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Growth Inhibitory Effect of Low Fat Diet on Prostate Cancer Cells: Results of a Prospective, Randomized Dietary Intervention Trial in Men With Prostate Cancer

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Abstract

Purpose—A high fat Western diet and sedentary lifestyle may predispose men to prostate cancer through changes in serum hormones and growth factors. We evaluated the effect of a low fat diet on serum factors affecting prostate cancer cell growth by performing a prospective, randomized dietary intervention trial in men with prostate cancer.

Materials and Methods—We randomized 18 men with prostate cancer who did not receive prior therapy to a low fat (15% kcal), high fiber, soy protein supplemented diet or a Western (40% kcal fat) diet for 4 weeks. Fasting serum was collected at baseline and after the intervention to measure prostate specific antigen, sex hormones, insulin, insulin-like growth factor I and II, insulin-like growth factor binding proteins, lipids and fatty acids. LNCaP cells (ATCC®) were cultured in medium containing pre-intervention and post-intervention human serum to assess the in vitro effect of the diet on prostate cancer cell proliferation.

Results—Subjects in each group were highly compliant with the dietary intervention. Serum from men in the low fat group significantly decreased the growth of LNCaP cells relative to Western diet serum ($p = 0.03$). There were no significant between group changes in serum prostate specific antigen, sex hormones, insulin, insulin-like growth factor I and II, and insulin-like growth factor binding proteins. Serum triglyceride and linoleic acid (ω -6) levels were decreased in the low fat group ($p = 0.034$ and 0.005 , respectively). Correlation analysis revealed that decreased ω -6 and increased ω -3 fatty acid correlated with decreased serum stimulated LNCaP cell growth ($r = 0.64$, $p = 0.004$ and $r = -0.49$, $p = 0.04$, respectively).

Conclusions—In this prospective, randomized dietary intervention trial a low fat diet resulted in changes in serum fatty acid levels that were associated with decreased human LNCaP cancer cell growth. Further prospective trials are indicated to evaluate the potential of low fat diets for prostate cancer prevention and treatment.

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Keywords

prostate; prostatic neoplasms; dietary fats; fatty acids; ω -6

Epidemiological studies suggest that environmental factors associated with the Western lifestyle may promote clinical prostate cancer development and progression. One such factor that is implicated is dietary fat. Case-control and cohort studies show positive associations of total fat intake, and saturated, monounsaturated and polyunsaturated fat intake with prostate cancer risk.¹⁻³ Epidemiological studies support an inverse association between marine derived ω -3 fatty acid intake and the prostate cancer risk.⁴ Animal feeding studies using human prostate cancer xenografts and transgenic mouse models also support the potential for dietary fat modification to prevent prostate cancer development and progression.^{5,6} The mechanisms by which dietary fat impacts prostate cancer development and progression remain to be defined, including effects on the IGF system, sex hormone metabolism, free radical damage and fatty acid metabolic pathways.⁵ Soy protein, which is consumed in high quantities in the typical Asian diet but at low levels in the American diet, may also be protective for prostate cancer.⁷ In preclinical studies our group noted that combining soy protein with decreased dietary fat reduced the growth of human prostate cancer xenografts in mice.⁸

Prospective clinical trials in men with prostate cancer suggest that diet and lifestyle changes may potentially impact tumor cell biology and serum PSA levels.⁹⁻¹² Using an ex vivo bioassay developed at our laboratory we observed that a short-term low fat, high fiber diet and exercise intervention in overweight men led to a 30% decrease in serum stimulated growth of LNCaP cells in vitro.¹³ In this bioassay we compared LNCaP cell proliferation in medium containing human serum obtained before and after the diet and exercise intervention, and found decreased serum stimulated growth of LNCaP cells in post-intervention serum relative to that in pre-intervention serum. This growth inhibitory effect of post-intervention serum was likely due to decreased serum IGF-I and increased serum IGFBP-1 levels.¹³ Based on results of our prior preclinical and clinical studies we performed a prospective, randomized trial comparing a low fat (15% kcal), high fiber diet supplemented with soy protein to a Western diet (40% kcal fat) in men with untreated prostate cancer. The primary aim was to determine the effects of the diets on human serum mitogenicity on LNCaP cells. Secondary aims were to determine the feasibility of the dietary intervention and the effects on serum levels of lipids, fatty acids, sex hormones, IGF-I and II, and IGFBP.

