Appendix A.

A.1 Primary Search Strategy

1. exp cardiovascular diseases/
2. Adhesion molecule expression.mp.
3. Angiographic progression.mp.
4. Angioplast$.mp.
5. (atherogen$ or antiartherogen$).mp.
6. (arrhythmi$ or Antiarrhythmi$).mp.
7. Antithrombo$.mp.
8. endotheli$.mp.
9. exp endothelium, vascular/
10. Beta-thromboglobulin.mp.
11. Cardi$.mp.
12. CHD.mp.
13. Coronary.mp.
14. Hypotens$.mp.
15. Hypotriglyceridem$.mp.
16. heart disease$.mp.
17. Myocardial infarct$.mp.
18. Platelet adhesi$.mp.
19. (postprandial adj (lipemia or lipoprotein$)).mp.
20. Pulmonary Embol$.mp.
21. Heart failure$.mp.
22. Arteriosclerosi$.mp.
23. cardioprotect$.mp.
24. Homocystine/
25. exp Homocysteine/
26. homocyst$.mp.
27. Cystine/
28. cystine.mp.
29. exp Acute-Phase Proteins/
30. acute phase protein$.mp.
31. Acute-Phase Reaction/
32. acute phase react$.mp.
33. exp Blood Coagulation Factor Inhibitors/
34. exp Blood Coagulation Factors/
35. blood coagulation factors$.mp.
36. exp Cell Adhesion Molecules/
37. cell adhesion molecule$.mp.
38. exp Interleukins/
39. interleukin$.mp.
40. Lipid Peroxidation/
41. lipid peroxidat$.mp.

42. exp Hemostasis/
43. hemosta$.mp.
44. haemosta$.mp.
45. exp Diagnostic Techniques, Cardiovascular/
46. or/1-45
47. exp fatty acids, omega-3/
48. fatty acids, essential/
49. Dietary Fats, Unsaturated/
50. linolenic acids/
51. exp fish oils/
52. (n 3 fatty acid$ or omega 3).tw.
53. docosahexa?noic.tw,hw,rw.
54. eicosapenta?noic.tw,hw,rw.
55. alpha linolenic.tw,hw,rw.
56. (linolenate or cervonic or timnodonic).tw, hw,rw.
57. menhaden oil$.tw,hw,rw.
58. (mediterranean adj diet$).tw.
59. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
60. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
61. (fish adj2 oil$).tw.
62. (cod liver oil$ or marine oil$ or marine fat$).tw.
63. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
64. (fish consumption or fish intake or (fish adj2 diet$)).tw.
65. diet$ fatty acid$.tw.
66. or/47-65
67. dietary fats/
68. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
69. random$.tw.
70. exp clinical trials/ or evaluation studies/
71. follow-up studies/ or prospective studies/
72. or/68-71
73. 67 and 72
74. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
75. (omega 3 or n 3).mp.
76. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
77. 75 and 76
78. 66 or 73 or 74 or 77
79. 46 and 78
80. limit 79 to (addresses or bibliography or biography or congresses or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or

letter or news or newspaper article or patient education handout or
periodical index or review of reported cases)
81. 79 not 80
82. limit 81 to human
83. (guidelines or practice guideline or meta analysis or review or revewi,
academic or review, tutorial or review literature).pt.
84. 82 and 83
85. limit 84 to english language
86. 84 not 85
87. (random$ or rct$).tw.
88. exp randomized controlled trials/
89. exp random allocation/
90. exp double-blind method/
91. exp single-blind method/
92. randomized controlled trial.pt.
93. clinical trial.pt.
94. (clin$ adj trial$).tw.
95. ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.
96. exp placebos/
97. placebo$.tw.
98. exp comparative study/
99. exp clinical trials/
100. follow-up studies/
101. (follow up or followup).tw.
102. exp case-control studies/
103. (case adj20 control).tw.
104. exp longitudinal studies/
105. longitudinal.tw.
106. exp cohort studies/
107. cohort.tw.
108. exp prospective studies/
109. exp evaluation studies/
110. or/87-109
111. (82 and 110) not 83
112. limit 111 to english language
113. 111 not 112
114. 82 not (111 or 83)
115. limit 114 to english language
116. 114 not 115

A.2 Diabetes Search Strategy

1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. (mediterranean adj diet$).tw.
12. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
13. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
14. (fish adj2 oil$).tw.
15. (cod liver oil$ or marine oil$ or marine fat$).tw.
16. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
17. (fish consumption or fish intake or (fish adj2 diet$)).tw.
18. diet$ fatty acid$.tw.
19. menhaden oil$.tw,hw,rw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. or/20,27-28,31
33. limit 32 to (addresses or bibliography or biography or congresses or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education handout or periodical index or review of reported cases)
34. Case Report/
35. 32 not (33 or 34)
36. exp Diabetes Mellitus/
37. diabet$.af.
38. 35 and (36 or 37)
39. limit 38 to human

40. limit 39 to english language
41. limit 40 to (guideline or meta analysis or review or review, academic or review, multicase or review, tutorial or review literature)
42. 40 not 41

A.3 Nut Search Strategy

1. exp Nuts/	964
2. exp Cardiovascular Diseases/	1123117
3. (nut or nuts).tw.	1762
4. 1 or 3	2318
5. 4 and 2	145
6 limit 5 to (human and english language)	122

A.4 Risk Factor Update Search Strategy

1. exp fatty acids, omega-3/
2. exp fish oils/
3. (n 3 fatty acid$ or omega 3).tw.
4. docosahexa?noic.tw,hw,rw.
5. eicosapenta?noic.tw,hw,rw.
6. alpha linolenic.tw,hw,rw.
7. (linolenate or cervonic or timnodonic).tw,hw,rw.
8. (fish adj2 oil$).tw.
9. or/1-8
10. limit 9 to human
11. limit 10 to english language
12. exp "Lipoprotein(a)"/
13. c-reactive protein.mp.
14. insulin.mp.
15. exp Factor VIII/
16. exp von Willebrand Factor/
17. heart rate variab$.mp.
18. ankle brachial index.mp.
19. ankle-arm blood pressure index.mp.
20. exp Hemoglobin A, Glycosylated/
21. glycohemoglobin hgb a1c.mp.
22. hgb a1c.mp.
23. exp Apolipoproteins B/
24. apolipoprotein b-100.tw.
25. intima media thickness.mp.
26. carotid doppler.mp.
27. exp Heart Function Tests/
28. exp PLETHYSMOGRAPHY/
29. exp Ultrasonography, Doppler/
30. glycated hemoglobin.mp.
31. or/12-30
32. 11 and 31

Appendix B
Whole Animal Result Form

Animal Characteristic

Subjects and Controls

(Give brief descriptions for each groups. Control group is the group with No intervention or Placebo; or the group with lowest amount of N-3 intakes)

Initial number of animals used: ND

Number of groups used: ND

Control group:

Tx Arm 1:

Tx Arm 2:

Tx Arm 3:

Tx Arm 4:

Comments on Subjects and Controls and/or Study Designs

Animals' Diets

Diet composition of the reference diet:

Total fat: ND

Saturated fatty acids (SFA): ND

Monounsaturated fatty acids (MUFA): ND

Polyunsaturated fatty acids (PUFA): ND

ALA (18:3n-3): ND

EPA (20:5n-3): ND

DPA (22:5n-3): ND

DHA (22:6n-3): ND

Only EPA+DHA: ND

Other n-3 FA reporting: ND

Comments on Animals' Reference/Baseline Diets:

Control Group Characteristics

Control Group

Control (No intervention or Placebo) -- Number enrolled: ☐ ND

Mean Age: ☐ ND

+/- SD/SE: ☐ ND

Age Range: to ☐ ND

Sex of control animals? ☐ ND

- ☐ Only males
- ☐ Only Females
- ☐ Males and Females (give numbers of % distribution)

Control's mean/median age? ☐ ND

Are ages different between groups? ☐ ND

- ☐ No
- ☐ Yes (give brief description)

Is sex different between groups? ☐ ND

- ☐ No
- ☐ Yes (give brief description)

Are body weight different between groups? ☐ ND

- ☐ No
- ☐ Yes (give brief description)

Is control group's diet same as reference diet? ☐ ND

- ☐ Yes
- ☐ No

If controls' diet is NOT reference diet, what is the composition of controls' diet?

Total fat: ☐ ND

Saturated fatty acids (SFA): ☐ ND

Monounsaturated fatty acids (MUFA): ☐ ND

Polyunsaturated fatty acids (PUFA): ☐ ND

ALA (18:3n-3): ☐ ND

EPA (20:5n-3): ☐ ND

DPA (22:5n-3): ☐ ND

DHA (22:6n-3): ND

Only EPA+DHA: ND

Other n-3 FA reporting: ND

Comments on Control Animals' Diets:

Tx Arm No.

DUPLICATE THIS SECTION FOR EACH TREATMENT ARM

Do Not Use The Template (titled Tx Arm No.) to Enter Data.

Name each new section by an appropriate Brief Description (eg, Fish Oil, O3 Diet)

Number each new section's Section ID Tx Arm number from the ANIMAL CHARACTERISTICS section

Treatment Arm #:

Number of animals in Tx Arm #:

Tx Arm's Diets

Diet composition of the Tx Arm's diet:

Total fat: ND

Saturated fatty acids (SFA): ND

Monounsaturated fatty acids (MUFA): ND

Polyunsaturated fatty acids (PUFA): ND

ALA (18:3n-3): ND

EPA (20:5n-3): ND

DPA (22:5n-3): ND

DHA (22:6n-3): ND

Only EPA+DHA: ND

Other n-3 FA reporting: ND

Tx Arm's Outcomes

Check ND if no outcome reported for this Tx Arm. DO NOT skip any outcome.

Tx Arm # vs. Controls

Effect observed for Outcome 1: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 2: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 3: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 4: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 5: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 6: ND

Number of animals: ND

% of change: ND

ND

Other outcomes or comments for outcomes (Tx Arm # vs. Controls):

Other Comparisons of Outcomes

DUPLICATE THIS SECTION FOR EACH COMPARISONS OTHER THAN COMPARING TO CONTROLS

Do Not Use The Template (titled Tx Arm 1 vs. 2) to Enter Data.

Comparison groups:

Check ND if no outcome reported for this Tx Arm. DO NOT skip any outcome.

Effect observed for Outcome 1: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 2: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 3: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 4: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 5: ND

Number of animals: ND

% of change: ND

ND

Effect observed for Outcome 6: ND

Number of animals: ND

% of change: ND

ND

Other outcomes or comments for outcomes:

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
Abeywardena, 1995	Country: Australia Animal: Wistar rats Funding: Industry	Mean age: ND Age grp: ND Sex: Males	9 months	Standard rat chow (Milling Industries, Adelaide, Australia)	SSO SBO FO (MaxEPA)	15* %w/w or 32* %kcal	0.9 2.8 1.4	0 0 22	59* 44* 7*	13* 21* 28*	22* 25* 15*	
al Makdessi, 1995	Country: Germany Animal: Wistar rats Funding: ND	Mean age: ND Age grp: Young Sex: Males	10 weeks	Low-fat (<1% w/w) standard chow from (Altromin GmbH & Co.)	FO (sardine oil) Coconut oil	10% w/w	1. 3 0.9	29 0	ND ND	31* >60*	ND ND	
Anderson, 1996	Country: Australia Animal: Sprague-Dawley rats Funding: Government	Mean age: ND Age grp: Adult Sex: Males	8 weeks	Total fat: 3.5%	FO (MaxEPA) Safflower oil	Initially given at 0.6 ml and + 0.1 ml/wk up to 1.0 ml w/ increasing body weight	ND 0	ND 0	0 75	10 25	28 15	Total n3 = 41%
Billman, 1994	Country: US Animal: Mongrel dogs Funding: Government	Mean age: ND Age grp: ND Sex: ND	Infusion study	ND	Saline (n=3) or I.V. infusion (n=5) Emulsion of fish oil	100 ml of Intralipid, a 10% lipid emulsion 10 ml FO concentrate (n=4) 5 ml same FO concentrate + 5 ml TG concentrate (n=4)	7 ND ND	0 70 65	ND ND ND	ND ND ND	ND ND ND	

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
Billman, 1999	Country: US Animal: Mongrel dogs Funding: Government	Mean age: ND Age grp: ND Sex: ND	Infusion study	ND	SBO lipid emulsion (n=7) or saline (n=7)	ND	7~8 in SBO	0	ND	ND	ND	
					EPA		0	E=98 D=1	ND	ND	ND	
					DHA		0	E=1 D=91	ND	ND	ND	
					ALA		>99	0				
Charnock, 1992	Country: Australia Animal: Wistar rats Funding: ND	Mean age: > 3 years old Age grp: Adult Sex: ND	30 months	ND	SSO	12* %w/w or 28 %kcal	1.1	0	ND	23*	23*	N3/n6 = 0.02
					FO		1.4	20	ND	29*	26*	= 2.0
Charnock, 1991	Country: Australia Animal: Wistar rats Funding: ND	Mean age: near 1 yr old Age grp: Adult Sex: males	12 months	NDMilling Industries Australia. Total fat: 3 %w/w	SF/SSO	16* %w/w or 35 %kcal	ND	ND	19	45	29	TT n-3 =1.1 TT n6 =19
					SF/FO		ND	ND	12	41	29	TT n-3 =13 TT n6 =12
Chen, 1994	Country: Taiwan Animal: rabbits Funding: Government	Mean age: ND Age grp: ND Sex: Males	2 weeks.	Standard rabbit chow (Purina 5321, St. Louis, MO, USA)	HC (1% CHOL-enriched diet)	40 %kcal (1% chol)	ND	ND	ND	ND	ND	
					HCF (1% CHOL and 10% FO)	40% energy (1% chol +10% fish oil)	ND	52	ND	ND	ND	

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
Culp, 1980	Country: US Animal: Mongrel dogs Funding: Government	Mean age: ND Age grp: ND Sex: ND	36 to 45 days	Standard dog chow (Friskies Dinner)	Standard dog chow FO (Menhaden)	ND +25 %kcal	ND ND	0. 1 13	ND ND	32 32	34 20	
Germain, 2003	Country: France Animal: Sprague-Dawley rats Funding: Government	Mean age: ND Age grp: ND Sex: Females	>= 3 weeks	APAE, Jouy en Josas, France.	Palm oil DHASCO (DHA fom purified TGs)	+15% of total fat	ND ND	ND ND	ND ND	high MUFA level ND	ND ND	
Hartog JM 1987	Country: Netherlands Animal: Yorkshire piglets Funding: Dutch Heart Foundation	Mean age: 5 weeks Age grp: Unclear Sex: ND	16 weeks	ND	Lard fat (9% w/w) ML (4.5% mackerel oil + 4.5% lard fat)	ND	1 1	0 13	ND ND	36 32	ND ND	
Hock, 1990	Country: US Animal: Sprague-Dawley rats Funding: Government	Mean age: ND Age grp: Weanling Sex: ND	4 weeks	Fat-free purified diet	CO (corn oil) MO (Menhaden oil)	12 %kcal or 5 %w/w	1 2	0 20	59 5	14* 33*	25* 27*	n3/n6= 0.02 =6.06
Hock, 1987	Country: US Animal: Sprague-Dawley rats Funding: Government	Mean age: ND Age grp: Adult Sex: Males	4 weeks	Fat-free purified diet	CO (corn oil) MO (Menhaden oil)	12 %kcal or 5 %w/w	1 2	0 21	59 4	14* 31*	25* 27*	n3/n6= 0.02 =7.99

