(n-3) Polyunsaturated Fatty Acids Modulate the Expression of Functionally Associated Molecules on Human Monocytes In Vitro¹,²,³

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ABSTRACT Diets rich in (n-3) polyunsaturated fatty acids (PUFA) are associated with suppression of the immune system, but the mechanisms are unclear. Specific immune responses are initiated by antigen-presenting cells. This study examines the in vitro effect of the (n-3) PUFA eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) on the expression of cell surface molecules required for normal antigen-presenting cell function on human blood monocytes. Monocytes were incubated with or without EPA or DHA for 48 h at 37°C. Following incubation, expression of major histocompatibility complex (MHC) class II molecules (HLA-DR, -DP and -DQ) and adhesion molecules [intercellular adhesion molecule-1 (ICAM-1) and leucocyte function associated antigen-1] was quantified by flow cytometry. In the presence of EPA alone there was a significantly lower median intensity of expression of HLA-DR and ICAM-1 relative to incubations without EPA. In contrast, significantly greater median intensities of expression of HLA-DR and -DP were observed following incubation with DHA. In parallel experiments, where monocytes were simultaneously activated by the addition of interferon-gamma to the cultures, median expression intensities of HLA-DR, -DP and ICAM-1 were significantly lower in the presence of either EPA or DHA compared with incubations without the (n-3) PUFA. These findings support previous animal studies that suggest that (n-3) PUFA can influence immune reactivity by modulating antigen-presenting cell function. J. Nutr. 126: 603–610, 1996.

INDEXING KEY WORDS:
- (n-3) polyunsaturated fatty acids
- major histocompatibility complex class II
- monocytes • humans • adhesion molecules

Diets rich in (n-3) polyunsaturated fatty acids (PUFA) are associated with suppression of the immune system (Maki and Newberne 1992), and it has been reported that dietary supplementation with fish oils [rich in (n-3) PUFA] can improve the condition of patients suffering from a number of disorders involving overreactive immune responses, such as rheumatoid arthritis (Kremer 1991).

Several in vitro studies have tried to elucidate the mechanism of this immunosuppressive effect of (n-3) PUFA. Most studies have concentrated on examining the effects of fatty acids on lymphocyte function (recently reviewed by Yaqoob and Calder 1993) because of the central role that this cell type plays in orchestrating immune responses. Less attention has been given to the effect of dietary fatty acids on the mononuclear phagocyte cell types, which initiate cell-mediated immune responses by processing and subsequently expressing antigens on their surface membranes for recognition by appropriate T cells (Unanue and Cerottini...
MATERIALS AND METHODS

(n-3) Polyunsaturated fatty acids. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were obtained from Sigma (Poole, Dorset, U.K.) and solubilized in 95% ethanol. Stock concentrations were stored under nitrogen until immediately prior to use.

Antibodies for immunostaining. The following MAb were used to investigate the modulatory effects of the fatty acids on cell surface antigen expression: anti-HLA-DR, -DP and -DQ (Becton Dickinson, Oxford, U.K.), anti-CD54 [ICAM-1] (Serotec, Oxford, U.K.) and anti-CD11a (LFA-1) (Serotec). Fluorescein isothiocyanate (FITC)-labeled rabbit anti-mouse immunoglobulin F(ab')2 fragment (Dako, High Wycombe, U.K.) was used as a second layer antibody to detect MAb binding. This FITC-labeled antibody was also used alone to control for nonspecific binding. Anti-CD45 (common to all leucocytes, Serotec) was used as a positive control.

Subjects. The monocytes used in this study were obtained by venepuncture from healthy, non-smoking, adult volunteers. Although several volunteers were recruited into both studies, the EPA and DHA experiments were performed on separate occasions. For the EPA study the volunteers were four males and six females (mean age 31 y, range 24–38 y). Monocytes from two males and six females (mean age 30 y, range 24–34 y) were used in the DHA study. No volunteers were receiving medication, and none had been consuming fish oil supplements or were regular consumers of oily fish. The study was approved by the Institute of Food Research ethics committee.