METHODS

Patient Enrollment

The study protocol was approved by our institutional internal review board. Men with a new diagnosis of prostate cancer within the previous 2-years that had not received any prostate cancer therapies were invited to enroll. Subjects were recruited from the prostate cancer clinic at the Veterans Administration Greater Los Angeles Healthcare System from June 2001 through June 2003. These subjects either elected active surveillance or had not yet decided on a primary therapy for their prostate cancer.

Primary and Secondary End Points, and Power Calculation

The primary end point of the trial was the difference in serum stimulated LNCaP cell growth between the Western and low fat diet groups. Secondary end points were changes in weight, percent body fat, sex hormones, lipids, fatty acids, insulin, IGF-I and II, IGFBP and PSA,

and correlation analysis comparing changes in those variables with changes in serum stimulated LNCaP cell growth.

Based on pilot data from a previous 1-arm trial a sample size of 40 subjects was estimated to detect a 20% difference in the mean change in cell proliferation in the ex vivo bioassay between the groups with greater than 90% power using the Wilcoxon rank sum test. Interim analysis was done after 20 subjects were enrolled. Two subjects withdrew from the trial, including 1 before randomization for personal reasons and 1 after 9 days on the Western diet after a gout attack. Analysis in the remaining 18 subjects revealed a statistically significant difference in the change in ex vivo bioassay results between the 2 groups and, thus, enrollment was discontinued. Data on the 2 subjects who withdrew from the trial were not included in the data analysis.

Baseline Procedures and Dietary Intervention

All subjects provided a history, and underwent physical examination and a morning fasting blood draw at baseline and after 4 weeks. Body composition was determined by bioelectrical impedance and the Fred Hutchinson Cancer Research Center food frequency questionnaire was completed. Questionnaires were analyzed elsewhere. Subjects were randomly assigned (1:1) to a low fat or a Western diet group. Dietary interventions were designed to maintain patient weight. The low fat diet consisted of 15% kcal from fat, 30% kcal from protein, including 35 gm soy protein per day, and 55% kcal from carbohydrates, including 35 gm fiber per day. The Western diet consisted of 40% kcal from fat, 30% kcal from protein without soy supplementation and 30% kcal from carbohydrates providing, 10 gm fiber per day. All meals were prepared by UCLA clinical research center nutrition staff. Study subjects picked up the packaged meals 2 or 3 days per week and returned uneaten food, which was weighed by the dietary staff. Compliance was determined by the research dietitian based on weekly meetings with subjects and measurement of uneaten foods.

Serum Measurements

PSA, sex hormones (estradiol and total testosterone), insulin and lipid panels were measured at the UCLA clinical laboratory. IGF I and II, and IGFBP-1, 2 and 3 were measured at the laboratory of one of us (PC) using previously described enzyme-linked immunosorbent assay techniques.¹⁴ Serum fatty acid analysis was done at the UCLA center for human nutrition laboratory using established techniques.¹⁵ Serum was stored at -70°C and batch tested.

Ex Vivo Proliferation Bioassay

LNCaP cells were grown as previously described.⁶ The mitogenic effect of human serum on LNCaP proliferation was studied using an in house bioassay. Cells were plated at 5×10^3 per well in 96-well plates and incubated for 24 hours before changing to fresh medium containing 10% human serum or 10% fetal bovine serum as the control. Each serum sample from an individual study subject was tested twice in duplicate and the mean of these measurements was used for data analysis. Cell proliferation in medium containing human serum was measured by the CellTiter 96® Assay as previously described⁶ after 48-hour incubation at 37°C . Data are expressed as a percent of proliferating cells grown in medium containing 10% fetal bovine serum. Interassay and intra-assay coefficient of variation for the ex vivo bioassay is 6.95 and 2.98, respectively.

Statistical Analysis

Quantitative measures were compared between the groups using the 2-tailed Student t test calculated by Prism® 3.0. The paired t test was used to perform within group comparisons

before and after intervention. The 2-sample unpaired t test was used to compare groups at specific time points and the change in scores between the groups with $p < 0.05$ considered significant. Data are presented as the mean $\pm$ SEM. Correlations between outcome variables were calculated using the Spearman correlation coefficient with STATA® 9.2.