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
Isensee H 1994	Country: Germany Animal: Wistar rats Design: A Funding: Alfred Teufel-Stiftung research foundation	Mean age: 2 months Age grp: Young Sex: Males	10 weeks	Low-fat (<1 %w/w) basic diet (Altromin GmbH, Lage, Germany)	CO LO (Linseed oil) FO	10 %w/w	1 52 0.3	0 0 29	50 20 12	16 9 31	31 16 26	
Kinoshita, 1994	Country: Japan Animal: Mongrel dogs Diseased: Funding: ND	Mean age: ND Age grp: Adult Sex: ND	8 weeks	Standard diet (Oriental Yeast Co.)	Standard diet EPA ester	ND Mochida Pharmaceutical Co	ND ND	ND 100 mg/kg BW/d	ND ND	ND ND	ND ND	
Lo, 1991	Country: Taiwan Animal: Mongrel dogs Funding: ND	Mean age: ND Age grp: ND Sex: MixSex : "either sex"	Infusion study	Same dogs were infused control buffer or different dosages of ALA.	Control buffer ALA infusion	ND	ND 1, 5, 10, 20, 30, or 60 mg/kg	ND ND	ND ND	ND ND	ND ND	
McLennan, 1996	Country: Australia, Switzerland Animal: spontaneously hypertensive Wistar rats Funding: ND	Mean age: ND Age grp: ND Sex: Males	5 weeks	ND	Olive oil EPA DHA EPA+DHA	5% w/w from olive oil 0.5% from n-3; 4.5% from olive oil	ND ND ND ND	ND E:0.5 w/w D:0.5 w/w ND	ND ND ND ND	ND ND ND ND	ND ND ND ND	

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
McLennan, 1995	Country: Australia Animal: Sprague-Dawley rats Funding: ND	Mean age: 12 weeks Age grp: Adult Sex: Males	12 weeks	Nonpurified lab rat diet. Total fat = 4% w/w	CAN SBO SSO	15 %w/w or 32 %kcal	8 7 5	0 0 0	21 52 64	12 19 12	60 22 23	N3/n6 = 0.37 = 0.14 =0.008
McLennan, Bridle, 1993	Country: Australia Animal: Marmoset monkeys Funding: Government	Mean age: ND Age grp: Old Sex: 50% Males	16 weeks	Low-fat marmoset diet (Milling Industries, Adelaide, Australia) Total fat = 6% w/w	SF/SSO (8% sheep perirenal fat + 2% SSO) SF/FO (7% SF + 3% FO)	16 %w/w	0.8 0.8	1 11	20 10	48 47	ND ND	N3/n6 = 0.12 =1.25
McLennan, 1993	Country: Australia Animal: Sprague-Dawley rats Funding: International Olive Oil Council	Mean age: 30 weeks Age grp: Old Sex: ND	12 weeks	Basic laboratory diet (Milling Industries, Adelaide, Australia) Total fat = 4% w/w	SSO FO	15 %w/w or 32 %kcal	ND ND	ND ND	56 8	15 40	25 25	Total n3 = 4% =17%
McLennan, 1992	Country: Australia Animal: Marmoset monkeys Funding: ND	Mean age: 2 years Age grp: Unclear Sex: breeding pairs	30 months	Total fat: 4 %w/w SFA: 37.3% MUFA: ND PUFA: 18.3%	SSO TFO (tuna fish oil)	12 %w/w or 29 %kcal	ND ND	ND ND	54 11	23 29	ND ND	ND Total n3 = 23%
McLennan, 1990	Country: Australia Animal: Sprague-Dawley rats Funding: Government	Mean age: 2 months Age grp: Adult Sex: Males	18 months	Standard lab rat diet. Total fat = 4% w/w	SF+SSO SF+TFO	16 %w/w or 35 %kcal	0 ND	0 23	58 9	16 31	ND ND	

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
McLennan, 1988	Country: Australia Animal: Wistar rats Funding: Government	Mean age: "age-matched" Age grp: Unclear Sex: Males	12 months	Standard lab rat diet. Total fat = 4% w/w	SSO TFO	16 %w/w or 35 %kcal	ND ND	0 23	58 9	ND ND	ND ND	
Oskarsson, 1993	Country: US Animal: Mongrel dogs Funding: ND	Mean age: ND Age grp: ND Sex: “Mixed Sex”	6 weeks	ND	No fish oil Rx MaxEPA	ND	ND ND	ND 0.1 g/kg/d	ND ND	ND ND	ND ND	
Otsuji, 1993	Country: Japan Animal: Mongrel dogs Funding: ND	Mean age: ND Age grp: Adult Sex: MixSex : No data on the distribution	8 weeks	Standard diet prepared by Oriental Yeast Co.	Standard dog chow EPA ester	30 g/kg BW /day 100 mg/kg BW/day	ND ND	ND ND	ND ND	ND ND	ND ND	
Pepe, 1996	Country: Australia Animal: Wistar rats Funding: ND	Mean age: 16 weeks Age grp: Young Sex: Males	16 weeks	Nonpurified diet fed to all rats (Milling Industries, Adelaide, Australia). Total fat = 7.6%	SAT (sheep perirenal fat) FO	15.3% w/w	1. 5 1.2	1 36	8 8	55 25	ND ND	

Appendix C

Evidence Table 1: Whole Animal Studies

Part 1

Author, yr	Study Characteristics	Animal Model	Exposure Duration	Ref. Diet	Dietary Characteristics							
					Groups	Total Fat	% of Total Fatty Acids					Other
							ALA	E+D	n-6	SFA	MUFA	
Yang, 1993	Country: US Animal: Sprague-Dawley rats Funding: Government	Mean age: ND Age grp: ND Sex: Males	5 days	Standard rat nonpurified diet (Purina Mills, St. Louis, MO) Total fat = 5 %kcal	Butter FO (fish oil rich pellets)	17 %kcal	ND ND	ND 32	ND 23	ND 25	ND 15	

* estimated values, not reported in original paper

Types of study design:

A = N-3 PUFAs vs. n-6 PUFAs
B = N-3 PUFAs vs. MUFAs
C = N-3 PUFAs vs. SFAs
D = N-3 PUFAs vs. Standard chows

Appendix C

Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Abeywardena, 1995	VPB VT (%) VF (%) AS Deaths	Myocardial ischemia and reperfusion model. 5-min regional myocardial ischemia. Arrhythmias induced by reperfusion were assessed during a 10-min period after releasing the occlusion and restoring blood flow.	VPB/10 min [SBO vs. SSO] n=18 vs. 18, p>0.05 Increased +176% Estimated [FO vs. SSO] n= 18 vs. 18, p>0.05 Decrease -13% Estimated [FO vs. SBO] n= 18 vs. 18, Decrease -68% Estimated VT (%) during reperfusion [SBO vs. SSO] n=18 vs. 18, Increased 76%/39% Reported [FO vs. SSO] n=18 vs. 18, Decrease 22%/39% Reported VF (%) during reperfusion [SBO vs. SSO]n= 18 vs. 18, Increased 23%/11% Reported [FO vs. SSO] n= 18 vs. 18, Decrease 5%/11% Estimated AS (severity of arrhythmia) during reperfusion [SBO vs. SSO] n= 18 vs. 18, p<0.05 Increase (sig.), +107% Estimated [FO vs. SSO] n= 18 vs. 18, p>0.05 Decrease, -40% Estimated [FO vs. SBO] n= 18 vs. 18, Decrease -71% Estimated Total Deaths [SBO vs. SSO] n= 18 vs. 18, No change 2/18 vs. 1/18 Reported [FO vs. SSO] n= 18 vs. 18, Decrease 0/18 vs. 1/18 Reported VT (%) during ischemia [SBO vs. SSO] n=: 18 vs. 18, No change 44%/39% Reported [FO vs. SSO] n=: 18 vs. 18, Decrease 6%/39% Reported	Sex diff? No Age diff? ND BW diff? No No statistics were performed for FO vs. SBO comparison in the original study
al Makdessi, 1995	AR (%) SIZ (%)	Arrhythima (AR) was defined as salves of extrasystoles and/or ventricular flutter and fibrillation. The preconditioning = in situ by means of 2 cycles of 3 min left anterior descending coronary artery occlusion - 10 min reperfusion.	[FO vs. HCO] (results in figure) AR (%): n= 8 vs. 5, Decrease AR (%) w/ precondition: n= 8 vs. 6, No change SIZ (%): n= 8 vs. 5, No change SIZ (%) w/ precondition: n= 8 vs. 6, No change	Sex diff? No Age diff? No BW diff? ND No statistics were done for FO vs. HCO comparisons in the original study.

Appendix C

Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Anderson, 1996	VPB VT (%) VF (%) AS	Myocardial ischemia and reperfusion model. 20-min regional myocardial ischemia. Arrhythmias induced by reperfusion were assessed during reperfusion.	Hearts that experienced instability (VPB, VT, and/or VF) during the equilibration period or sustained VT and/or VF during the last 30 s of the occlusion period were excluded from analysis of reperfusion-induced arrhythmias. [FO vs. SO in reperfusion] VPB: n= 8 vs. 6, p>0.05 No change –31% Estimated VT (%): n= 8 vs. 6, p>0.05, 38%/50% Reported VF (%): n= 8 vs. 6, p>0.05, 13%/33% Reported AS: n= 8 vs. 6, p>0.05 Decrease, -54% Estimated	Sex diff? No Age diff? ND BW diff? ND Sustained VT and/or VF were excluded from the analyses.
Billman, 1994	VF (%)	Exercise-plus-ischemia (2-min occlusion) test. VF was induced in one additional animal by the combination of cocain (1.0 mg/kg i.v.) and the exercise-plus-ischemia test.	Ctrl: saline or I.V. infusion VF (%) Ventricular flutter (which degenerates to VF) was reproducibly induced with each presentation of the control (both saline and Intralipid infusions) exercise-plus-ischemia tests. The cocaine exercise-plus-ischemia test induced a similar response. Data for all animals that developed VF have therefore been combined. [FO infusion vs. Ctrl] n= 8 vs. 8, p<0.005 Decrease (sig.) 12.5%/100% (4 ctrl animals developed VF shortly after the treadmill stopped, whereas 4 animals developed malignant arrhythmias while running) Reported.	Sex diff? ND Age diff? ND BW diff? ND
Billman, 1999	VF (%)	Exercise-plus-ischemia (2-min occlusion) test.	Ctrl: Soybean oil lipid emulsion (containing 7%~8% ALA) VF (%). [EPA infusion vs. Ctrl] n= 7 vs. 7, p=0.0105 Decrease (sig.), 2/7 vs. 7/7 Reported [DHA infusion vs. Ctrl] n= 8 vs. 7, p=0.0035 Decrease (sig.), 2/8 vs. 7/7 Reported [ALA infusion vs. Ctrl] n= 8 vs. 7, p=0.0035 Decrease (sig.), 2/8 vs. 7/7 Reported	Sex diff? ND Age diff? ND BW diff? ND
Charnock, 1992	VFT Sustaned VF (%)	Arrhythmias were induced by electrical stimulation protocol in normoxic and ischemic hearts.	VFT [FO vs. SSO in normoxic)] n=ND, No change [FO vs. SSO in ischemia)] n=ND, No change Sustained VF (%) [FO vs. SSO in normoxic)] n=ND, Decrease 8%/13% Reported [FO vs. SSO in ischemia)] n=ND, Decrease 0%/13% Reported	Sex diff? ND Age diff? ND BW diff? ND The procedures for induced-arrhythmias were not reported in the study, but presumably same as McLennan, 1992 & McLennan, Bridle, 1993.

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Charnock, 1991	VT (%) VF (%) VPB/15 min AS	15-min ischemia model	[SF/FO vs. SSO] VT (%) in ischemia: n=10 vs. 10, p>0.05 No Change 70%/100% Reported VF (%) in ischemia: n=10 vs. 10, p<0.05 Decreased (sig.) 0%/60% Reported VPB/15 min in ischemia: n=10 vs. 10, p<0.05 Decreased (sig.) –72% Estimated AS in ischemia: n=10 vs. 10, p<0.05 Decreased (sig.) –59% Estimated	Sex diff? No Age diff? No BW diff? No
Chen, 1994	VPB Deaths	In the short-term ischemia study, the ligation was maintained for 10 min in each rabbit and was followed by a reperfusion for 1 hr. In the long-term ischemia study, the ligation was maintained for 1 hr in each rabbit and was followed by a reperfusion for 4 hr.	VT/VF Deaths (%) during ischemia [HCF vs. HC (short term study)] n= 12 vs. 14, p>0.05 Decrease 8%/21% Reported [HCF vs. HC (long term study)] n= 14 vs. 15, p>0.05 No change 21%/27% Reported VPB (%) during ischemia [HCF vs. HC (short term study)] n= 11 vs. 11, p>0.05 Decrease 18%/36% Reported [HCF vs. HC (long term study)] n= 11 vs. 11, p>0.05 No change 36%/55% Reported VT/VF Deaths (%) during reperfusion [HCF vs. HC (short term study)] n= 11 vs. 11, p>0.05 No change 0%/0% Reported [HCF vs. HC (long term study)] n= 11 vs. 11, p>0.05 No change 0%/0% Reported VPB (%) during reperfusion [HCF vs. HC (short term study)] n= 11 vs. 11, p>0.05 No change 18%/18% Reported [HCF vs. HC (long term study)] n= 11 vs. 11, p>0.05 No change 27%/36% Reported	Sex diff? No Age diff? ND BW diff? ND
Culp, 1980	Sudden death Infarct size (%) VPB	Coronary artery thrombosis induced by electrical stimulations.	Ctrl: standard dog chow [FO vs. Ctrl] n= 10 vs. 17 Sudden death (%): No change 30%/29% Reported Infarct size (%): p=0.08 Decrease -52% Estimated Frequency of ectopic beats rose from < 10% at the beginning of the experiment to about 80% after 19 to 247 hrs of stimulation among controls. In contrast, the fish-oil-fed dogs maintained a more normal ECG pattern, showing less than 30% ectopic beats after 19 hours.	Sex diff? ND Age diff? ND BW diff? No

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Hartog JM 1987	VPB VT (%) VF (%) Death	Myocardial ischemia and reperfusion models: 5-min ischemia; 10-min reperfusion.	Ctrl: Lard fat (9% w/w) [ML vs. Ctrl] VPB during occlusion: n= 7 vs. 6, p>0.05 No change, +53% Estimated VPB during reperfusion: n= 7 vs. 6, p<0.05 Decrease (sig.) -65% Estimated VT (%) n= 7 vs. 6, No change 29%/17% Reported (all events were occurred during ischemia) VF (%) n= 7 vs. 6, Increased 3/7 vs. 0/6 Reported Of the three animals in ML group had VF, defibrillation was unsuccessful in one animal, which died of ventricular systole during the fifth reperfusion.	Sexdiff? ND Age diff? No BW diff? ND
Hock, 1990	VF (%) AS Deaths	Myocardial ischemia and reperfusion models: 15-min ischemia; 6-hr and 24-hr reperfusion.	[MO vs. CO] VF (%) in 6-hr model: n= 7 vs. 10, p<0.02 Decrease (sig.) 14%/91% Reported AS in 6-hr model: n= 7 vs. 10 p<0.01 Decrease (sig.) -77% Estimated Total Deaths (%) in 24-hr model: n= 21 vs. 22, p<0.05 Decrease (sig.) 24%/69% Reported	Sex diff? ND Age diff? ND BW diff? No
Hock, 1987	VPB Deaths	Ischemia model. “Acute” left main coronary artery ligation was performed. Arrhythima outcomes were observed 15 min after the acute ligation.	[MO vs. CO] Arrhythmia death (%): n= 13 vs. 14, No change 2/13 vs. 2/14 Reported VPB: n= 11 vs. 12, p>0.05 No change	Sex diff? No Age diff? ND BW diff? No

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Evidence Table 1: Whole Animal Studies