Purification of monocytes. Monocytes were purified by density gradient centrifugation, by the method previously described in detail (Hughes et al. 1992). Briefly, peripheral blood (usually 60 mL) from each volunteer was collected into syringes containing EDTA. Leucocyte-rich plasma was obtained by Dextran 500 sedimentation and subjected to a period of hyperosmolality. The plasma was then layered onto NycoPrep 1.068 [Nycomed Ltd, Birmingham, U.K.] in 15-mL tubes [diameter 13 mm, Falcon 2097; Becton Dickinson] that were centrifuged for 15 min at 600 × g at 22°C. The monocyte-containing fraction was aspirated and washed twice in 0.15 mol/L NaCl containing 0.04 mol/L EDTA and 10 g/L albumin by centrifuging at 600 × g for 7 min. The recovered cells were resuspended in 1 mL of culture medium [HEPES-buffered RPMI containing 5% heat-inactivated fetal calf serum, 2 mmol/L L-glutamine, 10^5 iu/L penicillin, 0.07 mmol/L streptomycin; Gibco BRL, Paisley, U.K.], counted and adjusted to 5 × 10^6 cells/L. The monocytes were greater than 95% viable, as assessed by trypan blue exclusion.
Cell culture with (n-3) PUFA. Monocytes (8 × 10^6) in a total volume of 8 mL of culture medium were cultured in 15-mL polystyrene tubes (Falcon 2097). The stock solutions of EIA and DHA were diluted in culture medium immediately before being used (to minimize oxidation) and added to the cultures at final concentrations of 66 and 61 μmol/L, respectively. Control cells were given equivalent amounts of 95% ethanol (final concentration, 0.1% ethanol). In addition, cultures in the absence or presence of EIA or DHA were performed with the further addition of IFN-γ [Genzyme, West Malling, U.K.] to upregulate surface molecule expression. This recombinant form of human IFN-γ (produced using a cDNA for IFN-γ from activated human splenocytes) was used at a previously determined optimal concentration of 4 × 10^5 units/L. After a 48-h incubation at 37°C, the cells were placed on ice for 40 min to loosen any adherent monocytes. The cells were washed twice in minimal essential medium (MEM; Gibco BRL), counted using trypan blue exclusion to assess viability (which was always greater than 90% after culture with or without [n-3] PUFA) and adjusted to a concentration of 5 × 10^6 cells/L in MEM for staining prior to flow cytometry.

Immunofluorescence. The cells were stained with the various MAb by the technique described by Parker and Haslam (1989). Briefly, 5 × 10^6 cells in 100 μL of MEM were incubated with an optimal concentration of each MAb for 30 min at 4°C. The cells were washed in MEM containing 10% Haemocell (Hoechst, Hows- low, U.K.) to reduce cell clumping, followed by the addition of the FITC rabbit anti-mouse immunoglobulin, for 30 min at 4°C. After a further washing, the cells were fixed in MEM containing 5% Haemocell and 50% methanol and then washed in PBS. The cell nuclei were then stained with propidium iodide (0.025 g/L) in the presence of ribonuclease (0.25 g/L) for 20 min at 37°C immediately prior to flow cytometric analysis.

Analysis of surface marker expression by flow cytometry. A 488-nm laser line was used to simultaneously excite FITC and propidium iodide. The instrument was calibrated daily using fluorescent 1-μm latex beads [Fluoresbrite, Polysciences, Warrington, PA]. Log FITC fluorescence was detected via a 530-nm band-pass filter and linear propidium iodide fluorescence emission via a 610-nm band-pass filter. Forward angle and 90° light scatter characteristics were also recorded for each cell, to give an indication of size and granularity, respectively, to aid in distinguishing the different populations. Monocytes were identified on this basis and gated appropriately. Therefore, the large majority of any contaminating lymphocytes present in the samples will be excluded from the subsequent fluorescence analysis, because they are generally smaller and less granular than monocytes. The percentages of FITC-positive cells (exhibiting a higher fluorescence intensity than the upper limit of the FITC-only controls without MAb) in the gated populations were determined. Cells within the gated population were greater than 90% anti-CD14 positive [as assessed using the anti-CD14 clone, B-A8 (Serotec), which reacts primarily with monocytes and, unlike some other anti-CD14 antibodies, does not react with B lymphocytes]. Contaminating lymphocytes were less than 6% anti-CD3 positive (expressed on T lymphocytes; Serotec) in all cases, and we previously observed that this separation technique produces minimal (<1%) contamination by B cells, as assessed by the expression of CD22.