RESULTS

Table 1 lists subject baseline characteristics. There was no significant difference in age, race, prostate cancer characteristics, PSA, BMI or percent body fat between the groups. Most patients in each group were overweight or obese with a mean overall BMI of $29.7 \pm 4.2 \text{ kg/m}^2$. The mean fat mass determined by bioelectrical impedance and expressed as a percent of body weight was also increased in each group at a mean of $30.1\% \pm 3.0\%$ at baseline. The mean percent body fat mass in healthy American men 65 to 74 years old is 24.6%. Analysis of food frequency questionnaires showed that the mean intake of fat, protein and carbohydrates at baseline expressed as a percent of total energy intake was $35.8\% \pm 6.0\%$, $19.1\% \pm 2.7\%$ and $43.9\% \pm 6.9\%$, respectively.

Subjects in each group were compliant with the dietary intervention with $96.5\% \pm 6.0\%$ of prepared food consumed in the Western diet group and $98.9\% \pm 1.2\%$ consumed in the low fat group. Subjects in the low fat group lost a mean of $2.2 \pm 0.7 \text{ kg}$ during the study course and subjects in the Western diet group lost a mean of $0.4 \pm 0.7 \text{ kg}$ ($p = 0.014$ and 0.58 , respectively). The weight change was not significantly different between the groups. Post-intervention serum from subjects in the low fat group decreased LNCaP cell proliferation by $16.0\% \pm 2.4\%$ relative to pre-intervention serum ($p = 0.006$, see figure). There was a $2.4\% \pm 5.4\%$ decrease in LNCaP proliferation in post-intervention Western diet serum vs pre-intervention serum. When comparing the change in LNCaP proliferation between the low fat and Western diet groups, the decrease in proliferation was greater in the low fat group than in the Western diet group ($p = 0.03$).

There were no significant between group changes in serum levels of PSA, sex hormones, insulin, IGF-I and IGF-II, and IGFBPs (table 2). Analysis of within group changes revealed that IGF-I levels increased significantly in each group with an increase of $24.0 \pm 9.0 \text{ ng/ml}$ (11.6% increase from baseline) in the Western diet group ($p = 0.029$) and an increase of $58.0 \pm 16.4 \text{ ng/ml}$ (24.0% increase) in the low fat group ($p = 0.008$). In analyzed lipids the only significant change was a $102.5 \pm 36.4 \text{ mg/dl}$ decrease in the mean triglyceride level in the low fat group ($p = 0.034$). In the low fat group there was a significant 20.3% decrease in the mean linoleic acid (ω -6) level, and increased EPA and DHA levels (each an ω -3 fatty acid) (34.5% and 18.8%, respectively, table 2).

To decipher factors that may be responsible for the effects of the dietary intervention on LNCaP proliferation in the ex vivo bioassay correlation analysis was done to compare serum hormones, lipids, fatty acids, IGF and IGFBP levels, and weight changes against proliferation bioassay results. This was done in the group as a whole (Western and low fat groups combined). The change in triglyceride, total ω -6 fatty acid and linoleic acid (ω -6) levels positively correlated with bioassay changes (table 3). The greater the decrease in serum total triglyceride and total ω -6 fatty acid levels, of which linoleic acid is the most predominant, the greater the decrease in LNCaP proliferation when cultured in human serum. Conversely the change in total ω -3 fatty acid levels, and EPA (ω -3) and linolenic acid (ω -3) levels correlated negatively with the ex vivo bioassay results (table 3). Weight loss did not correlate with decreased LNCaP proliferation ($p = 0.078$). There was no significant correlation between the change in IGF-I or II, IGFBPs, cholesterol or serum hormone levels (testosterone and estradiol) and the proliferation bioassay.

DISCUSSION

Our trial shows that a short-term intervention consisting of decreased dietary fat, and increased soy protein and fiber intake in men with untreated prostate cancer decreased the mitogenic effects of patient serum on androgen sensitive LNCaP cells grown in an ex vivo bioassay. Correlation analysis suggests that this effect was due in part to the alteration in serum ω -6 and ω -3 fatty acids. Decreased serum ω -6 fatty acids such as linoleic acid and increased ω -3 fatty acids such as EPA were associated with decreased LNCaP proliferation on the bioassay. These findings are consistent with prior in vitro and preclinical studies showing that ω -6 fatty acids such as linoleic acid promote the growth of prostate cancer cell lines and xenografts, whereas ω -3 fatty acids have growth inhibitory effects.^{5,15} In a prior short-term study incorporating a low fat diet and exercise with resultant weight loss the 30% decrease in LNCaP proliferation was greater than the 16% decrease in the low fat group in our trial, suggesting that exercise and/or weight loss has the potential to have a greater effect on serum factors that are mitogenic for prostate cancer cells.¹³