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Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Isensee H 1994	Time in normal sinus rhythm VF (%) VT (%) SIZ (%)	Myocardial ischemia and reperfusion models: 20-min ischemia; 20-min reperfusion	VT (%) during ischemia [FO vs. CO] n= 9~10/grp, Decrease (sig.) 0% vs. 44% Reported [LO vs. CO] n= 9~10/grp, No change 60%/40% Reported [FO vs. LO] n= 9~10/grp, p<0.05 Decrease (sig.) 0%/60% Reported VF (%) during ischemia (results in figure) [FO vs. CO] n= 9~10/grp, p<0.05 Decrease (sig.) 10% vs. (about 45%) Reported [FO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [LO vs. CO] n= 9~10/grp, p>0.05 No change [LO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [FO vs. LO] n= 9~10/grp, p<0.05 Decrease (sig.) 10% vs. (about 40%) Reported [FO vs. LO w/ Aspirin during ischemia] n= ND, p>0.05 No change VF (%) during reperfusion [FO vs. CO] n= 9~10/grp, p>0.05 No change 40%/67% Reported [LO vs. CO] n= 9~10/grp, No change 60%/67% Reported [FO vs. LO] n= 9~10/grp, No change 40%/60% Reported SIZ (%) at end of ischemia (results in figure) [FO vs. CO] n= 9~10/grp, No change [FO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [LO vs. CO] n= 9~10/grp, p>0.05 No change [LO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [FO vs. LO] n= 9~10/grp, p>0.05 No change [FO vs. LO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change Length of time in normal sinus rhythm after occlusion (results in figure) [FO vs. CO] n= 9~10/grp, p<0.05 Increase (sig.) [FO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [LO vs. CO] n= 9~10/grp, p>0.05 No change [LO vs. CO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change [FO vs. LO] n= 9~10/grp, p<0.05 Increase (sig.) [FO vs. LO w/ Aspirin during ischemia] n= 9~10/grp, p>0.05 No change The length of time in normal sinus rhythm after occlusion was sig. longer, VF incidence was sig. higher, and the size of the ischemic zone was sig. larger when no Aspirin added during ischemia among the FO group. The length of time in normal sinus rhythm after occlusion was sig. longer, VF incidence was sig. higher, and the size of the ischemic zone was sig. larger when no Aspirin added during ischemia among the LO group.	Sex diff? No Age diff? No BW diff? ND

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Evidence Table 1: Whole Animal Studies

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Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Kinoshita, 1994	VF (%) VT (%) AS VPB	Ischemia model: 3-hr coronary ligation Digitalis-induced arrhythmia model: Digoxin (0.025 mg/kg/min) was administrated intravenously over a 60 sec period to 5 dogs in each group immediately after ischemia	Ctrl: Standard diet [EPA vs. Ctrl] Ventricular extra beats (VEBs) in ischemia: n= 10 vs. 10, p<0.05 Decrease (sig.) -44% Estimated VF (%) in ischemia: n= 10 vs. 10, p>0.05 No change 2/10 vs. 2/10 Reported AS in ischemia: n= 10 vs. 10, p<0.05 Decrease (sig.) -55% Estimated Time in developing digitalis-induced VT or VF: n= 5 vs. 5, Increased >25 min vs. 10-15 min Reported	Sex diff? ND Age diff? ND BW diff? ND
Lo, 1991	VT (%) VPB	Normal conditions.	No events of VT or VPB were observed when infusing control buffer, ALA=1, 5, or 10 mg/kg (n= 8, same dogs for all groups) [ALA vs. Ctrl buffer n=8, same dogs for all groups] VT (%) ALA=20, or 30 mg/kg, p>0.05 Increased 13%, or 38% respectively Reported ALA=60 mg//kg, p=0.013 Increase (sig.) 63% Reported VPB (%) ALA=20 mg/kg, p>0.05 Increased 25% Reported ALA=30 mg/kg, p=0.003 Increase (sig.) 75% ALA=60 mg/kg, p=0.0007 Increase (sig.) 88% Reported All ventricular arrhythmia occurred within 3 seconds after injection and recovered spontaneously within 5 minutes. A significant depression of myocardial contractility (the change in maximal left ventricular dp/dt during systole) was noted at a dose of 5 mg/kg. When the dose of ALA was increased, a more prominent myocardial depression was observed. In contract, and injection of the control buffer solution did not alter left ventricular dp/dt.	Sex diff? No Age diff? ND BW diff? ND Injections of ALA invariably result in acute pulmonary edema within 5 minutes (unpublished observation). Thus, whether or not the observed CVD effect was due to the direct effect of ALA was questionable. Possibly cumulative effect should be considered because various testing doses were repeatedly given in each dog.
McLennan, 1996	VF (%) AS	Ischemia model	Ctrl: Olive oil AS (results in figure) [EPADHA vs. Ctrl] n= "n=10", p<0.02 Decrease (sig.) [EPA vs. Ctrl] n=ND, p>0.05 No change [DHA vs. Ctrl] n= "n=10", p<0.02 Decrease (sig.) VF (%) [EPADHA vs. Ctrl] n=ND p<0.01 Inhibitory effects 10%/80% Reported [EPA vs. Ctrl] n=ND, p>0.05 No change 70%/80% Reported [DHA vs. Ctrl] n=ND ", p<0.03 Inhibitory effects 20%/80% Reported	Sex diff? No Age diff? ND BW diff? ND No statistics were performed for these comparisons in the original study.

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
McLennan, 1995	VPB VT (%) VF (%) AS Deaths	Myocardial ischemia and reperfusion models: 15-min ischemia; 10-min reperfusion. 5-min ischemia; 10-min reperfusion.	15-min ischemia; 10-min reperfusion model: VPB [CAN vs. SSO in ischemia] n= 16 vs. 14, No change -13% Estimated [SBO vs. SSO in ischemia] n= 13 vs. 14, No change -14% Estimated [CAN vs. SSO in reperfusion] n= 13 vs. 13, No change -43% Estimated [SBO vs. SSO in reperfusion] n= 11 vs. 13, No change -2% Estimated VT (%) [CAN vs. SSO in ischemia] n= 16 vs. 14, No change 75%/93% Reported [SBO vs. SSO in ischemia] n= 13 vs. 14, No change 62%/93% Reported [CAN vs. SSO in reperfusion] n= 13 vs. 13, No change 31%/69% Reported [SBO vs. SSO in reperfusion] n= 11 vs. 13, No change 3%/69% Reported VF (%) [CAN vs. SSO in ischemia] n= 16 vs. 14, No change 43%/43% Reported [SBO vs. SSO in ischemia] n= 13 vs. 14, No change 38%/43% Reported [CAN vs. SSO in reperfusion] n= 13 vs. 13, Decrease (sig.) 0%/23% Reported [SBO vs. SSO in reperfusion] n= 11 vs. 13, No change 27%/23% Reported VF Deaths [CAN vs. SSO in ischemia] n= 16 vs. 14, Increased 19%/7% Reported [SBO vs. SSO in ischemia] n= 13 vs. 14, Increased 15%/7% Reported [CAN vs. SSO in reperfusion] n= 13 vs. 13, Decrease (sig.) 0%/8% Reported [SBO vs. SSO in reperfusion] n= 11 vs. 13, Decrease (sig.) 0%/8% Reported AS [CAN vs. SSO in ischemia] n= 16 vs. 14, No change -11% Estimated [SBO vs. SSO in ischemia] n= 13 vs. 14, No change -18% Estimated [CAN vs. SSO in reperfusion] n= 13 vs. 13, No change -64% Estimated [SBO vs. SSO in reperfusion] n= 11 vs. 13, No change -12% Estimated 5-min ischemia; 10-min reperfusion model: VPB [CAN vs. SSO in reperfusion] n= 10 vs. 10, p>0.05 No change [SBO vs. SSO in reperfusion] n= 10 vs. 10, p>0.05 No change VT (%) [CAN vs. SSO in reperfusion] n= 10 vs. 10, No change 70%/70% Reported [SBO vs. SSO in reperfusion] n= 10 vs. 10, No change 90%/70% Reported VF (%) [CAN vs. SSO in reperfusion] n= 10 vs. 10, No change 10%/50% Reported [SBO vs. SSO in reperfusion] n= 10 vs. 10, No change 50%/50% Reported VF Deaths [CAN vs. SSO in reperfusion] n= 10 vs. 10, 0%/30% Reported	Sex diff? No Age diff? No BW diff? ND

See abbreviations in List of Acronyms, Abbreviations, and Parameters

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
McLennan, Bridle, 1993	VFT VF (%)	Ischemia was induced by 15-min coronary artery occlusion. Isoproterenol (ISO) was injected in 0.5 ug/kg BW/min. Arrhythmias were induced by electrical stimulation protocol in control, 5 min after ischemia, and 30 min after restoration of coronary blood flow during the infusion of isoproterenol.	Ctrl: SF/SSO (8% sheep perirenal fat+2% sunflower-seed oil) [SF/FO vs. Ctrl] VF (%) in control condition: n=10 vs. 9, No Change 60%/60% Reported VF (%) in ischemia: n=10 vs. 9, No Change 100%/100% Reported VF (%) in ISO (0.5 ug/kg body wt/min): n= 10 vs. 9, p<0.05 Decrease (sig.) 3/10 vs. 7/9 Reported. The other 2 out of the 10 animal in FO group developed VT. VF (%) in ISO (2.0 ug/kg body wt/min): n=: 10 vs. 9, p=0.033 Decrease (sig.) 5/10 vs. 9/9 Reported Among susceptible animals: VFT in control condition: n= 6 vs. 6, p<0.05 Increase (sig.) +133% Estimated VFT in ischemia: n= 10 vs. 10, p<0.05 Increase (sig.) +79% Estimated VFT in ISO (0.5 ug/kg body wt/min): n= 5 (VF+VT) vs. 7, p<0.05 Increased +55% Estimated VFT in ISO (2.0 ug/kg body wt/min): n= 5 vs. 9, p>0.05 Increased +75% Estimated	Sex diff? No Age diff? ND BW diff? No

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
McLennan, 1993	Time in normal sinus rhythm VPB VT (%) VF (%) AS Deaths	Myocardial ischemia and reperfusion models: 15-min ischemia; 5-min reperfusion. 5-min ischemia; 5-min reperfusion.	15-min ischemia; 5-min reperfusion model: VPB [FO vs. SSO in ischemia] n= 14 vs. 13, No change -10% Estimated [FO vs. SSO in reperfusion] n= 14 vs. 12, No change -31% Estimated VT (%) [FO vs. SSO in ischemia] n= 14 vs. 13, Decrease 35%/92% Reported [FO vs. SSO in reperfusion] n= 14 vs. 12, p<0.05 Decrease (sig.) 21%/67% Reported VF (%) [FO vs. SSO in ischemia] n= 14 vs. 13, Decrease (sig.) 0%/38% Reported [FO vs. SSO in reperfusion] n= 14 vs. 12, p>0.05 No Change, 0%/8% Reported Time in sinus rhythm [FO vs. SSO in ischemia] n= 14 vs. 13, No change +12% [FO vs. SSO in reperfusion] n= 14 vs. 12, p>0.05 No Change Deaths [FO vs. SSO in ischemia] n= 14 vs. 13, Decrease (sig.) 0%/8% Reported [FO vs. SSO in reperfusion] n= 14 vs. 12, No change 0%/0% Reported AS [FO vs. SSO in ischemia] n= 14 vs. 13, , p<0.05 Decrease (sig.) -41% Estimated [FO vs. SSO in reperfusion] n= 14 vs. 12, p<0.05 Decrease (sig.) –63% Estimated 5-min ischemia; 5-min reperfusion model VPB [FO vs. SSO in reperfusion n= 10 vs. 12, No change -27% Estimated VT (%) [FO vs. SSO in reperfusion] n= 10 vs. 12, No change 60%/80% Reported VF (%) [FO vs. SSO in reperfusion] n= 10 vs. 12, Decrease 10%/25% Reported Time in sinus rhythm [FO vs. SSO in reperfusion] n= 10 vs. 12, No change +16% Estimated Deaths [FO vs. SSO in reperfusion] n= 10 vs. 12, Decrease (sig.) 0%/8% Reported AS [FO vs. SSO in reperfusion] n= 10 vs. 12, Decrease -48% Estimated	Age diff? No BW diff? No No statistics were performed for FO vs. SSO comparisons in the original study.

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
McLennan, 1992	VFT VF (%) Deaths	Ischemia was induced by 15-min coronary artery occlusion. Isoproterenol (ISO) was injected in 0.5 ug/kg BW/min. Arrhythmias were induced by electrical stimulation protocol in control, 5 min after ischemia, and 30 min after restoration of coronary blood flow during the infusion of isoproterenol.	VF (%) [TFO vs. SSO in control condition] n= 16 vs. 13, No change 10/16 vs. 8/13 Estimated from graph [TFO vs. SSO in ischemia] n= 16 vs. 13 No change 12/16 vs. 8/13 Estimated from graph [TFO vs. SSO in ISO] n= 16 vs. 13 No change 7/16 vs. 10/13 Estimated from graph In TFO fed animals, 80% of VF episodes were of less than 5 seconds' duration compared with only 25% of SSO (p=0.054 n.s.) animals. VFT in susceptible marmosets (results in figure) [TFO vs. SSO in control condition] n= 10 vs. 8, p>0.05 No change [TFO vs. SSO in ischemia] n= 12 vs. 8, p>0.05 No change [TFO vs. SSO in ISO] n= 7 vs. 10, >0.05 No change Total VF Deaths, combining the Deaths in control condition, ischemia, and isoproterenol models. [TFO vs. SSO] n= 16 vs. 13, Decrease (sig.) 0/16 vs. 3/13 Reported	Sex diff? ND Age diff? No BW diff? No Isoproterenal induced a sig. increase in the proportion of inducible animals having sustained episodes of VF in all dietary groups; as well as a sig. proportion of animals suffering fatal VF and cardiac arrest compared to the control condition.
McLennan, 1990	Time in normal sinus rhythm VPB VT (%) VF (%) AS Deaths	Myocardial ischemia and reperfusion models: 15-min ischemia; 10-min reperfusion.	VPB [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, p>0.05 No change [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, p<0.05 Decrease (sig.) -24% Estimated VT (%) [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, p>0.05 No change 57%/57% Reported [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, p>0.05 No change 71%/86% Reported VF (%) [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, p>0.05 No change 14%/29% Reported [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, p>0.05 No change 29%/29% Reported Time in sinus rhythm [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, p>0.05 No change [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, p>0.05 No change VT/VF Deaths [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, No change 0%/0% Reported [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, No change 0%/0% Reported AS (results in figure [SF/TFO vs. SF/SSO in ischemia] n= 7 vs. 7, p>0.05 No change [SF/TFO vs. SF/SSO in perfusion] n= 7 vs. 7, p>0.05 No change	Sex diff? No Age diff? No BW diff? Yes SSO group had significant lower body weight after 18 months

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
McLennan PL 1988	VT (%) VF (%) AS Ischemic region (%)	Myocardial ischemia and reperfusion models: 15-min ischemia, followed by reperfusion.	VT (%) [TFO vs. SSO in ischemia] n= 10 vs. 10, p<0.01 Decrease (sig.) 37% vs. 77%* Reported [TFO vs. SSO in reperfusion] n= 10 vs. 10, p<0.05 Decrease (sig.) 50%* vs. 80%* Estimated VF (%) [TFO vs. SSO in ischemia] n= 10 vs. 10, p<0.01 Decrease (sig.) 0% vs. 10%* Reported [TFO vs. SSO in reperfusion] n= 10 vs. 10, p<0.05 Decrease (sig.) 0% vs. 30% Estimated AS (results in figure) [TFO vs. SSO in ischemia] n= 10 vs. 10, p>0.05 No change [TFO vs. SSO in reperfusion] n= 10 vs. 10, p<0.05 Decrease (sig) -44% Estimated IS [TFO vs. SSO] n= 10 vs. 10, No change +7% Estimated No animal died in TFO and SSO groups.	Sex diff? No Age diff? No BW diff? Yes SSO=512 gm; TFO=566 gm
Oskarsson, 1993	SIZ (%)	Myocardial ischemia and reperfusion models: 90-min ischemia; 30-min reperfusion.	Ctrl: No fish oil Rx [MaxEPA vs. Ctrl] Myocardial infarct size (%): n= 10 vs. 12, p<0.05 Decrease (sig.) 13%/29% Reported Amount of myocardium at risk for severe ischemia (%): n= 10 vs. 12, p>0.05 No change 41.2%/39.3% Reported	Sex diff? ND Age diff? ND BW diff? No
Otsuji, 1993	Deaths Infracted area Size of the area at risk (%)	Coronary artery occlusion (ischemia model)	Ctrl: Standard dog chow [EPA-ester vs. Ctrl] VF Deaths: n= 10 vs. 15, p<0.05 Decrease (sig.) 0%/33% Reported Ultimate size of the infarcted area: n= 10 vs. 10, p<0.01 Decrease (sig.) 17.6%/29.2% Reported Size of the area at risk (%): n= 10 vs. 10, p>0.05 No change	Sex diff? ND Age diff? ND BW diff? ND

