Omega-3 nutritional supplementation improves amyloid-beta immunity through specialized pro-resolving mediators

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Alzheimer disease and Minor cognitive impairment (MCI) patients have a defect in the phagocytosis of amyloid-beta 1-42 (Abeta1-42) and abnormally low or high activation of inflammation. Objectives: We are studying the effects of the omega-3 drink (Smartfish, Oslo, Norway) and the specialized pro-resolving mediators (SPMs) resolvins, protectins and maresins on phagocytosis, inflammation and cognition. Methods: Phagocytosis of FITC- Abeta1-42 was measured by flow cytometry (expressed as mean fluorescence intensity (MFI)) and fluorescence microscopy; resolvin D1 (RvD1) by ELISA; inflammation by RNA-Seq of PBMCs; cognition by Minimental state examination (MMSE) score; and macrophage phenotype by the M1 markers CD54 (ICAM-1) and CD80 (costimulatory protein) and the M2 markers CD163 (scavenger receptor) and CD206 (mannose receptor). Results: 12 MCI patients and 2 pre-MCI patients have been followed on daily nutritional supplementation with omega-3 fatty acids (DHA 1 gm and EPA 1 gm in the Smartfish drink, Oslo Norway) for 5-18 months (the first visit was without supplementation and subsequent visits on supplementation). MFI increased from 530 on the first visit to 1306 on the last visit ($P<0.016$). RvD1 (n=6) increased in 3 and did not change in 3 patients. MMSE score (n= 8) improved in 7 but later declined in 4 (related to disease or noncompliance) and declined in one ApoE4 patient. Most patients had mixed macrophage phenotype with highest expression of CD54 and CD206; two had an inflammatory type but one switched to a mixed type on a subsequent visit. On the initial visit, FITC- Abeta1-42 phagocytosis by macrophages of most patients was improved more by in vitro treatment with resolvin D1, resolvin D2 or maresin D1 than by omega-3 emulsion (Fig.1A), whereas on later visits omega-3 was generally more effective (Fig.1B). RNA sequencing (n=4) showed inflammatory signature in 2 and non-inflammatory signature in 2. Conclusions: In MCI patients, omega-3 have positive effects on immunity against Abeta1-42 through SPMs.

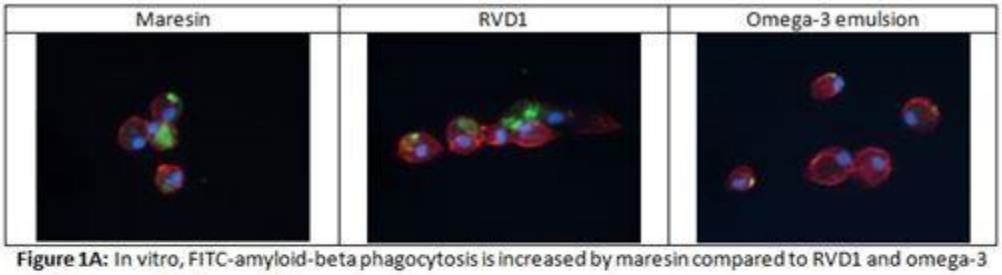

Figure 1A: In vitro, FITC-amyloid-beta phagocytosis is increased by maresin compared to RVD1 and omega-3 emulsion respectively on visit 1.

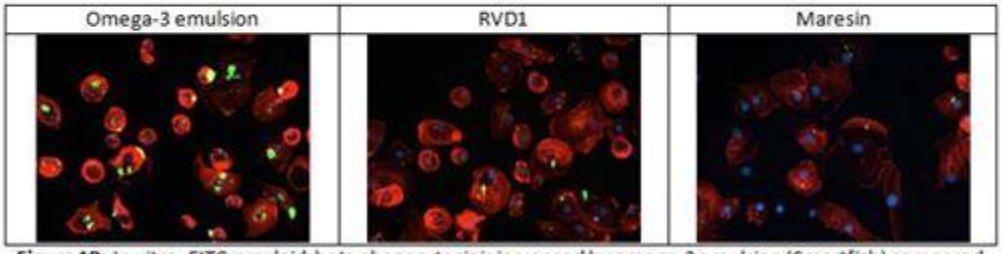

Figure 1B: In vitro, FITC-amyloid-beta phagocytosis is increased by omega-3 emulsion (Smartfish) compared to RVD1 and maresin respectively on visit 6.

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