Dietary intake was strictly controlled by having all meals prepared by UCLA clinical research center kitchen staff and compliance was extremely high. This rigorous controlled feeding regimen was useful in our trial but future long-term trials must incorporate outpatient dietary and monitoring regimens. These types of long-term regimens are feasible in patients with prostate cancer, as previously noted by our group in a 4-year trial,¹⁶ by Ornish et al⁹ in a 1-year trial and by Parsons et al in a 6-month telephone-based dietary counseling trial.¹⁷ At issue is whether long-term low fat dietary intervention trials are feasible for prevention trials in men at risk for prostate cancer. Pilot feasibility studies are required to evaluate this issue further. Our trial shows that men with prostate cancer are willing to be randomized to a low fat or a Western diet in future clinical trials.

IGF-I increased in the low fat and Western diet groups, although between group changes in IGF-I levels were not significant. Prior investigators observed that increasing dietary protein results in increased IGF-I levels.¹⁸ The amount of protein provided in the dietary intervention in our trial was 30% of the daily energy intake, whereas the mean baseline protein intake of subjects before initiating the study diet was 19.1%. Decreased serum IGF-I levels after a low fat diet and exercise intervention previously correlated with decreased mitogenicity of patient serum on LNCaP growth, suggesting that increased serum IGF-I levels in our trial may have limited the antiproliferative effects of the low fat diet seen on the ex vivo bioassay.¹³ High protein diets raise a number of concerns in regard to prostate cancer, given that increased IGF-I levels in men are associated with an increased risk of clinical prostate cancer and IGF-I is a well-known potent mitogen for androgen sensitive and androgen independent prostate cancer.^{13,19} Also, a recent large, prospective cohort study showed that high dietary intake of protein was associated with an increased risk of prostate cancer.²⁰ The issue of protein intake and the potential for increasing cancer risk is somewhat complicated by the fact that high protein diets that incorporate protein based meal replacements may be a useful tool in weight loss programs. The effects of protein intake on the IGF axis and prostate cancer outcomes must be addressed in future preclinical and clinical trials.

In our trial we did not expect to see an increase in serum levels of fish derived EPA and DHA (ω -3 fatty acids) in the low fat group relative to baseline since the amount of fish servings and type of fish served in the low fat and Western diet groups were the same. The increase in serum EPA and DHA levels in the low fat group may potentially be a direct effect of soy protein on the liver, resulting in increased expression of δ -6 desaturase, which converts the plant based ω -3 fatty acid α -linolenic acid to DHA and EPA,²¹ although this must be verified in future clinical trials. Of great interest is that the change in serum ω -3

levels negatively correlated with LNCaP cell proliferation on the ex vivo bioassay. Recent preclinical studies by our group and others showed that decreasing the ratio of ω -6 to ω -3 fatty acids directly impacts prostate cancer development and progression in animal models, possibly by affecting the cyclooxygenase-2/prostaglandin E2 pathway, and proliferation and apoptotic pathways.^{15,22} Based on the results of these prior preclinical and clinical trials we are now performing a prospective, randomized trial incorporating decreased dietary fat and fish oil capsules to evaluate serum and tissue biomarkers in men who undergo radical prostatectomy with final results expected in 2010.

We developed the ex vivo proliferation bioassay at our laboratory to ultimately function as a surrogate biomarker for prospective, randomized trials of biologically meaningful end points, such as prostate cancer development and progression. Given that diet and lifestyle interventions require long-term, costly prospective trials, it would be ideal if valid surrogate biomarkers were available to predict the end points of clinical trials. The ex vivo bioassay was previously used in a number of human trials to assess the effect of diet, supplements and lifestyle interventions on serum induced proliferation and apoptosis in androgen sensitive and androgen independent prostate cancer cell lines.^{9,13,23} Ultimately to determine whether the ex vivo bioassay is a valid surrogate biomarker it must be incorporated in clinical trials with biologically relevant end points associated with prostate cancer development and progression.