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Evidence Table 1: Whole Animal Studies

Part 2

Author, yr	Outcomes	Experimental Protocols	Results	Comment/ Biases/ Limitations
Pepe, 1996	VPB VT (%) VF (%) VFT	Myocardial ischemia and reperfusion models: 15-min ischemia; 10-min reperfusion. Electrical Stimulation (independent of myocardial ischemia model)	[FO vs. SAT] Ischemia-reperfusion model: VPB during ischemia: n= 20 vs. 20, p<0.05 Decrease (sig.) -73% Estimated VT (%) after ischemia-reperfution: n= 20 vs. 20, p<0.05 Decrease (sig.) 10%/70% Reported VF (%) after ischemia-reperfution: n= 20 vs. 20, p<0.05 Decrease (sig.) 0%/80% Reported Electrical Stinulation: The threshold current for VF induction was reduced in all dietary groups in ischemia but remained significantly higher in the mackerel-oil-fed group than in the saturated-fat-fed group (n=10 per group).	Sex diff? No Age diff? No BW diff? ND
Yang, 1993	VF (%) or VF (%)	Myocardial ischemia and reperfusion models: 15-min ischemia; 10-min reperfusion.	[FO vs. Butter] VT (%) or VF (%): n= 8 vs. 9, p<0.05 Decrease (sig.) 3/8 vs. 7/9 Reported	Sex diff? No Age diff? ND BW diff? ND

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies

Part 1

Author, yr	Country Funding	Species Stage Sex	Exp-osure Dura-tion (weeks)	Group [Sample Size]	Total Fat (omega-3 fatty acids)	Unit	SFA	MUFA	PUFA	ALA	EPA	DHA	Other omega-3 fatty acids
Benedik-tsdottir, 1988	Iceland U	Rats Adult Male	16	Corn oil (CO) [ND] Cod-liver oil (CLO) [ND]	10 %w 10 %w	% total fatty acids	14.5 22.0	24.5 47.0	57.8 27.2	ND ND	0.0 6.9	0.0 7.2	0.0[3] 0.9[3]
Black, 1989	Canada G	Rats Adult Male	4	STD [6] STD+FO [6]	 0.5ml/kg/day	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	
Chemla, 1995	France G	Rats Adult Male	4	N-3 [15] N-6 [15]	15%w 15%w	%TFA	20.0 19.8	57.7 58.9	11.4 20.7	0.8 0.5	4.3 0.0	4.1 0.0	
Chen, 1994	Taiwan G	Rabbits Adult Male	2	High cholesterol (HC) [11-15] HC+FO [11-12]	40 %kcal 40 %kcal (10 %kcal from fish oil)	% w/w	ND ND	ND ND	ND ND	ND ND	ND 30.2	ND 21.5	
Croset, 1989a	USA G[1]	Mouse Weanling Male	2	STD [10] STD+0.4 %w/w DHAe[10] STD+0.8 %w/w DHAe[10] STD+ 4%w/w DHAe [10]	0 %w 10 %w/w 10 %w/w 10 %w /w	Mol%	11.8 11.7 11.5 5.3	31.7 28.8 25.7 9.3	56.1 59.1 61.6 85.3	0.0 0.0 0.0 0.0	ND ND ND ND	0.0 0.1 0.2 0.8	
Croset, 1989b	USA G	Mouse Weanling Male	2	OO+ALA e [6] OO+EPA e [6] OO+DHA e [6]	1.5+0.5%w 1.5+0.5%w 1.5+0.5%w	Mol%	27.6 30.3 27.5	44.5 49.8 47.3	27.9 19.9 25.1	20.5 1.0 0.5	0.2 8.1 0.9	0.1 1.9 16.5	
Demai-son, 1993	France G	Rats Weanling Male	8	SF [32] LIN [29]	100g/Kg 100g/kg	% TFA	11.8 8.7	16.2 20.3	71.7 71.0	0.2 53.5	ND ND	ND ND	
Gillis, 1992	Canada G	Rabbits Weanling ND	6	SAF (9) FO (9)	10%w 10%w	%w	9.6 23.5	13.1 29.2	77.3 47.3	0.0 1.4	0.0 26.5	0.0 8.6	0.0[3] 2.3[3]

See abbreviations in List of Acronyms, Abbreviations and Parameters

Appendix C

Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies

Part 1

Author, yr	Country Funding	Species Stage Sex	Exp-osure Dura-tion (weeks)	Group [Sample Size]	Total Fat (omega-3 fatty acids)	Unit	SFA	MUFA	PUFA	ALA	EPA	DHA	Other omega-3 fatty acids
Gudmundsdottir, 1991	Iceland U	Rats Adult Male	20	CO [5] CLO (4)	10%w 10%w	%w	13.6 18.1	24.6 51.0	58.6 27.7	2.6 0.0	0.0 7.1	0.0 8.1	
		Rats Aged Male	88	CO [5] CLO (4)	10%w 10%w	%w	13.6 18.1	24.6 51.0	58.6 27.7	2.6 0.0	0.0 7.1	0.0 8.1	
Heard, 1992	USA U	Rats Adult Male	4	SAF [18] MenO+SAF [18]	20%w 19.5%+0.5 %w	ND	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	
Honen, 2002	Austra-lia G	Rats Adult Male	3	Canola oil (6) FO(6) G	3ml/d 3ml/d	% TFA	6.2 1.7	60.0 15.8	33.8 77.7	12.1 0.5	0 48.0	0 26.2	
Karmazyn, 1987	Canada G	Rats Weanling Male/ Female	12	STD [14] STD+Cod liver oil (CLO) [14]	10%w	ND	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	
Kinoshita, 1994	Japan U	Dogs Adult ND	8	STD (15) STD+EPAe (15)	100mg/kg	mg/kg/d	ND ND	ND ND	ND ND	ND ND	ND 100	ND ND	
Ku, 1997	Japan G	Rats Aged Female	12	HC (5) HC+EPA (5) HC+DHA (5)	5.1%w 5.1%w (300mg/kg) 5.1%w (300mg/kg)	ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	ND ND ND	
Lamers, 1988	Neth.; Italy G	Pigs Weanling Male/ Female	8	LARD [8] FO +LARD [8]	9%w 4.5% +4.5%w	%TFA	36 32	46 40	15 11	1 1	0 8	0 5	
Laustiola, 1986	Finland U	Rats Weanling Male	16	STD [20] STD+CLO [33]	10%na	% TFA	26.2 22.8	23.6 46.5	49.7 28.6	5.3 1.7	1.3 6.4	2.7 8.2	0.2[3] 2.7[4] 0.7[3] 8.2[4]

See abbreviations in List of Acronyms, Abbreviations and Parameters

Appendix C

Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies

Part 1

Author, yr	Country Funding	Species Stage Sex	Exp-osure Dura-tion (weeks)	Group [Sample Size]	Total Fat (omega-3 fatty acids)	Unit	SFA	MUFA	PUFA	ALA	EPA	DHA	Other omega-3 fatty acids
Leifert, 2000a	Austra-lia G	Rats Young Adult Male	3	LARD [6-8] FO [6-8] G5	29% E (74kJ fat/d) 29% E (74kJ fat/d)	% w	58.0 27.3	39.4 28.2	2.6 44.6	0.7 1.1	0.1 24.3	0.0 12.1	0.0[3] 2.3[3]
Leifert, 2001	Australia I+NP	Rats Adult Male	3	SF (6) FO (6)	17%w (10%w) 17%w (10%w)	%w	36.4 18.6	55.1 44.0	8.5 37.4	1.2 0.9	0 17.8	0 8.9	0.0[3] 1.7[3]
Maixent, 1999	France G+NPI	Rats Adult Male	8	STD [11] STD+FO [10]	0.5g of oil/kg	mg/g of oil	ND ND	ND ND	ND ND	ND ND	ND **180**	ND **120**	
Minaro-vic, 1997	Slovak G	Rats Young Adult Male	2	HF [10] FO [10]	300g/kg 100g/kg	% w	47.0 13.0	39.7 29.4	13.3 57.6	ND ND	ND ND	ND ND	
Pepe, 1999	USA U	Rats Young Adult Male	6	N-6 (6) FO (5)	15.6% w (11.7%w) 15.6%w (11.7%w)	ND	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND	ND ND
Reig, 1993	Spain U	Rats Young Adult Male	5	HF (20) HF+FO (20)	37%w 31%+6%w	%TFA	36.7 30.0	40.0 33.0	19.4 37.1	2.2 3.4	0.0 4.6	0.0 3.4	0.0[3] 1.0[3]
Swan-son, 1989	USA G	Mouse Weanling Male	2	SAF+CO (9) SAF+MenO (9)	12%w (2%+10%w) 12%w (2%+10%w)	%w	14.5 28.5	24.2 26.1	60.9 44.7	1.0 1.8	0.0 12.9	0.0 9.1	0.0[3] 2.0[3]
Taffet, 1993	USA G	Rats Young Adult Female	3	CO [11] CO+MenO [12]	20%w 3%+17%w	Mol %	14.3 39.9	26.3 28.3	59.3 31.9	0.0 1.3	0.0 16.5	ND ND	