The intensity of expression of the cell surface markers on monocytes was determined using a previously reported method [Hughes et al. 1992]. The anti-log of the green (530-nm) fluorescence emission was used to calculate the linear median intensity values for the monocytes stained with MAb and for the controls without MAb. The intensity of FITC fluorescence relating to bound MAb was obtained by subtracting the median linear intensity value for the control monocytes. The results are thus expressed as relative median intensity values.

Statistical analysis. Differences between pairs of [n-3] PUFA-treated and untreated samples were analyzed using the paired t test [Altman 1991]. Significance level was set at P < 0.05. Results are expressed as means and SEM unless otherwise stated.

RESULTS

Effect of eicosapentaenoic acid on surface molecule expression by monocytes

Unstimulated monocytes. After incubation for 48 h in the absence [control] or presence of 66 μmol/L EPA, no significant differences were seen in the percentage of the MHC class II molecules, but a significantly lower percentage of ICAM-1 positive cells was observed (P < 0.05) when incubations included EPA (Table 1). There was also a significantly lower median intensity of expression of both HLA-DR and ICAM-1 on the monocytes cultured in the presence of EPA (P < 0.05).

No significant differences in cell viability (as assessed by trypan blue exclusion) or in the expression of any of the surface molecules studied were observed between monocytes cultured in medium alone and monocytes cultured with 0.1% ethanol (data not shown).

Interferon-gamma-stimulated monocytes. After incubation for 48 h in the additional presence of IFN-γ, there was a significantly lower percentage of monocytes incubated with EPA expressing the MHC class II molecules HLA-DR (P < 0.01) and HLA-DP (P < 0.05) and the adhesion molecule ICAM-1 (P < 0.05) (Table 2). There was also a significantly lower intensity of expression of HLA-DR (P < 0.001) and HLA-DP (P < 0.01) and of ICAM-1 (P < 0.01) compared with con-
Control cultures. No significant differences in the expression of LFA-1 were observed.

Effect of varying the concentration of eicosapentaenoic acid. Eicosapentaenoic acid apparently had a concentration-dependent effect on the percentage of monocytes expressing ICAM-1, in both the presence and absence of IFN-γ (Fig. 1a). The percentages of monocytes expressing HLA-DR seemed to show a dose-dependent decrease only in the presence of IFN-γ. Cell viability as assessed by trypan blue exclusion was monitored at each concentration of EPA, and a slight reduction seemed to occur at concentrations of EPA greater than 66 μmol/L following the 48-h incubation period. Cell viabilities were as follows: 0 μmol/L, 97.3 ± 0.6%; 33 μmol/L, 97.3 ± 1.2%; 50 μmol/L, 96.0 ± 1.0%; 66 μmol/L, 96.3 ± 1.5%; 100 μmol/L, 94.7 ± 2.3%; 132 μmol/L, 93.0 ± 1.0% (means ± SD, n = 3).

Incubation with EPA produced a dose-dependent decrease in the median intensity of expression of HLA-DR and ICAM-1, in both the presence and absence of IFN-γ (Fig. 1b).

Effect of docosahexaenoic acid on surface molecule expression by monocytes

Unstimulated monocytes. Table 3 shows the percentages of monocytes expressing the various surface molecules after incubation for 48 h in the absence (control) or presence of 61 μmol/L DHA. In contrast to EPA, there was a significantly greater percentage of HLA-DR (P < 0.001) and HLA-DP (P < 0.05) positive monocytes following incubation with DHA. There was also a significantly greater median intensity of expression of both HLA-DR (P < 0.001) and HLA-DP (P < 0.05) on the monocytes cultured in the presence of DHA.

Interferon-gamma-stimulated monocytes. After incubation for 48 h in the additional presence of IFN-γ, there were significantly lower percentages of monocytes expressing each of the MHC class II molecules and adhesion molecules (P < 0.05) when cells were incubated with DHA (Table 4). There was also a significantly lower intensity of expression of all the surface molecules studied (P < 0.01).

