommendations (alpha-linolenic acid and long omega 3 fatty acids) showing a reduction of 37%.

death. However, the highest protection against all-cause death occurred in participants meeting both recommendations (ALA and long ω-3 FA) showing a reduction of 37%. Interestingly, in these analyses we found that ALA intake was highly correlated with walnut consumption, reinforcing the high amount of ALA present in walnuts, the highest amount of ALA among nuts (8.493g/100g dry roasted walnuts).[11] In fact, the health promoting benefits of the consumption of walnuts and other types of nuts have been widely ascribed but not limited to its fatty acid profile.[12–14] Therefore, as a complex matrix of different macro- and micronutrients and antioxidant molecules, nuts may act on different modulatory pathways to exhibit their beneficial health properties including CVD prevention.

Overall, beyond dietary quantity and quality of fat, the different types of unsaturated FA play an important role on health. Results from PREDIMED support and reinforce the beneficial properties of ω-3 FA intake, and demonstrate the fact that even in a context of frequent high consumption of seafood, ALA is inversely associated to all-cause death even though protection from cardiovascular and cardiac death is limited to long ω-3 (EPA plus DHA). Importantly, higher protective role is found when both recommendations are met. This suggests that marine and vegetable ω-3 FA act synergistically and are partners rather than competitors in reducing death risk.

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