See abbreviations in List of Acronyms, Abbreviations and Parameters

Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Benedikt-sdottir, 1988	IPIM	Sarcolemma	Ambient	None	Yes	CLO vs. CO - NC in Na^+K^+ATPase (n=ND; p>0.05)
Black, 1989	IPIM	Sarcoplasmic reticulum	Ambient	None	ND	STD+FO vs. STD - NC in sarcoplasmic reticulum calcium transport activity (n=6;p>0.05)
Chemla, 1995	CP	Myocardium	Ambient	None	ND	N-3 vs. N-6 - NC in force-velocity relationship characteristics (n=15; p>0.05)
Chen, 1994	IPIM	Myocardial mitochondria	Sham ischemic	None	ND	HC+FO vs. HC - NC in mitochondrial calcium concentrations (n=5/group; p>0.05)
			Short-term Ischemia (Occl-10min Rep-1hr) Long-term Ischemia (Occl-1hr Rep-4hr)	None	ND	HC+FO vs. HC - NC in mitochondrial calcium concentrations after short or long term ischemia (n=11/group; p>0.05)
Croset, 1989a	IPIM[1]	SR vessicles[2]	Ambient	None	Yes	All DHA diets vs. STD - NC in maximum velocity of SR Ca2+, Mg2+-ATPase with incremental levels of DHA (n=10/group; p>0.05)
		Myocardial mitochodria	Ambient	0.15 uM oligomycin	Yes	STD+0.4%DHAe. vs. STD - Increased maximum velocity of mitochondrial oligomycin-sensitive ATPase (%=ND)(n=10/grp, p<0.02) STD+0.8%DHAe. vs. STD - Increased maximum velocity of mitochondrial oligomycin-sensitive ATPase (%=ND)(n=10/grp, p<0.05) STD+4%DHAe. vs. STD - NC in maximum velocity of mitochondrial oligomycin-sensitive ATPase (n=10/grp, p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Croset, 1989b	IPIM	SR vesicles	Ambient	None	Yes	OO+ALAe. vs. Safflower oil - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p<0.05) OO+EPAe. vs. Safflower oil - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p<0.04) OO+DHAe. vs. O Safflower oil - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p<0.03)
						OO+ALAe. vs. OO+EPAe. - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p=ND) OO+ALAe. vs. OO+DHAe. - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p=ND) OO+EPAe. vs. OO+DHAe. - Decreased Ca^{2+} transport measured a maximum rate of Ca^{2+} accumulation in cardiac SR vesicles (%=ND) (n=3; p=ND) OO+EPAe. vs. OO+SA - NC in maximum specific activity (V_{max}) and affinity for Ca^{2+} and ATP of $Ca^{2+}Mg^{2+}$ATPase associated with CA2+ uptake (n=3;p>0.05) OO+DHAe. vs. OO+SA - NC in maximum specific activity (V_{max}) and affinity for Ca^{2+} and ATP of $Ca^{2+}Mg^{2+}$ATPase associated with CA2+ uptake (n=3;p>0.05)
Demaison, 1993	CP	Isolated Working heart	Ambient (Perfusion)	None	Yes	LIN vs. SF - NC in contractility (n=29-32; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Gillis, 1992	BEP	SR vesicles	Ambient	None	Yes	FO vs. SAF - NC in mean baseline QRS (n=9; p>0.05) - NC in mean baseline QT interval duration (n=9; p>0.05)
			Electrical	None	Yes	FO vs. SAF - NC in mean baseline left ventricular effective refractory period (VERP) (n=9; p>0.05) - NC in mean baseline epicardial MAP duration (n=9; p>0.05) - NC in mean baseline endocardial MAP duration (n=9; p>0.05) - NC in strength - interval relations (mean threshold current at each coupling interval) (n=9; p>0.05)
			Electrical	None	Yes	FO vs. SAF - NC in mean diastolic threshold (n=9; p>0.05) - NC in absolute refractory period (n=9; p>0.05) - NC in relative refractory period (n=9; p>0.05)
Gudmundsdottir, 1991	ICH	Sarcolemma	Ambient	NIT	Yes	CLO vs. CO at 20 weeks - NC in the affinity ($1/K_d$) and binding (B_{max}) of slow Ca2+ channels for [3H NIT] (n=4-5;p>0.05) CLO vs. CO at 88 weeks - Decreased the affinity (1/K) and binding (B_{max})of slow Ca2+ channels for [3H NIT] (n=4-5;p<0.05)
Heard, 1992	CP	Atrial tissue	Ambient	Saline	ND	FO+SAF vs. SAF - NC in force of contraction indexed to body weight (FOC/BW) (n=6; p>0.05) - NC in maximum rate of rise of contraction (dF/dt) (n=6; p>0.05) - NC in maximum rate of relaxation (-dF/dt) (n=6; p>0.05) - NC in atrial rate (beats/min) (n=6; p>0.05)
	CP	Atrial tissue	Ambient	LPS (20mg/kg)	ND	FO+SAF vs. SAF - Increased force of contraction indexed to body weight (FOC/BW) (n=11; p<0.05) - Increased maximum rate of rise of contraction (dF/dt) (n=11; p<0.05) - Increased maximum rate of relaxation (-dF/dt) (n=11; p<0.05) - Decreased atrial rate (beats/min) (n=ND; p<0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
	CP	Atrial tissue	Ambient	ISO (0.1, 0.5, 1.0 and 5.0uM)	ND	FO+SAF vs. SAF - NC in atrial force of contraction indexed to body weight (FOC/BW) as a function of Iso concentration (n=ND; p>0.05)
Honen, 2002	IPIM	Atrial myocytes	Ambient	None	Yes	FO vs. RO - NC in mean area of Ca2+ sparks n=5; p>0.05) - NC in mean duration of Ca2+ sparks (n=5; p>0.05) - NC in mean frequency of Ca2+sparks (n=5; p>0.05) - Increased the proportion of "ideal' sparks (rapid rise and exponential fall by 9.1% (n=5; p<0.05) - NC in proportion of "very slow rise and fall sparks" (n=5; p>0.05) - Decreased the proportion of "marked step/plateau in the decay phase" sparks by 63% (n=5; p<0.05)
Karma-zyn, 1987	IPIM	Ventricular myocytes	Ischemia-Reperfusion	None	Yes	STD+CLO vs STD - Time dependent (10-80mins) increase in Ca^{2+} uptake by 135-159% (n=5-9; p<0.01) - NC in Ca^{2+} efflux (n=5-9; p>0.05)
	BEP	Ventricular myocytes	Ischemia-Reperfusion	None	Yes	STD+CLO vs STD - NC in developed or resting tension (n=5-9; p>0.05)
Kinoshita, 1994	IPIM	Myocardial microsomal vesicles	Ambient (non-infarct)	None	Yes	STD+EPAe. vs. STD - Increased Ca^{2+}-Mg^{2+}ATPase V_{max} by 48% (n=6; p<0.01) - NC in Km (n=6; p>0.05)
		Myocardial microsomal vesicles	Ischemia	None	Yes	STD+EPAe. vs. STD - Increased Ca^{2+}-Mg^{2+}ATPase V_{max} by 45% (n=6; p<0.01) - NC in Km (n=6; p>0.05)
		Myocardial microsomal vesicles	Ambient (non-infarct)	Oua	Yes	STD+EPAe. vs. STD - NC in Na^{2+}-K^{2+}ATPase V_{max} (n=6; p>0.01) - NC in the amount of ouabain needed to induce 50% inhibition (IC_{50}) of Na^{2+}-K^{2+}ATPase activity.(n=6; p>0.05)
		Myocardial microsomal vesicles	Ischemia	Oua	Yes	STD+EPAe. vs. STD - NC in Na^{2+}-K^{2+}ATPase V_{max} (n=6; p>0.01) - NC in the amount of ouabain needed to induce 50% inhibition (IC_{50}) of Na^{2+}-K^{2+}ATPase activity.(n=6; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Ku, 1997	CP	Isolated Heart	Ambient	None	Yes	HC+EPA vs. HC - NC in recovery of heart rate (n=5; p>0.05)
			Ambient	None	Yes	HC+DHA vs. HC - NC in recovery of heart rate (n=5; p>0.05)
			Ambient	None	Yes	HC+DHA vs HC+EPA - NC in recovery of heart rate (n=5; p>0.05)
Lamers, 1988	IPIM	Sarcolemma	Ambient	Ca^{2+}	Yes	FO+LARD vs LARD - Increased Ca^{2+} pumping ATPase activity by 68% (n= 6; p< 0.05)
			Ischemia (5 min) Reperfusion (10 min)	Ca^{2+}	Yes	FO+LARD vs LARD - Increased Ca^{2+} pumping ATPase activity by 43% (n=6; p< 0.05)
Laustiola, 1986	CP	Atrial myocytes	High O2	None	Yes	STD+CLO vs STD - Decreased contraction amplitude by 25% (n=7-11; p<0.001) - Decreased heart rate by 24% (n=7-11; p<0.001)
			High O2	NA($1x10^{-6}$/90sec)	Yes	STD+CLO vs STD - NC in contraction amplitude (n=4-11; p>0.05) - NC in heart rate (n=4-11; p>0.05)
			Hypoxia	NA($1x10^{-6}$/90sec)	Yes	STD+CLO vs STD - Decreased contraction amplitude by 58% (n=4-11; p<0.001) - Decreased heart rate by 13% (n=4-11; p<0.001)
			Reoxy O2 5min	NA ($1x10^{-6}$/90sec)	Yes	STD+CLO vs STD - NC in contraction amplitude (n=4-11; p>0.05) - NC in heart rate (n=4-11; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Leifert, 2000a	CP	Ventricular myocytes	Ambient		Yes	FO vs. LARD - NC in resting or diastolic cell length (voltage required to stimulate 90% of cells to contract) (n=29-36; p>0.05) - NC in systolic cell length (peak cell shortening during steady state) (n=29-36; p>0.05) - NC in percent cell length (systolic-diastolic/diastolic*100) (n=29-36; p>0.05) - NC in post-rest potentiation (post rest contraction length/steady state contraction length*100) (n=29-36; p>0.05)
			Ambient	ISO (0.01-3uM/3min)	Yes	FO vs. LARD - Decrease and delay in the development of ISO induced asynchronous contractile activity (n=6 animals/gr; p<0.05) - EC_{50} values were 892 ± 130nM and 347 ± 91 nM for FO and LARD, respectively.
			Ambient	FRGS (2.3mM purine; 7mU/ml xanthine oxidase/20mins)	Yes	FO vs. LARD - Decreased development of FRGS induced asynchronous contractions over the entire time course (3-20mins) (n=6-9 animals/gp; p<0.01) - Increased the time taken until 50% of cardiomyocytes contracted in an asynchronous manner (30%) (n=6-9animals/gp; p<0.01)
			Ambient	None	Yes	FO vs. LARD - NC in voltage dependence of Na^+ current activation parameters G_{max}; V_{50}; E_{rev} or K (n=28; p>0.05) - NC in voltage dependence of Na^+ current inactivation parameters I_{max} and K (n=28; p>0.05) - More negative V_{50} for the voltage dependence of Na^+ current inactivation (n=28; p<0.05)
			Ambient	None	Yes	FO vs. LARD - NC in I_{to} current activation parameters I_{max}; V_{50} or K (n=17-28; p>0.05) - NC in I_{to} current inactivation parameters I_{max}; V_{50} or K (n=17-28; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Leifert, 2001	CP	Cardio-myocytes	Ambient	ISO (0.1-3uM)	Yes	FO vs. SF - Decreased the time of onset of asynchronous contractile activity (%=ND)(n=6 animals; p<0.001) - No change in the number of asynchronously contracting myocytes (n= 29-32; *p>0.05*) - Prevented asynchronously contraction during Ca2+ transient measurements (n= 29-32; p<0.05)
	IPIM		Ambient	None	Yes	FO vs. SF - NC in SR Ca2+ transient under steady state conditions and after 30sec rest period (n=8/grp; p>0.05)
			Ambient	Caffeine (20mM) – induced SR Ca2+ release	Yes	FO vs. SF - NC in SR Ca2+ content (n=8/grp; p>0.05)
			Ambient	DBHQ (10uM/4m): SR Ca2+ ATPase inhibitor	Yes	FO vs. SF - NC in value of the peak Ca2+ transient (n=32; p>0.05) - Increased the time constant of decay (tau) of the Ca2+ transient (%=ND) (n=8/grp; p<0.05), indicating a more rapid Ca2+ efflux via sarcolemmal Ca2+ exchangers in the SF group.
			Ambient	None	Yes	FO vs. SF - Increased the time constant of the decay phase of the Ca2+ transient (%=ND) (n=8/grp; p<0.05) - NC in end-diastolic Ca2+ concentration (n=8/grp; p>0.05) - NC in systolic peak Ca2+ concentration (n=8/grp; p>0.05) - NC in developed Ca2+ concentration (systolic-end diastolic) (n=8/grp; p>0.05)

Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
			Ambient	ISO (0.5uM): increase the cellular Ca2+ load	Yes	FO vs. SF - Increased the time constant of the decay phase of the Ca2+ transient by 13% (n=8/grp; p<0.01), indicating a more rapid Ca2+ efflux via SR and/or sarcolemmal Ca2+ exchangers in the SF group. - NC in end-diastolic Ca2+ concentration (n=8/grp; p>0.05) - NC in systolic peak Ca2+ concentration (n=8/grp; p>0.05) - NC in developed Ca2+ concentration (systolic-end diastolic) (n=8/grp; p>0.05)
Maixent, 1999	IPIM	Myocardial microsomal vesicles	Ambient	OUA (10^{-7} to 10^{-4}M)	Yes	STD+FO vs. STD - NC in ouabain-sensitive Na^+K^+ATPase activity (n=4; p>0.05) - NC in relative contribution of Na^+K^+ATPase a2 isoform (high affinity) - NC in relative contribution of Na^+K^+ATPase a1 isoform (low affinity) - NC in IC_{50} value of Na^+K^+ATPase a2 isoform (high affinity) - Lower IC_{50} value of Na^+K^+ATPase a1 isoform (low affinity)
Minarovic, 1997	ICU	Ventricular myocytes	Ambient	None	Yes	FO vs. HF - NC in rates of activation and the fast component of inactivation of the Ca^{2+} current (n=ND; p>0.05) - More negative half–inactivation potential (n=5-8;p<0.05) suggesting that these channels are less prone to inactivation - NC in voltage dependence of the peak I_{Ca} amplitude (n=ND; p>0.05)
			Ambient	Verapamil (ND)	Yes	FO vs. HF - No effect on the binding characteristics of the calcium channel blockers or the parameters of the I_{Ca}-V curves (n=ND; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
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Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
			Ambient	Diltiazem: (ND)	Yes	FO vs. HF - No effect on the binding characteristics characteristics of the calcium channel blockers or the parameters of the I_{Ca}-V curves (n=ND; p>0.05)
Reig, 1993	BEP	Ventricular Tissue	Ambient	None	Yes	HF+FO vs. HF - Decreased ventricular refractory period by 14% (n=5 animals; *p<0.05*)
	CP	Ventricular Tissue	Ambient	None	Yes	HF+FO vs. HF - No change in proportion of animals with heart rate >750 beats/min by 50% (n=10animals; *p>0.05)*
Pepe, 1999	IPIM	Myocardial mitochondria	Ambient	None	Yes	FO vs. N-6 in young animals - NC in response of mitochondrial Ca2+concentration (n=5-6; p>0.05) FO vs. N-6 in aged animals - NC in response of Ca2+concentration (n=5-6; p>0.05) FO vs. FO (aged vs. young) - NC in response of Ca2+concentration (n=5-6; p>0.05)
			Ambient	Norepinephrine (10^{-7} M): ß-adrenergic receptor stimulation	Yes	FO vs. N-6 in young animals - Decreased response of Ca2+concentration by 32% (n=5-6; p<0.05) FO vs. N-6 in aged animals - Decreased response of Ca2+concentration by 35% (n=5-6; p<0.05) FO vs. FO (aged vs. young) - NC in response of Ca2+concentration (n=5-6; p>0.05)
			15-min low-flow ischemia, and 5-min reperfusion	None		FO vs. N-6 in young animals - Decreased response of Ca2+concentration (n=6; p<0.0001) FO vs. N-6 in aged animals - Decreased response of Ca2+concentration (n=6; p<0.05)

Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
Swanson, 1989	IPIM	SR vesicles	Ambient	None	Yes	SAF+MenO vs SAF+CO - Decreased relative activity of Ca2+-Mg2+ ATPase activity by 86% (n= 3 pools of 3 hearts per replicate; p<0.05) SAF+MenO vs SAF+CO - Decreased the initial (0-5 min) calcium transport rate by 60% (n= 3 pools of 3 hearts per replicate; p<0.05) SAF+MenO vs SAF+CO - Decreased maximum sarcoplasmic reticulum calcium uptake by 62% (n= 3 pools of 3 hearts per replicate; p<0.01)
Taffet, 1993	IPIM	Ventricular SR vesicle	Ambient	None	Yes	CO+FO vs. CO - Decreased oxalate facilitated ATP dependent SR Ca2+ uptake by 30% (n=11-12; p<0.05)
			Ambient	Calcium 40uM +ATP 50um	Yes	CO+FO vs. CO - Decreased $Ca^{2+}Mg^{2+}$ ATPase activity by 25% (n=11-12; p<0.05) - Decreased Ca^{2+}ATPase activity (independent of Mg-ATPase activity) by –27% (n=11-12; p<0.05)
			Ambient	Calcium 40uM +ATP 50um +Ionomycin (800mM)	Yes	CO+FO vs. CO - Decreased $Ca^{2+}Mg^{2+}$ATPase activity by 27% (n=11-12; p<0.05) - Decreased $Ca^{2+}Mg^{2+}$ ATPase activity (independent of Mg^{2+}ATPase activity) by 27% (n=11-12; p<0.05) - NC in Mg-ATPase activity (independent of Ca^{2+}ATPase activity) (n=11-12; p>0.05)

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Evidence Table 2. Whole-Animal Isolated Organ and Cell Studies
Part 2