### Table 1

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Positive monocytes</th>
<th>Relative median intensity of expression</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
<td>EPA</td>
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<tr>
<td></td>
<td>%</td>
<td>%</td>
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<tr>
<td>HLA-DR</td>
<td>63.1 ± 7.3</td>
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<tr>
<td>HLA-DP</td>
<td>33.8 ± 5.0</td>
<td>33.1 ± 5.7</td>
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<tr>
<td>HLA-DQ</td>
<td>13.2 ± 4.4</td>
<td>13.4 ± 3.8</td>
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<tr>
<td>ICAM-1</td>
<td>62.7 ± 8.2</td>
<td>53.6 ± 8.7</td>
</tr>
<tr>
<td>LFA-1</td>
<td>58.6 ± 10.0</td>
<td>63.0 ± 8.8</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, n = 10. *P < 0.05 (paired t test) compared with controls.

2 Abbreviations used: HLA, human leucocyte antigen; ICAM-1, intercellular adhesion molecule-1; LFA-1, leucocyte function associated antigen-1.

### Table 2

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Positive monocytes</th>
<th>Relative median intensity of expression</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
<td>EPA</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>HLA-DR</td>
<td>93.0 ± 1.2</td>
<td>83.2 ± 3.8</td>
</tr>
<tr>
<td>HLA-DP</td>
<td>79.7 ± 3.5</td>
<td>69.3 ± 5.9</td>
</tr>
<tr>
<td>HLA-DQ</td>
<td>43.7 ± 9.6</td>
<td>34.9 ± 9.2</td>
</tr>
<tr>
<td>ICAM-1</td>
<td>86.3 ± 2.5</td>
<td>72.8 ± 5.8</td>
</tr>
<tr>
<td>LFA-1</td>
<td>66.4 ± 5.0</td>
<td>55.7 ± 5.7</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, n = 10. *P < 0.05, **P < 0.01, ***P < 0.001 (paired t test) compared with controls.

2 Abbreviations used: HLA, human leucocyte antigen; ICAM-1, intercellular adhesion molecule-1; LFA-1, leucocyte function associated antigen-1.
Effect of varying the concentration of DHA. The percentages of monocytes expressing HLA-DR and ICAM-1 seemed to show a dose-dependent decrease only in the presence of IFN-γ (Fig. 2a). In common with EPA, there seemed to be a slight reduction in cell viability at concentrations of DHA greater than 61 μmol/L following the 48-h incubation period. Cell viabilities were as follows: 0 μmol/L, 95.7 ± 0.6%; 30 μmol/L, 96.0 ± 1.0%; 46 μmol/L, 94.3 ± 1.6%; 61 μmol/L, 94.7 ± 0.6%; 92 μmol/L, 93.3 ± 1.2%; 122 μmol/L, 92.0 ± 1.0% (means ± SD, n = 3).

An apparent DHA concentration-dependent decrease in the median intensity of expression of HLA-DR and ICAM-1 in the combined presence of DHA and IFN-γ was observed (Fig. 2b).

DISCUSSION

The findings in this study demonstrate that the (n-3) PUFA EPA and DHA modulate both the number of monocytes expressing surface molecules involved in their adherence and antigen-presenting function and also the amount of these surface molecules on the cells. Variability in the expression of these functionally associated molecules is capable of altering the degree of immune responsiveness of an individual to antigenic stimulation (Janeway et al. 1984). The differences in surface molecule expression were observed at levels of EPA and DHA that are achievable in blood plasma with relatively low supplementation with fish oil capsules (3 g/d) (Marangoni et al. 1993). Although the two fatty acids had opposite effects on the expression of HLA-DR by unstimulated monocytes, they both significantly inhibited the expression of HLA-DR and ICAM-1 on INF-γ-stimulated cells. Differences in the control values of monocytes expressing each surface molecule were observed between the subjects studied in the EPA study (Table 1) and those in the DHA study (Table 3).

**FIGURE 1** Effect of increasing doses of eicosapentaenoic acid on (a) the percentage of human monocytes expressing human leucocyte antigen (HLA)-DR and intercellular adhesion molecule-1 (ICAM-1) in the absence or presence (+IFN) of interferon-gamma, and (b) the median intensity of expression of these molecules, following incubation at 37°C for 48 h. Values are means ± SEM for three separate experiments.