There are a number of limitations in the current trial. Sample size was small with 9 subjects evaluable per group and the study duration was short at 4 weeks. Also, multiple comparisons were reported when evaluating differences in metabolic changes in serum and reporting correlation analysis. Performing multiple comparisons increases the likelihood of finding statistical significance in 1 comparison. Given that they were exploratory analyses of secondary aims, we do not consider our findings conclusive but rather hypothesis generating.

Our results build on a number of important trials of dietary fat modification and/or lifestyle changes in men with prostate cancer. In men on expectant management Ornish et al noted that 1-year intervention consisting of a low fat vegan diet combined with soy, selenium, fish oil, vitamin C and E, and lifestyle changes decreased PSA by 4% relative to baseline in the intervention group while PSA increased by 6% in the control group.⁹ They subsequently reported that this intervention resulted in changes in gene expression of pathways relevant for tumorigenesis in benign prostate tissue.²⁴ Lin et al also observed significant changes in gene expression in benign prostate epithelium in men given a low fat, low glycemic load dietary intervention.¹² In a prospective intervention trial using historical controls Demark-Wahnefried et al noted that decreased dietary fat with flaxseed supplementation decreased proliferation and increased apoptosis in prostatectomy tissue.¹⁰ Together these trials, and other preclinical and clinical trials show the potential biological activity of diet and lifestyle modifications on benign and malignant prostate tissue.¹¹

CONCLUSIONS

In men with prostate cancer decreased dietary fat with increased fiber and soy intake reduced the mitogenic effects of patient serum on androgen sensitive LNCaP cells. This anticancer effect may be due in part to decreased serum ω -6 fatty acids and increased serum ω -3 fatty acids resulting from the diet intervention. Further prospective trials are indicated to evaluate low fat diets with varying levels of ω -6 and ω -3 fatty acids for prostate cancer prevention and treatment.

Abbreviations and Acronyms

BMI	body mass index
DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
IGF	insulin-like growth factor
IGFBP	IGF binding protein
PSA	prostate specific antigen

Acknowledgments

Study received institutional internal review board approval.

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Effect of low fat and Western diets on serum stimulated LNCaP cell growth in vitro. Cell proliferation was measured after 48-hour incubation in medium containing 10% serum from individuals. All experiments were done in duplicate and repeated twice. Data are shown as percent of LNCaP growth in medium containing 10% fetal bovine serum. Between group difference in LNCaP proliferation change was statistically significant ($p = 0.03$). Bars indicate mean $\pm$ SE in 9 subjects per diet group. White bars represent predietary intervention serum. Black bars represent post-dietary intervention serum. Asterisk indicates statistically significant LNCaP proliferation within group change in low fat group ($p = 0.006$).

Table 1

Research subject baseline characteristics

	Mean $\pm$ SEM Western Diet	Mean $\pm$ SEM Low Fat Diet
No. race:		
White	6	6
Black	3	3
Age	64.7 $\pm$ 2.7	63.8 $\pm$ 2.3
Wt (kg)	92.4 $\pm$ 6.0	90.9 $\pm$ 6.2
BMI (kg/m ²)	29.9 $\pm$ 2.1	29.5 $\pm$ 2.0
% Body fat	30.4 $\pm$ 1.6	29.7 $\pm$ 1.3
PSA (ng/ml)	7.0 $\pm$ 1.4	8.0 $\pm$ 1.9
Gleason grade	6.2 $\pm$ 0.2	6.2 $\pm$ 0.2

Table 2

Effect of Western and low fat diets on PSA, serum hormones, lipids and fatty acids in 9 subjects per group