Author, yr	Outcome Category	Cell or Tissue	Expt Condition	Agent	Change in Membrane Composition	Results (n=cells)
			Ambient	40uM calcium+ 1mM ATP +Ionomycin (800mM)	Yes	CO+FO vs. CO - Decreased $Ca^{2+}Mg^{2+}$ATPase activity by 23% (n=11-12; p<0.05) - Decreased Ca^{2+}ATPase activity (independent of Mg^{2+}ATPase activity) by 23% (n=11-12; p<0.05) - Decreased Mg^{2+}ATPase activity (independent of Ca^{2+}ATPase activity (%=ND); (n=11-12; p<0.05) - Decreased calcium accumulation by isolated SR by 27% (n=11-12; p<0.05) - NC in iononycin stimulation (n=11-12; p>0.05) - NC in acylphosphate (EP) (n=4; p>0.05) - Decreased turnover (Ca-ATPase/total EP) by 24% (n=11-12; p<0.05) - Decreased turnover (Ca-ATPase/CaEP) by 17% (n=11-12; p<0.05) - NC in coupling (ATP/Ca uptake) (n=11-12; p<0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
Bayer, 1979	Germany, U	Cat Adult heart in situ	ALA-Na 2mg/kg/min Free IV	5 min	BEP	Ambient	INDO	ALA vs. Ctrl - No change in intra-atrial conduction time - No change in atrioventricular conduction time - No change in functional refractory period of the atrium - No change in functional refractory period of atrio-ventricular conducting system
Bogdanov, 1998	Russia/USA U	Rat Adult Ventricular	DHA 5µM Free	3-12 mins	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_{to} by 40% (n=ND; p=ND) which were not observed when 4-AP (5µM/ND) was present in the bath medium - Decreased I_{to} amplitude by 60% (n=ND; p=ND) - Increased I_{to} delay (n=ND; p=ND) - Decreased time constant of I_{to} inactivation (t) evoked by a voltage step from –70 to +60MV by 33% within 3mins (n=4; p<0.02). - Effects were reversible by BSA
			DHA 5µM Free	3-12 mins	ICU	Ambient	INDO (10µM) Added with FA	DHA+INDO vs. Ctrl+INDO - Presence of INDO did not modify effects on I_{to} indicating that effects of DHA were not related to its cyclooxygenase products (n=ND; p>0.05)
			DHA 50µM Free	3-12 mins	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_{SUS} by 32% (n=ND; p=ND) - No change in I_{KI} at voltages between -120 to -80mV (n=5; p>0.05)
			EPA 5-10µM Free	3-12 mins	ICU	Ambient	None	EPA vs. Ctrl - No change in of I_{SUS} (n=4; p>0.05)
			EPA 20µM Free	3-12 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_{SUS} by 16% (n=4; p<0.05)
			EPA 50µM Free	3-12 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_{to} by 73% (n=4; p<0.05) - Decreased I_{SUS} by 56% (n=4; p<0.05) - No change in I_{KI} at voltages between -120 to -80mV (n=5; p>0.05)
			EPA 5-10um Free	10-15 mins	BEP	Ambient	None	EPA vs. Ctrl - Increased AP (% in fig) (n=ND; p=ND) - No change in APA (n=ND; p>0.05)
			EPA 20uM Free	10-15 mins	BEP	Ambient	None	EPA vs. Ctrl - Increased APD (% in fig) (n=ND; p=ND) - Decreased APA (% in fig) (n=ND; p<0.05) - Decreased V_{max} (% in fig) (n=ND; p=ND)
			DHA 10-50µM Free	10-15 mins	BEP	Ambient	None	DHA vs. Ctrl - Similar effects as EPA on APD, APA and V_{max} (data not shown)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
Courtois, 1992	France G	Rat Neonatal Ventricular	SM3-Na-BSA (ALA+EPA) 28.3+29.9 % of total FA's Bound	24 hour s	CP	Ambient	None	SM3 vs. Ctrl - No change in contraction rate (n=5; p>0.05) - No change in CD_{80} (n=5; p>0.05) - No change $+C_{max}$ (n=5; p>0.05) - No change in $-C_{max}$ (n=5; p>0.05) SM3 vs. SM6 - No change in contraction rate (n=5; p>0.05) - No change in CD_{80} (n=5; p>0.05) - Increased $+C_{max}$ (n=5; p<0.01) - No change in $-C_{max}$ (n=5; p>0.05)
			SM3-Na-BSA (ALA+EPA) 28.3+29.9 % of total FA's Bound	24 hour s	CP	Ambient	ISO (10^{-7} M) Added after FA	SM3+ISO vs. Ctrl+ISO - Decreased contraction rate by10% (n=5; p<0.05) - No change in CD_{80} (n=5; p>0.05) - No change in $+C_{max}$ (n=5; p>0.5) - No change in $-C_{max}$ (n=5; p>0.05) SM3+ISO vs. SM6+ISO - No change in contraction rate (n=5; *p>0.05*) - No change in CD_{80} (n=5; *p>0.05*) - No change in $+C_{max}$ (n=5; *p>0.05*) - No change in $-C_{max}$ (n=5; *p>0.05*) SM3+Iso vs. SM3 - Increased contraction rate by 18% (n=5; p<0.01) - Decreased CD_{80} by –12% (n=5; p<0.01) - No change $+C_{max}$ (n=5; p>0.05) - Decreased $-C_{max}$ by 13% (n=5; p<0.01)
de Jonge, 1996	Netherlands G	Rat Neonatal Ventricular	EPA 214µM Bound	4-5 days	CP	Ambient	None	EPA vs. Ctrl - Decreased irregularity of spontaneous contractions (n=4; p<0.05)
Durot, 1997	France G	Rat Neonatal Ventricular	SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	BEP	Ambient	None	SM3 vs. SM6 - Increased V_{max} by 16% (n=9; p<0.05) - No change in MDP (n=9; p>0.05) - No change in OS (n=9; p>0.05) - No change in AP (n=9; p>0.05) - No change in APA (n=9; p>0.05) - No change in APD_{40} (n=9; p>0.05) - No change in APD_{80} (n=9; p>0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	BEP	Hypoxia (N_2)	None	SM3 vs. SM6 - Decreased APA (% in fig)(n=5; p<0.05) - Decreased APD_{40} (% in fig) (n=5; p<0.01) - Decreased APD_{80} (% in fig)(n=5; p<0.05) - No change in MDP (n=5; p>0.05) - No change in AP (n=5; p>0.05) - No change in upstroke velocity (n=5; p>0.05) - No change in V_{max} (n=5; p>0.05)
Durot, 1997	France G	Rat Neonatal Ventricular	SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	BEP	Reoxy (O_2 for 1.5 hrs)	None	SM3 vs. SM6 - No change in APA (n=5; p>0.05) - No change in APD_{40} (n=5; p>0.05) - No change in APD_{80} (n=5; p<0.05) - Recovery of MDP was significantly increased i.e. improvement (n=5, p<0.01) - No change in V_{max} (n=5; p>0.05)
			SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	CP	Ambient	None	SM3 vs. SM6 - No change in tC_{20} (n=6, p>0.05) - No change in CD_{20} (n=6, p>0.05) - No change in CD_{80} (n=6, p>0.05) - No change in $+C_{max}$, (n=6, p>0.05) - No change in $-C_{max}$ (n=6, p>0.05)
			SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	CP	Hypoxia (N_2)	None	SM3 vs. SM6 - No change in tC_{20} (n=6, p>0.05) - No change in CD_{20} (n=6, p>0.05) - No change in CD_{80} (n=6, p>0.05) - No change in $+C_{max}$ (n=6, p>0.05) - No change in $-C_{max}$ (n=6, p>0.05)
			SM3 media containing 25µM EPA-Al + 25µM DHA-Al Bound	4 days	CP	Reoxy (O_2 for 1.5 hrs)	None	SM3 vs. SM6 - No change in tC_{20} (n=6, p>0.05) - No change in CD_{20} (n=6, p>0.05) - No change in CD_{80} (n=6, p>0.05) - No change in $+C_{max}$ (n=6, p>0.05) - No change in $-C_{max}$ (n=6, p>0.05)
Ferrier, 2002	Canada G	Guinea Pig Adult Ventricular	DHAm.e. 10µM Free	20 mins	ICU	Ambient	None	DHAm.e. vs. Ctrl - Inhibition in the magnitude of the peak $I_{ca.L}$ by 85% (n=18-24; p<0.001)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHAm.e. 10µM Free	20 mins	CP	Ambient	None	DHAm.e. vs. Ctrl - Decreased amplitude of CICR induced contractions by 93% (n=18-24; p<0.001) - No change in VSRM induced contractions (n=18-24; p>0.05)
Fournier, 1995	France G/ NP	Rat Neonatal Ventricular	EPA 100µM Bound DHA 100µM Bound	4 days	CP	Ambient	None	EPA vs. DHA - No change in tC_{20} (n=11; p>0.05) - No change in CD_{20} (n=11; p>0.05) - No change in CD_{80} (n=11; p>0.05) - No change in $+C_{max}$ (n=11; p>0.05) - No change in $-C_{max}$ (n=11; p>0.05)
Fournier, 1995	France G/ NP	Rat Neonatal Ventricular	EPA 100µM Bound DHA 100µM Bound	4 days	BEP	Ambient	None	EPA vs. DHA - Increased APA due to a higher plateau phase (%in fig) (n=11; p<0.05) - Increased OS (% in fig) (n=11; p<0.05) - No change in MDP (n=11;p>0.05) - No change in ADP_{40} (n=11;p>0.05) - No change in ADP_{80} (n=11;p>0.05) - No change in AP (n=11;p>0.05) - No change in V_{max} (n=11;p>0.05)
Goel, 2002	Canada G/NP	Pig Adult Ventricular SL vesicles	EPA 10µM Free	90+/- 30s	IPIM	Ambient	None	EPA vs. Ctrl - No change in H^+dependent Na^+ uptake (Na^+/H^+exchange) (n=3-5; p>0.05)
			EPA 25µM Free	90+/- 30s	IPIM	Ambient	None	EPA vs. Ctrl - No change in H^+dependent Na^+ uptake (Na^+/H^+exchange) (n=3-5; p>0.05)
			EPA 50µM Free	90+/- 30s	IPIM	Ambient	None	EPA vs. Ctrl - Decreased H^+dependent Na^+ uptake by 24% (Na^+/H^+exchange) (n=3-5; p<0.05) which occurred at all reaction times (2-60 secs) and at all extravesicular pH values except pH 6 - No change in passive Na^+ efflux (n=6; p>0.05)
			EPA 100µM Free	90+/- 30s	IPIM	Ambient	None	EPA vs. Ctrl - Decreased H^+dependent Na^+ uptake (Na^+/H^+exchange) (% in fig) (n=3-5; p<0.05) which occurred at all reaction times (2-60 secs) and at all extravesicular pH values except pH 6
			DHA 10µM Free	90+/- 30s	IPIM	Ambient	None	DHA vs. Ctrl - No change in H^+dependent Na^+ uptake (Na^+/H^+exchange) (n=3-5; p>0.05)
			DHA 25µM Free	90+/- 30s	IPIM	Ambient	None	DHA vs. Ctrl - Decreased H^+dependent Na^+ uptake (Na^+/H^+exchange) (% in fig) (n=3-5; p<0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA 50µM Free	90+/- 30s	IPIM	Ambient	None	DHA vs. Ctrl - Decreased H^+dependent Na^+ uptake (Na^+/H^+exchange) by 34% (n=3-5; p<0.05) - No change in passive Na^+ efflux (n=6; p>0.05)
			DHA 100µM Free	90+/- 30s	IPIM	Ambient	None	DHA vs. Ctrl - Decreased H^+dependent Na^+ uptake (Na^+/H^+exchange) (% in fig) (n=3-5; p<0.05)
			ALA 50µM Free	90+/- 30s	IPIM	Ambient	None	ALA vs. Ctrl - No change in H^+dependent Na^+ uptake (Na^+/H^+exchange) (n=3-5; p>0.05)
			DHA 50µM Free	90+/- 30s	IPIM	Ambient	Na^+ (0.05, 25 or 10mM)	DHA vs. Ctrl - Decreasd H^+ dependent Na^+ uptake (Na^+/H^+exchange) as a function of Na^+ by 30-40% (n=3-4; p<0.05)
Grynberg, 1988	France G	Rats Neonatal Ventricular	SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	BEP	Ambient	None	SM3 vs. SM6 - No change in AP (n=11, p>0.05) - No change in APA (n=11, p>0.05) - No change in APD_{40} (n=11, p>0.05) - No change in APD_{80} (n=11, p>0.05) - No change in MDP (n=11, p>0.05) - No change in OS (n=11, p>0.05) - No change in V_{max} (n=11, p>0.05)
			SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	BEP	Hypoxia (N_2)	None	SM3 vs. SM6 - No change in AP (n=11; p>0.05) - Decreased APA (n=11, p<0.01). - No change in APD_{40} (n=11, p>0.05) - No change in APD_{80} (n=11, p>0.05) - No change in MDP (n=11, p>0.05) - Decreased OS (n=11, p<0.05) - No change in V_{max} (n=11, p>0.05)
			SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	BEP	Reoxy (O_2)	None	SM3 vs. SM6 - No change in AP (n=11, p>0.05) - Increased APA (n=11, p<0.01) - No change in APD_{40} (n=11, p>0.05) - No change in APD_{80} (n=11, p>0.05) - No change in MDP (n=11, p>0.05) - Increased OS (n=11, p<0.05) - No change in V_{max} (n=11, p>0.05)

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Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	CP	Ambient	None	SM3 vs. SM6 - No change in tC_{20} (n=11, p>0.05) - No change in CD_{80} (n=11, p>0.05)
			SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	CP	Hypoxia (N_2)	None	SM3 vs. SM6 - No change in tC_{20} (n=11, p>0.05) - No change in CD_{80} (n=11, p>0.05)
			SM3 media containing 57% ALA+7%LA +0.2% AA as Na-Al	24 hours	CP	Reoxy (O_2)	None	SM3 vs. SM6 - No change in tC_{20} (n=11, p>0.05) - No change in CD_{80} (n=11, p>0.05)
Grynberg, 1995	France G/NP	Rat Neonatal Ventricular	EPA-Na-BSA 100µM DHA-Na-BSA 100µM Bound	4 days	CP	Ambient	None	EPA vs. DHA - No change in spontaneous beating frequency (n=12; p>0.05) - No change in CD_{20} (n=12; p>0.05) - No change in CD_{80} (n=12; p>0.05) - No change in $+C_{max}$ (n=12; p>0.05) - No change in $-C_{max}$ (n=12; p>0.05)
			EPA-Na-BSA 100µM DHA-Na-BSA 100µM Bound	4 days	CP	Ambient	ISO (10^{-7} M) Added after FA	EPA+ISO vs. DHA+ISO - Decreased spontaneous beating frequency by 40% (n=6; p<0.05) - No change in normalized CD_{80} (n=6; p>0.05) EPA+ISO vs. EPA - Increased spontaneous beating frequency by 30% (n=6; p<0.05) DHA+ISO vs. DHA - Increased spontaneous beating frequency by 50% (n=6; p<0.05)
			EPA-Na-BSA 100µM DHA-Na-BSA 100µM Bound	4 days	CP	Ambient	Phe (3×10^{-6} M) Added after FA	EPA+Phe vs. DHA+Phe - No change in spontaneous beating rate (n=6; p>0.05) - No change in CD_{80} (n=6; p>0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			EPA-Na-BSA 100µM DHA-Na-BSA 100µM Bound	4 days	CP	Ambient	dBcAMP (10^{-73}M) Added after FA	EPA+dBcAMP vs. DHA+dBcAMP - Decreased spontaneous beating rate (% in fig) (n=6; p<0.05) EPA+dBcAMP vs. EPA - Increased spontaneous beating rate by 40% (n=6; p=ND) DHA+dBcAMP vs. DHA - Increased spontaneous beating rate by 60% (n=6; p=ND)
Grynberg, 1996	France U	Rat Neonatal Ventricular	EPA-Albumin 0.1mM Bound DHA-Albumin 0.1mM Bound	4 days	CP	Ambient	None	- EPA vs. DHA - No change in spontaneous rate (n=10; p>0.05) - No change in CD_{20} (n=10; p>0.05) - No change in CD_{80} (n=10; p>0.05) - No change in $+C_{max}$ (n=10; p>0.05) - No change in $-C_{max}$ (n=10; p>0.05)
			EPA-Albumin 0.1mM Bound	4 days	CP	Ambient	Phe ($3x10^{-6}$M)	EPA+Phe vs. DHPA+Phe - No change in contraction rate (n=10; p>0.05)
Grynberg, 1996	France U	Rat Neonatal Ventricular	EPA-Albumin 0.1mM Bound DHA-Albumin 0.1mM Bound	4 days	CP	Ambient	ISO (10^{-6}M)	EPA+ISO vs. DHA+ISO - Decreased contraction rate (% in fig) (n=10; p<0.01)
			EPA-Albumin 0.1mM Bound DHA-Albumin 0.1mM Bound	4 days	CP	Ambient	dBcAMP (10^{-3}M)	EPA+dBcAMP vs. DHA+dBcAMP - Decreased contraction rate (% in fig) (n=10; p<0.01)

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Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			EPA-Albumin 0.1mM Bound DHA-Albumin 0.1mM Bound	4 days	BEP	Ambient	None	EPA vs..DHA - Increased APA by 3% (n=10; p<0.05) - Increased OS by 13% (n=10; p0<0.05) - No change in MDP (n=10; p>0.05) - No change in APD_{80} (n=10; p>0.05) - No change in V_{max} (n=10; p>0.05)
Hallaq, 1990	USA/Germany G	Rat Neonatal Cardiac	EPA 5µM Bound	3-5 days	CP	Ambient	None	EPA vs. Ctrl - No change in amplitude of contraction (n=6; *p>0.05*) - No change in beats/min (n=6; *p>0.05*)
			EPA 5µM Bound	3-5 days	CP	Ambient	OUA (0.1mM) Added after FA	EPA+OUA vs. Ctrl+OUA - Increased amplitude of contraction by 156% (n=6; *p<0.001*) - Decreased beats/min by 67% (n=6; *p<0.001*) EPA vs. EPA+OUA - Increased amplitude of contraction by 33% (n=6; *p<0.001*) - Decreased beats/min by 31% (n=6; *p<0.001*)
			EPA 5µM Bound	3-5 days	IPIM	Ambient	None	EPA vs. Ctrl - No change in cytosolic free Ca^{2+} (n=8; p>0.05)
			EPA 5µM Bound	3-5 days	IPIM	Ambient	OUA (1µM) Added after FA	EPA+OUA vs. Ctrl+OUA - No change in time averaged cytosolic free Ca^{2+} induced by OUA (n=3; *p>0.05*)
			EPA 5µM Bound	3-5 days	IPIM	Ambient	OUA (0.1mM) Added after FA	EPA+OUA vs. Ctrl+OUA - Decreased time averaged cytosolic free Ca^{2+} induced by OUA by 75% (n=5; *p<0.001*)
Hallaq, 1990	USA/Germany G	Rat Neonatal Cardiac	EPA 5µM Bound	3-5 days	IPIM	Ambient	OUA (0.1mM) Added after FA	EPA+OUA vs. Ctrl+OU A - No change in OUA sensitive Na, K-ATPase (pump activity) measured as the rate of influx of ^{86}Rb into myocytes (n=10; p>0.05) - No change in OUA sensitive Na, K-ATPase (pump activity) measured using NADH-coupled enzyme assay to determine rate of ATP hydrolysis by Na, K-ATPase (n=3; p>0.05)
			EPA 5µM Bound	3-5 days	IPIM	Ambient	BUME (10µM) Added after FA	EPA+BUME vs. Ctrl+BUME - No change in BUME sensitive Na, K-ATPase (pump activity) measured as the rate of influx of ^{86}Rb into myocytes which also indicates that the facilitated cotransport pathway for Na^+, K^+ and $2Cl^-$ is not affected by EPA (n=11; p>0.05)
			EPA 5µM Bound	3-5 days	IPIM	Ambient	OUA+BUME (0.1mM+10 µM) Added after FA	EPA+OUA+BUME vs. Ctrl+OUA+BUME - No change in total Na, K-ATPase (pump activity) measured as the rate of influx of ^{86}Rb into myocytes (n=11; p>0.05)