### TABLE 3

Effect of incubation with docosahexaenoic acid (DHA) on the expression of surface molecules on unstimulated human monocytes

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Positive monocytes</th>
<th>Relative median intensity of expression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
<td>DHA</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>HLA-DR</td>
<td>37.5 ± 5.4</td>
<td>66.2*** ± 5.3</td>
</tr>
<tr>
<td>HLA-DP</td>
<td>16.2 ± 2.8</td>
<td>27.6* ± 5.1</td>
</tr>
<tr>
<td>HLA-DQ</td>
<td>8.3 ± 1.9</td>
<td>11.5 ± 2.9</td>
</tr>
<tr>
<td>ICAM-1</td>
<td>72.9 ± 7.5</td>
<td>75.3 ± 8.9</td>
</tr>
<tr>
<td>LFA-1</td>
<td>77.4 ± 6.1</td>
<td>71.0 ± 8.4</td>
</tr>
</tbody>
</table>

1 Values are means ± SEM, n = 8. * P < 0.05, *** P < 0.001 (paired t test) compared with controls.

2 Abbreviations used: HLA, human leucocyte antigen; ICAM-1, intercellular adhesion molecule-1; LFA-1, leucocyte function associated antigen-1.
particularly regarding HLA-DR expression. This probably reflects the previously reported variation in the expression of MHC class II molecules on monocytes obtained from healthy individuals (Gonwa et al. 1986). In spite of the large interindividual variation in surface molecule expression, the consistent differences observed following incubation with either EPA or DHA suggest that one of the mechanisms whereby these fatty acids may affect cell-mediated immune responses is by modulating the function of antigen-presenting cells, a crucial step in mounting an immune response.

One question raised by this study is whether a fish oil–rich diet reduces the ability of the immune system to respond to infection, with an increased risk of mortality. Chang et al. (1992) reported that fish oil consumption increased the mortality rate of mice challenged with Salmonella typhimurium, but this was observed in mice fed a diet containing 20 g/100 g fish oil. In a human supplementation study we examined the effect of 3 g fish oil/d on the expression of MHC class II molecules and adhesion molecules on peripheral blood monocytes (Hughes et al. 1996) and found that, although there was no significant difference in the percentage of monocytes expressing these molecules following 3 wk of supplementation, there was a significant reduction in the amount of each molecule present on the monocytes. In spite of these changes, the level of suppression of surface molecule expression was probably insufficient to cause a major reduction in normal immune function, because most post-supplementation levels of expression still fell within the ranges observed in a comparison group of healthy control subjects. However, the ability of [n-3] PUFA to inhibit the expression of these molecules supports the possibility that fish oil may be beneficial in the treatment of autoimmune disorders. A number of double-blind studies have reported that consumption of fish oil by patients with rheumatoid arthritis is associated with mild to moderate symptomatic improvement, including a reduction in morning stiffness and in the number of
tender joints [Kremer 1991]. The more striking inhibition of MHC class II molecules and ICAM-1 expression by EPA and DHA on IFN-γ-stimulated monocytes seen in this study may be particularly relevant to the treatment of rheumatoid arthritis, because patients with this disorder have been shown to have abnormally elevated expression of both MHC class II molecules [Firestein and Zvaifler 1987] and ICAM-1 [Wicks et al. 1992] in chronically inflamed joints. A reduction in the expression of these molecules could reduce helper T cell activation and thus decrease both the production of inflammatory cytokines and the production of antibodies by B cells at these localized sites of disease.

Several animal studies have shown that (n-3) PUFA can inhibit the expression of Ia molecules. Kelley and colleagues [1985] reported that dietary supplementation with fish oil suppresses autoimmune lupus in MRL-lpr mice and prevents an increase in macrophage surface Ia expression. Mosquera et al. [1990] showed that administration of fish oil to mice and rats by esophageal gavage reduced the percentage of peritoneal macrophages that expressed Ia in comparison with saline-gavaged controls, and Huang et al. [1992] demonstrated that fish oil-fed mice infected with Listeria monocytogenes had a reduced expression of Ia on the surface of peritoneal macrophages compared with mice fed other fat sources. In addition, EPA can inhibit the antigen-presenting function of mouse splenocytes [Fujikawa et al. 1992]. Dietary enrichment with EPA inhibited the ability of spleen cells to present antigens to murine helper T cell clones, and in vitro pretreatment of splenocytes with EPA also inhibited antigen-presenting cell function. Taken together, the results of these studies and the current study support the hypothesis that (n-3) PUFA suppress cell-mediated immune responses, at least in part, by inhibiting antigen-presenting cell function.