Serum Factor	Western Diet			Low Fat Diet			Between Group p Value
	Mean $\pm$ SE Before	Mean $\pm$ SE After	p Value	Mean $\pm$ SE Before	Mean $\pm$ SE After	p Value	
PSA (ng/ml)	7.28 $\pm$ 1.5	6.3 $\pm$ 3.6	0.36	9.2 $\pm$ 2.7	11.4 $\pm$ 5.0	0.39	0.23
Testosterone (ng/dl)	502.9 $\pm$ 88.3	519.2 $\pm$ 234.9	0.72	388.4 $\pm$ 55.2	371.3 $\pm$ 42.4	0.90	0.80
Estradiol (pg/ml)	31.1 $\pm$ 2.3	32.4 $\pm$ 4.6	0.46	26.4 $\pm$ 2.5	28.2 $\pm$ 2.3	0.25	0.86
Insulin (μ U/ml)	15.8 $\pm$ 3.2	9.7 $\pm$ 5.6	0.06	14.3 $\pm$ 3.9	9.5 $\pm$ 2.1	0.15	0.65
IGF (ng/ml):							
I	206.3 $\pm$ 24.9	230.3 $\pm$ 88.6	0.03	241.4 $\pm$ 27.4	299.4 $\pm$ 34.7	0.01	0.09
II	670.8 $\pm$ 68.6	659.3 $\pm$ 187.5	0.53	807.3 $\pm$ 75.0	842.1 $\pm$ 68.8	0.13	0.11
IGFBP (ng/ml):							
1	32.6 $\pm$ 7.8	43.2 $\pm$ 29.5	0.09	26.3 $\pm$ 10.5	50.1 $\pm$ 18.9	0.09	0.40
2	404.0 $\pm$ 52.5	383.0 $\pm$ 127.7	0.54	278.7 $\pm$ 62.7	376.4 $\pm$ 63.4	0.10	0.08
3	1,869 $\pm$ 168	1,861 $\pm$ 489	0.88	2,178 $\pm$ 170	2,260 $\pm$ 138	0.21	0.27
Triglycerides (mg/dl)	141.9 $\pm$ 21.3	130.4 $\pm$ 118.6	0.71	240.1 $\pm$ 43.4	137.6 $\pm$ 15.1	0.03	0.09
Cholesterol (mg/dl):							
Total	188.6 $\pm$ 14.9	194.3 $\pm$ 26.6	0.69	197.5 $\pm$ 15.0	184.2 $\pm$ 17.0	0.36	0.65
High density lipoprotein	42.4 $\pm$ 5.3	44.6 $\pm$ 13.2	0.89	37.6 $\pm$ 2.2	40.0 $\pm$ 4.0	0.66	0.64
Low density lipoprotein	129.0 $\pm$ 15.2	131.7 $\pm$ 28.8	0.27	112.0 $\pm$ 16.7	117.2 $\pm$ 13.5	0.89	0.39
ω -6 (μ mol/l):							
Linoleic acid	3,076 $\pm$ 257	2,956 $\pm$ 148	0.67	3,793 $\pm$ 244	3,023 $\pm$ 221	0.01	0.08
Arachidonic acid	573.9 $\pm$ 66.7	550.7 $\pm$ 49.9	0.58	575.2 $\pm$ 50.3	599.7 $\pm$ 54.1	0.41	0.34
ω -3 (μ mol/l):							
EPA	45.9 $\pm$ 8.2	46.4 $\pm$ 8.7	0.97	46.1 $\pm$ 7.4	62.0 $\pm$ 7.6	0.004	0.25
DHA	157.3 $\pm$ 14.0	178.8 $\pm$ 19.9	0.36	158.2 $\pm$ 13.4	188.0 $\pm$ 12.9	0.03	0.74
Linolenic acid	107.9 $\pm$ 15.4	74.4 $\pm$ 19.8	0.18	98.3 $\pm$ 19.7	89.0 $\pm$ 17.4	0.65	0.43
Total fatty acid (μ mol/l):							
ω -3	311.1 $\pm$ 30.5	299.6 $\pm$ 42.9	0.84	302.7 $\pm$ 31.2	339.0 $\pm$ 31.0	0.28	0.46
ω -6	3,665 $\pm$ 307	3,521 $\pm$ 174	0.65	4,386 $\pm$ 252	3,636 $\pm$ 232	0.01	0.13
ω -3/ ω -6	0.09 $\pm$ 0.01	0.09 $\pm$ 0.01	0.90	0.07 $\pm$ 0.01	0.09 $\pm$ 0.01	0.001	0.14

Table 3

Correlation analysis of change in weight, serum triglyceride and fatty acid vs change in the ex vivo proliferation bioassay

Clinical Variable	Spearman Correlation Coefficient	p Value
Wt	0.43	0.08
Triglyceride	0.50	0.05
Total fatty acids:		
ω -3	-0.49	0.04
ω -6	0.64	0.004
ω -3/ ω -6	-0.72	0.001
ω -6 Linoleic acid	0.68	0.002
ω -3:		
EPA	-0.52	0.03
DHA	-0.40	0.1
Linolenic acid	-0.47	0.05