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Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
Hallaq, 1992	USA G	Rat Neonatal Ventricular	DHA 5µM Free	1-2mins	CP	Ambient	None	DHA vs. Ctrl - No change in contractility (n=6; p>0.05)
			DHA 5µM Free	1-2mins	CP	Ambient	OUA (0.1mM) Added before or after FA	DHA+OUA vs. Ctrl+OUA - Prevented or Terminated arrhythmia's (n=10; p<0.05)
			DHA 5µM Free	1-2mins	CP	Ambient	NIT (0.5nM) Added with FA	DHA+NIT vs. NIT - Prevented the inhibitory effect of NIT on contractility (n=6; p<0.05)
			DHA 5µM Free	1-2mins	CP	Ambient	BAY (0.1µM) Added after FA	DHA+BAY vs. Ctrl+BAY - Prevented the inhibitory effects of BAY on contractility (n=4; p<0.05)
			DHA 5µM Free	1-2mins	CP	Ambient	VER (10µM) or DIL (1µM) Added with FA	DHA+VER or DIL vs. Ctrl+VER or DIL - Did not prevent the inhibitory effects of VER or DIL on contractility (n=3-4; p=ND)
			EPA 5µM Free	1-2mins	CP	Ambient	OUA (0.1mM) Added after FA	EPA+OUA vs. Ctrl+OUA - Prevented arrhythmia (n=ND; p<0.05)
			EPA 5µM Bound	4 days	ICH	Ambient	NIT (0.03^{-10} nM) Added after FA	EPA vs. Ctrl - Noncompetitive inhibition of the specific binding of NIT by reducing the maximal binding of [^{3}H] NIT - Decreased K_d value of high affinity binding site by 97% (n=5-10; *p<0.05*) - Decreased the number of high affinity binding sites (B_{MAX}) by –90% (n=5-10; *p<0.01*) - Decreased K_d value of low affinity binding site by 74% (n=5-10; *p<0.01*) - Decreased the number of low affinity binding sites (B_{MAX}) by 60% (n=5-10; *p<0.05*)
Hallaq, 1992	USA G	Rat Neonatal Ventricular	DHA 5µM Bound	4 days	ICH	Ambient	NIT (0.03^{-10} nM) Added after FA	DHA vs. Ctrl - K_d value of high affinity binding site was non detectable due to suppression by DHA (n=5-10; *p<0.001*) - Number of high affinity binding sites (B_{MAX}) was non detectable due to suppression by DHA (n=5-10; *p<0.001*) - Decreased K_d value of low affinity binding site by 78% (n=5-10; *p<0.01*) - Decreased the number of low affinity binding sites (B_{MAX}) by 64% (n=5-10; *p<0.05*)
			DHA 5uM Bound	4 days	IPIM	Ambient	OUA (0.1mM) $^{45}Ca2^{+}$	DHA+OUA vs. OUA - Decreased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 29% (n=4-11; p<0.025)
			DHA 5µM Bound	4 days	IPIM	Ambient	NIT (0.5nM) Added after FA	DHA+NIT vs. Ctrl+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 28% (n=5-14; p=ND) - DHA+NIT vs. DHA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA 5µM Bound	4 days	IPIM	Ambient	BAY (0.1µM) Added after FA	DHA+BAY vs. Ctrl+BAY - Decreased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 32% (n=5-14; p=ND) DHA+BAY vs. DHA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			DHA 5µM Bound	4 days	IPIM	Ambient	OUA+ NIT (0.1mM+0.5 nM) Added after FA	DHA+OUA+NIT vs. Ctrl+OUA+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 13% (n=5-14; p=ND) DHA+OUA+NIT vs. DHA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			DHA 5µM Bound	4 days	IPIM	Ambient	BAY+ NIT (0.1µM+ 0.5 nM) Added after FA	DHA+BAY+NIT vs. Ctrl+BAY+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 55% (n=5-14; p=ND) DHA+Bay+NIT vs. DHA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			EPA 5µM Bound	4 days	IPIM	Ambient	NIT (0.5nM) Added after FA	EPA+NIT vs. Ctrl+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 34% (n=5-14; p=ND) EPA+NIT vs. EPA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			EPA 5µM Bound	4 days	IPIM	Ambient	BAY (0.1µM) Added after FA	EPA+BAY vs. Ctrl+BAY - Decreased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 30% (n=5-14; p=ND) EPA+BAY vs. EPA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			EPA 5µM Bound	4 days	IPIM	Ambient	OUA+ NIT (0.1mM+0.5 nM) Added after FA	EPA+OUA+NIT vs. Ctrl+OUA+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 20% (n=5-14; p=ND) EPA+OUA+NIT vs. EPA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
			EPA 5µM Bound	4 days	IPIM	Ambient	BAY+ NIT (0.1µM+0.5 nM) Added after FA	EPA+BAY+NIT vs. Ctrl+BAY+NIT - Increased $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) by 39% (n=5-14; p=ND) EPA+BAY+NIT vs. EPA - No change in $^{45}Ca^{2+}$ uptake (Ca^{2+} influx) (n=5-14; *p>0.05*)
Honore, 1994	France G/NP	Mouse Neonatal Ventricular	DHA 30µM Free	ND	ICH	Ambient	None	DHA vs. Ctrl - Blocked delayed rectifier K^+ channel (Kv1.5) activity (% in fig) (n=5-11; p<0.05)
			ALA ND ND	ND	ICH	Ambient	None	ALA vs. Ctrl - No change in delayed rectifier K^+ channel (Kv1.5) activity (n=ND; p>0.05)
			DHA 30µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Intracellular DHA included in the pipette medium did not alter the Kv1.5 current (n=9; p>0.05) - Addition of DHA to the external medium inhibited the Kv1.5 current within 20 seconds indicating that binding occurs on an external site (n=9; p<0.05)

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			DHA 30µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - No change in inward rectifier K^+ current (n=4; p>0.05) - Decreased ultra rapid K^+ current (I_{KUR}) measured at +30mV by 52% (n=4; p<0.05)
Jahangiri, 2000	Australia U	Rat Adult Atrial	EPA 10µM Free	7 mins	CP	Ambient	ISO (10µM) Added with FA	EPA+ISO vs. Ctrl+ISO - Decreased the number of asynchronously contracting atrial myocytes by 76% (n=107/7hearts; p<0.01)
			DHA 10µM Free	7 mins	CPr	Ambient	ISO (10µM) Added with FA	DHA+ISO vs. Ctrl+ISO - Decreased the number of asynchronously contracting atrial myocytes by 69% (n=101/5 hearts; p<0.05)
			DHA m.e 10µM Free	7 mins	CP	Ambient	ISO (10µM) Added with FA	DHA m.e+ISO vs. Ctrl+ISO - No change in the number of asynchronously contracting atrial myocytes (n=71/4 hearts; p>0.05)
Juan, 1987	Austria U	Guinea Pigs Adult Isolated heart	EPA-Na $6x10^{-8}$mol/min Free	30mins	CP	Ambient	Antigen-ovalbumin (1mg/0.1ml) Added before FA	EPA+Antigen vs. Ctrl+Antigen - No change in duration of arrhythmia (n=8; p>0.05)
			EPA-Na $15x10^{-8}$mol/min Free	30mins	CP	Ambient	Antigen-ovalbumin (1mg/0.1ml) Antioxidant-esculetin ($1x10^{-7}$mol) Added before FA	EPA+antigen vs. Ctrl+Antigen - Decreased duration of arrhythmia by 56% (n=8; p<0.05) EPA+Antioxidant+Antigen vs. Ctrl+Antigen - Decreased duration of arrhythmia by 52% (n=5; p<0.05)
Kang, 1994	USA G	Rat Neonatal Cardiac	EPA 5-10µM Free	3 mins	CP	Ambient	None	EPA vs. Ctrl - Decreased contraction rate by 50 to 80% within 2 mins (n=46; p<0.05) and effects were reversed by BSA - No change in amplitude of contraction (n=ND; p>0.05)
			DHA 5-10µM Free	3 mins	CP	Ambient	None	DHA vs. Ctrl - Decreased contraction rate by 50 to 80% within 2 mins (n=32; p<0.05) and effects were reversed by BSA - No change in amplitude of contraction (n=ND; p>0.05)
Kang, 1994	USA G	Rat Neonatal Cardiac	EPA 5-10µM Free	3 mins	CP	Ambient	INDO (10-20µM/) BW755c (20 µM) BHT (0.005%/ Vitamin E (0.5uNIT/ml) and ETYA (ND) Added with FA	EPA+agents vs. Ctrl+agents - No change in EPA induced reductions in beating rate (n=ND; p>0.05)

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			EPA 5-10µM Free	3 mins	CP	Ambient	Ca^{2+} (7-10µM) Added before or after FA	EPA+Ca^{2+} vs. Ctrl+Ca^{2+} - Prevented or Terminated arrhythmia (n=ND; p<0.05) and the effects were reversible by BSA
			DHA 5-10µM Free	3 mins	CP	Ambient	Ca^{2+} (7-10µM) Added before or after FA	DHA+Ca^{2+} vs. Ctrl+Ca^{2+} - Prevented or Terminated arrhythmia (n=ND; p<0.05) and the effects were reversible by BSA
			EPA 5-10µM Free	3 mins	CP	Ambient	OUA (0.1mM) Added before FA	EPA+OUA vs. Ctrl+OUA - Terminated contractures/fibrillations (n=ND; p<0.05) and the effects were reversible by BSA
			DHA 5-10µM Free	3 mins	CP	Ambient	OUA (0.1mM) Added before FA	DHA+OUA vs. Ctrl+OUA - Terminated contractures/fibrillation (n=ND; p<0.05) and the effects were reversible by BSA
			ALA 5-10µM Free	3 mins	CP	Ambient	None	ALA vs. Ctrl - Decreased beating rate by 40% (mean of the range (n=5; p<0. 05) and the effects were reversible by BSA
			EPA e.e 5-10µM Free	3 mins	CP	Ambient	None	EPAe.e vs. Ctrl - No change in beating rate (n=3; p>0.05)
Kang, 1995a	USA G	Rats Neonatal Ventricular	EPA 10µM Free	2-5 mins	BEP	Ambient	None	EPA vs. Ctrl - Hyperpolarizing RMP by 5±1 mV (n=8, p<0.05). The effect was reversible by BSA (2mg/ml). - Depolarizing APT by 9±3 mV (n=8, p<0.05). The effect was reversible by BSA (2mg/ml). - Decreased APD_{75} by 21% (n=8, p<0.01) - No change in APA (n=8, p>0.05) - No change in V_{max} (n=8, p>0.05) - Decreased action-potential frequency by 50% after 3 minutes EPA addition (n=8, p<0.05) - Increased the stimulation strengths required to initiate action potentials by 49% (n=ND, p<0.01) Effect was reversible by BSA
Kang, 1995b	USA G/NP	Rat Neonatal Cardiac	EPA 5-10µM Free	5mins	CP	Ambient	ISO (3uM) Added before or after FA	EPA+ISO vs. ISO - Prevented or Terminated arrhythmia within 2-3 mins (n=8; p<0.05) - Decreased contraction rate (%=ND) (n=5; p=ND) - Effects were reversible by BSA
Kang, 1995b	USA G/NP	Rat Neonatal Cardiac	EPA 5-10µM Free	5 mins	CP	Ambient	ISO (3uM)+ INDO (20 uM/)+ BW (ND) Added before FA	EPA+ISO+INDO+BW vs. Ctrl+ISO+INDO+BW - Prevented arrhythmia (n=3; p<0.05)

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			DHA 5-10µM Free	5 mins	CP	Ambient	ISO (3uM)+ INDO (20 uM/)+ BW (ND) Added before FA	DHA+ISO+INDO+BW vs. Ctrl+ISO+INDO+BW - Prevented arrhythmia (n=3; p<0.05)
			EPA 5-10µM Free	5 mins	CP	Ambient	cAMP (250uM) Added after FA	EPA+cAMP vs. Ctrl+cAMP - Terminated arrhythmias w/in 3-5min (n=5; p<0.05)
			EPA 8µM Free	5 mins	CP	Ambient	Cholera toxin (2ug/ml) (Gs protein activator)	EPA+Cholera toxin vs. Cholera toxin - Decreased beating rate (%=ND) (n=4; p=ND) - Effects were reversed by BSA
Kang , 1996	USA G	Rat Neonatal Cardiac	EPA 10-15µM Free	3-7 mins	CP	Ambient	LPC (5-10 µM) Added before or 3-5 mins after FA	EPA+LPC vs. Ctrl+LPC - Prevented tachycardia and slowed beating rate with 2-3 mins and also terminated arrhythmia (n=5; p<0.05) - Effects were reversible by BSA
			DHA 10-15µM Free	3-7 mins	CP	Ambient	LPC (5-10 µM) Added before FA	DHA+LPC vs. Ctrl+LPC - Prevented tachycardia and slowed beating rate with 2-3 mins (n=5; p<0.05) - Effects were reversible by BSA
			ALA 10-15µM Free	3-7 mins	CP	Ambient	LPC (5-10 µM) Added before FA	ALA+LPC vs. Ctrl+LPC - Prevented tachycardia and slowed beating rate with 2-3 mins (n=5; p<0.05) - Effects were reversible by BSA
			EPA 10-15µM Free	3-7 mins	CP	Ambient	PTC (2-10 µM) Added before or after FA	EPA+PTC vs. Ctrl+LPC - Prevented or Terminated occurrence of arrhythmia (n=5;p<0.05) - Effects were reversible by BSA
			DHA 10-15µM Free	3-7 mins	CP	Ambient	PTC (2-10 µM) Added before or after FA	DHA+PTC vs. Ctrl+LPC - Prevented or Terminated occurrence of arrhythmia (n=5;p<0.05)
			ALA 10-15µM Free	3-7 mins	CP	Ambient	PTC (2-10 µM) Added before or after FA	ALA+PTC vs. Ctrl+LPC - Prevented or Terminated occurrence of arrhythmia (n=5;p<0.05)
			EPA 10-15µM Free	7mins	CP	Ambient	Ca^{2+}ionophore (5µM) Added before FA	EPA+ Ca^{2+} vs. Ctrl+ Ca^{2+} - Prevented or Terminated occurrence of arrhythmia (n=5;p<0.05)
			EPA 15µM Free	3-5mins	CP	Ambient	Electrical pacing (15V)	EPA vs. Ctrl - Decreased electrical automaticity/ excitability of the cardiac myocyte by 50% (n=7; p<0.01)
Kang , 1996	USA G	Rat Neonatal Cardiac	EPA 10-15µM Free	7mins	IPIM	Ambient	None	EPA vs. Ctrl - No change in systolic and diastolic (cytosolic) Ca^{2+} (n=6; p>0.05)