The results of the present study may also be of relevance to the suggested inverse relationship between long-term fish oil intake and atherosclerosis. There is increasing evidence of a chronic immune and inflammatory involvement in the formation of atherosclerotic lesions [Ross 1993], and the presence of chronically stimulated T cells within lesions and the expression of MHC class II molecules on lesional monocytes-macrophages indicate that these cells are actively participating in the local immune response occurring during atherosclerosis. Dietary fish oil supplementation studies have shown that EPA and DHA are incorporated into the lipids of advanced atherosclerotic plaques in humans [Rapp et al. 1991], and it is possible that a reduced expression of MHC class II molecules might inhibit the antigen-presenting function of the local macrophages, thereby delaying, if not preventing, lesion development.

There are several mechanisms that may be involved in the modulatory effect of (n-3) PUFA on surface molecule expression. It is possible that the incorporation of these fatty acids into the cell membrane can increase its fluidity and thus alter the expression of membrane proteins [Muller et al. 1983], possibly by influencing the vertical displacement of the proteins within the membrane. It has been shown that different proteins exhibit disparate changes in cell surface expression following alterations in membrane fluidity [Muller and Krueger 1986]. This might explain why, in contrast to HLA-DR and ICAM-1, no significant differences in HLA-DQ and LFA-1 expression were observed on unstimulated monocytes in this study. Interestingly, increasing the cholesterol content of human monocyte cell membranes, which causes a decrease in membrane fluidity, leads to a greater increase in the expression of HLA-DQ on resting monocytes than in the expression of HLA-DR and HLA-DP [Hughes et al. 1992]. However, the converse effect of EPA and DHA on the expression of HLA-DR on resting monocytes cannot readily be explained by this mechanism, because both fatty acids should increase cell membrane fluidity. The effect of these fatty acids on human monocyte membrane fluidity and the possible relationship between fluidity and the expression of these cell surface molecules are currently being examined.

It is possible that a change in eicosanoid production may also influence the expression of cell membrane molecules. An increased availability of (n-3) PUFA in membrane phospholipids results in a decreased cellular production of prostaglandin (PG) E2 and an increased production of PGE3. However, because PGE2 can inhibit the expression of Ia molecules on stimulated macrophages [Snyder et al. 1982], it is unlikely that this mechanism is a major contributor to the significant differences in surface molecules observed in this study.

In addition, it has been reported that the reduction in Ia expression by peritoneal macrophages seen in fish oil-fed mice and rats [Mosquera et al. 1990] was not related to PGE2 production by the peritoneal cells. However, because both EPA and DHA will antagonize arachidonic acid metabolism, the potential roles that eicosanoids and membrane fluidity might play in modulating cell surface molecule expression cannot be distinguished from the results of this study.

Because PUFA are more susceptible to lipid peroxidation than are monounsaturated and saturated fatty acids, an increase in monocyte cell membrane lipid peroxidation may affect the expression of cell surface molecules. It has already been demonstrated that free radicals can suppress the expression of HLA-DR [Gruner et al. 1986], and we are currently investigating the relationship between the expression of this molecule and the cellular levels of antioxidant nutrients such as vitamin E and β-carotene.

A further possibility is that EPA and DHA are directly or indirectly influencing the expression of mRNA for the various cell surface molecules. It has recently been shown that DHA can inhibit the expression of vascular cell adhesion molecule-1 (VCAM-1),
induced by interleukin-1 on human endothelial cells [De Caterina et al. 1994], in parallel with a decrease in vascular cell adhesion molecule-1 mRNA levels. De Caterina et al. (1994) concluded that the observed effect was pretranslational, but whether it resulted from a decrease in mRNA stability or a decrease in transcription remains undetermined.

In conclusion, we have shown that EPA and DHA can modulate the expression of surface molecules on human peripheral blood monocytes that are involved in their adherence and antigen-presenting function. The inhibition of MHC class II molecule and ICAM-1 expression on IFN-γ-stimulated monocytes supports the possibility that fish oil may be beneficial in the treatment of autoimmune disorders associated with abnormally elevated expression of these molecules.

LITERATURE CITED