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			EPA 10-15µM Free	7mins	IPIM	Arr	LPC (5-10 µM) Added before FA	EPA+LPC vs. Ctrl+LPC - Terminated intermittent fluctuation of Ca^{2+} (n=6; p<0.05)
Kang, 1997	USA G	Rats Neonatal Cardiac	EPA 20µM Bound	3-4 days	ICH	Ambient	None	EPA vs. Ctrl - No change in the number of Na+ channels per 10^6 cell, measured by the binding of [^{3}H] BTXB (n=4, p>0.05)
			EPA 20µM Bound	3-4 days	ICH	Ambient	MEX (20 uM)	EPA+MEX vs. Ctrl+ MEX - Decreased the number of Na+ channels per 10^6 cell by 40% to 50% (n=4, p<0.05) - Decreased the MEX induced increase in cardiac Na^+ channel expression
Leifert, 1999	Australia U	Rat Adult Ventricular	DHA 25µM Free	4 mins	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_{Na} peak current amplitude by 42% (n=7; p=ND)
			DHA 25µM Free	4 mins	ICU	Ambient	None	DHA vs. Ctrl - Shifted the voltage dependence of I_{Na} activation to more positive potentials as indicated by a decrease in G_{mas} by 35% and a shift of V' to a more positive potentialby 21% (n=5; p<0.01) - Shifted the voltage dependence of of I_{Na} inactivation to more negative potentials as indicated by a decrease in I_{max} by 36% and a shift of V' to more hyperpolarized potentials by 30% (n=5; p<0.01)
			EPA 25µM Free	4 mins	ICU	Ambient	None	EPA vs. Ctrl - Shifted the voltage dependence of I_{Na} activation to more positive potentials as indicated by a decrease in G_{mas} by-30% and a shift of V' to a more positive potential by 26% (n=10; p<0.001) - Shifted the voltage dependence of of I_{Na} inactivation to more negative potentials as indicated by a decrease in I_{max} by 35% and a shift of V' to more hyperpolarized potentials by 25% (n=10; p<0.01)
			ALA 25µM Free	4 mins	ICU	Ambient	None	ALA vs. Ctrl - Shifted the voltage dependence of I_{Na} activation to more positive potentials as indicated by a decrease in G_{mas} by 18% and a shift of V' to a more positive potential by 25% (n=6; p<0.001) - Shifted the voltage dependence of of I_{Na} inactivation to more negative potentials as indicated by a decrease in I_{max} by 25% and a shift of V' to more hyperpolarized potentials by 30% (n=6; p<0.01)
Leifert, 2000b	Australia U	Rat Adult Ventricular	DHA 10µM Free	ND	CP	Ambient	ISO (10um) Added 5 mins after FA	DHA+ISO vs. Docasanoic Acid+ISO - Decreased spontaneous contractions by 85% (n=5; p<0.01)
			DHA 10µM Free	ND	CP	Ambient	LPC (10um) Added 5 mins after FA	DHA+LPC vs. Stearic Acid+LPC - Decrease in spontaneous contractions by 77% (n=4; p<0.01)

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Leifert, 2000b	Australia U	Rat Adult Ventricular	DHA 10µM Free	ND	CP	Ambient	Electrical Stimulation (1Hz at 25 V)	DHA vs. Stearic Acid - Decrease in asynchronous contractions by 61% (n=4; p<0.05)
Li, 1997	USA G	Rat Neonatal Cardiac	EPA 10µM Free	ND	CP	Ambient	Eicosanoids PGD2+PGE2+PGF2 +U46619 (3µm-0.5µM)	EPA vs. Ctrl - Terminated the arrhythmias and contractures within 2-3 minutes (n=ND, p<0.05), followed by a slow beating rate.
Macleod, 1998	New Zealand G/NP	Rat Adult Ventricular	EPA 1-7.5uM Free	5 mins	CP	Ambient	None	EPA vs. Ctrl - Increased (prolonged) twitch size (%=ND) (n=6-8; p=ND)
			DHA 1-7.5uM Free	5 mins	CP	Ambient	None	DHA vs. Ctrl - Increased (prolonged) twitch size (%=ND) (n=6-8; p=ND)
			EPA >10M Free	5 mins	CP	Ambient	None	EPA vs. Ctrl - Decreased twitch size (%=ND) (n=6-8; p=ND)
			DHA >10M Free	5 mins	CP	Ambient	None	DHA vs. Ctrl - Decreased twitch size (%=ND) (n=6-8; p=ND)
			EPA 1-7.5uM Free	5 mins	BEP	Ambient	None	EPA vs. Ctrl - Dose dependant increase (lengthening of early plateau potential) in ADP_{80} (%=ND) (n=11-14; p=ND)
			DHA 1-7.5uM Free	5 mins	BEP	Ambient	None	DHA vs. Ctrl - Dose dependant increase (lengthening of early plateau potential) in ADP_{80} (%=ND) (n=11-14; p=ND)
			EPA >10M Free	5 mins	BEP	Ambient	None	EPA vs. Ctrl - Dose dependant decrease in ADP_{80} (%=ND) (n=11-14; p=ND)
			DHA >10M Free	5 mins	BEP	Ambient	None	DHA vs. Ctrl - Dose dependant decrease in ADP_{80} (%=ND) (n=11-14; p=ND)
			EPA 5,10 or 20uM Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Dose dependant decrease of the peak amplitude of the I_{Na} (%=ND) (n=6-8; p=ND)
			DHA 5,10 or 20uM Free	5 mins	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease of the peak amplitude of the I_{Na} (%=ND) (n=6-8; p=ND)

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			EPA 5,7.5 or 10uM Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Dose dependant decrease of the peak $I_{Ca.L}$ (%=ND) (n=5-8; p=ND)
Macleod, 1998	New Zealand G/NP	Rat Adult Ventricular	DHA 5,7.5 or 10uM Free	5 mins	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease of the peak $I_{Ca.L}$ (%=ND) (n=5-8; p=ND)
			EPA 0.1-10uM Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Dose dependant decrease of I_{to} (%=ND) (n=5-8; p=ND)
			DHA 0.1-10uM Free	5 mins	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease of I_{to} (%=ND) (n=5-8; p=ND)
			EPA 2um Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_K and I_{K1} by 30-40%(n=ND; p=ND)
			EPA 5um Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_K and I_{K1} by 50-60% (n=ND; p=ND)
		Guinea Pig Adult Ventricular	EPA 5-20µM Free	5 mins	CP	Ambient	None	EPA vs. Ctrl - Dose dependant decrease in twitch size (%=ND) (n=6-8; p=ND)
			DHA 5-20µM Free	5 mins	CP	Ambient	None	DHA vs. Ctrl - Dose dependant decrease in twitch size (%=ND) (n=6-8; p=ND)
			EPA 1-20µM Free	5 mins	BEP	Ambient	None	EPA vs. Ctrl - Dose dependant reduction in ADP_{80} (%=ND) (n=12-16; p=ND)
			DHA 1-20µM Free	5 mins	BEP	Ambient	None	DHA vs. Ctrl - Dose dependant reduction in ADP_{80} (%=ND) (n=12-16; p=ND)
			EPA 5,10 or 20µM Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Dose dependant decrease of the peak amplitude of I_{Na} (%=ND) (n=8-10; p=ND)
			DHA 5,10 or 20µM Free	5 mins	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease of the peak amplitude of I_{Na} (%=ND) (n=8-10; p=ND)

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			EPA 5,7.5 or 10µM Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Dose dependant decrease of the peak $I_{Ca.L}$ (%=ND) (n=6-10; p=ND)
Macleod, 1998	New Zealand G/NP	Guinea Pig Adult Ventricular	DHA 5,7.5 or 10µM Free	5 mins	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease of the peak $I_{Ca.L}$ (%=ND) (n=6-10; p=ND)
			EPA 2um Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_K and I_{Kl} by 10% (n=5-8; p=ND)
			EPA 5um Free	5 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_K and I_{Kl} by 30-40% (n=5-8; p=ND)
Negretti, 2000	Venezuela G/NP	Rat Adult Ventricular	EPA 10µM Free	3 mins	CP	Ambient	None	EPA vs. Ctrl - Increased resting cell length by 2% (n=6, p<0.001). - Decreased the spontaneous contraction frequency (n=47 out of 57; p<0.001) - Effects were reversible by BSA
			EPA 10µM Free	3 mins	IPIM	Ambient	None	EPA vs. Ctrl - Decreased the frequency of spontaneous waves of calcium release (n=47 out of 57; p<0.001) - Decreased the amplitude of the wave by 16% (n=41, p<0.001) - Effects were reversible by BSA
			EPA 10µM Free	3 mins	IPIM	Ambient	Ca^{2+} (10uM)	EPA vs. Ctrl - Decreased the basal level of [Ca2+] by 6% (n=46, p<0.005). The effect was reversible by BSA.
			EPA 5µM Free	3 mins	IPIM	Ambient	Caffeine (10mM)	EPA vs. Ctrl - Increased the SR calcium content indicated by an increase in the caffeine induced Na^{+}-Ca^{2+} exchange current by 41% (n=4, p<0.05).
			DHA 5µM Free	3 mins	IPIM	Ambient	Caffeine (10mM)	DHA vs. Ctrl - Increased the SR calcium content indicated by an increase in the caffeine induced Na^{+}-Ca^{2+} exchange current by 41% (n=4, p<0.05).
			EPA 10µM Free	3 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased the amplitude of $I_{Ca.L}$ (n=5; p<0.05)
			DHA 10µM Free	3 mins	ICU	Ambient	None	DHA vs. Ctrl - Decreased the amplitude of $I_{Ca.L}$ (n=5; p<0.05)

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O'Neill, 2002	UK/Venezuela G/NP	Rat ND Ventricular	EPA 10uM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased frequency of transient inward currents that accompany spontaneous waves of CICR by 33% (n=6; p<0.05) - Increased amplitude of currents activated by each wave by 29% (n-6; p<0.05)
			EPA 10uM Free	ND	IPIM	Ambient	None	EPA vs. Ctrl - Decreased resting cytosolic Ca^{2+} due to decrease Ca^{2+} influx across surface membrane and not due to increased activation of efflux pathways(n=6; p<0.05)
O'Neill, 2002	UK/Venezuela G/NP	Rat ND Ventricular	EPA 10uM Free	ND	IPIM	Ambient	None	EPA vs. Ctrl - Decreased wave frequency activated by Ca2+ efflux (% in fig) (n=6; p<0.01) - Increased efflux of Ca2+ activated by individual waves by 12% (n=6; p<0.05) - Decreased wave generated efflux per unit time by 19% (n=6; p<0.01) - Decreased total efflux (% in fig) (n=6; p<0.01)
			EPA 10uM Free	ND	IPIM	Ambient	Caffeine (10mM/ND)	EPA+Caffeine vs. Ctrl+Caffeine - No change in surface membrane Ca2+ efflux pathway (n=12; p>0.1)
Pepe, 1994	USA G	Rat Young Adult Cardiac	DHA 5µM Free	4 mins	CP	Ambient	None	DHA vs. Ctrl - No change in DL (n=6, p>0.05) - No change in TA_{t50} (n=6, p>0.05) - No change in VS/DL (n=6; p>0.05)
			DHA 5µM Free	4 mins	CP	Ambient	NIT (10nM)	DHA+NIT vs. Ctrl+NIT - Blocked NIT effect on TA (n=6, p<0.05) - Blocked NIT effect on VS/DL (n=6; p<0.05) - Effects were reversible by BSA
			DHA 5µM Free	4 mins	CP	Ambient	BAY (10nM)	DHA+BAY vs. Ctrl+BAY - Blocked NIT effect on TA (n=6, p<0.05) - Blocked NIT effect on VS/DL (n=6; p<0.05) - Effects were reversible by BSA
			DHA 5µM Free	4 mins	CP	Ambient	ISO (0.1-1uM)	DHA+ISO vs. Ctrl+ISO - No change in TA (n=6, p>0.05) - No change in DL (n=6; p>0.05) - Effects were reversible by BSA
			DHA 5µM Free	4 mins	ICU	Ambient	None	DHA vs. Ctrl - No change in peak $I_{Ca.L}$ amplitude (n=6; p>0.05) -
			DHA 5µM Free	4 mins	ICU	Ambient	NIT (10nM)	DHA+NIT vs. Ctrl+NIT - Increased peak $I_{Ca.L}$ amplitude by 50% (n=6; p<0.05) - Effects were reversible by BSA
			DHA 5µM Free	4 mins	ICU	Ambient	BAY (10nM)	DHA+BAY vs. Ctrl+BAY - Blocked the BAY induced increase in peak $I_{Ca.L}$ amplitude (n=6; p<0.05) - Effects were reversible by BSA

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA 5µM Free	4 mins	ICU	Ambient	ISO (0.1-1uM)	DHA+ISO vs. Ctrl+ISO - No change in peak $I_{Ca.L}$ amplitude (n=6; p>0.05) -
			DHA 5µM Free	4 mins	IPIM	Ambient	None	DHA vs. Ctrl - No change in $IFTA_{dias}$ and IFR_{t50} indicating no change in cytosolic Ca^{2+} and Cai^{2+} transient amplitude (n=6; p>0.05)
			DHA 5µM Free	4 mins	IPIM	Ambient	NIT (10nM)	DHA+NIT vs. Ctrl+NIT - Inhibited NIT blockage of the L-type calcium channel influx (n=6; p<0.05) - Blocked NIT effect on $IFTA_{dias}$ (n=6; p<0.05) - Effects were reversible by BSA
Pepe, 1994	USA G	Rat Young Adult Cardiac	DHA 5µM Free	4 mins	IPIM	Ambient	BAY (10nM)	DHA+BAY vs. Ctrl+BAY - Inhibited BAY induced potentiation of L-type calcium channel influx (n=6; p<0.05) - Blocked BAY effect on $IFTA_{dias}$ (n=6; p<0.05) - Effects were reversible by BSA
			DHA 5µM Free	4 mins	IPIM	Ambient	ISO (0.1-1uM)	DHA+ISO vs. Ctrl+ISO - No change in ISO induced increase in cytosolic calcium content (n=6; p>0.05)
Phiipson, 1985	USA G	Dog Adult Ventricular SL vesicles	ALA 30µM Free	1.5 sec	IPIM	Ambient	Ca^{2+}(10uM) Added before FA	ALA vs. Ctrl - Increased Na^{+}-Ca^{2+} exchange measured as Na^{+} dependent Ca^{2+} uptake by 112% (n=9, p<0.05) - Preincubation with ALA to ensure complete incorporation resulted in the max imal stimulation of Na+ dependent Ca2+ influx being about 40% less than when the vesicles were only briefly exposed to ALA.
			ALA 20µM Free	2 mins	IPIM	Ambient	Preloaded Ca^{2+} (47.9 nMl)	ALA vs. Ctrl - Increased passive Ca2+ efflux by 147% (n=3, p<0.05)
Phiipson, 1987	USA G	Dog Adult Ventricular SL vesicles	ALA 60µM Free	1.5 sec	IPIM	Ambient	Ca^{2+}(10uM)	ALA vs. Ctrl - Increased Na^{+}-Ca^{2+} exchange measured as Na^{+} dependent Ca^{2+} uptake by 87% (n=3, p<0.05)
			ALA 30µM Free	2 minutes	IPIM	Ambient	Preloaded Ca^{2+} (52.3 nM)	ALA vs. Ctrl - Increased passive Ca2+ efflux by 170% (n=4, p<0.05)
Ponsard, 1999	France NP	Rat Neonatal Ventricular	EPA+DHA-Albumin 4.6+6.5% Bound	4 days	CP	Ambient	None	EPA+DHA vs. Ctrl - No change in CR (n=13; *p>0.05*) - No change in CD_{20} (n=13; *p>0.05*) - No change in CD_{80} (n=13; *p>0.05*) - No change in $+C_{max}$ (n=13; *p>0.05*) - No change in $-C_{max}$ (n=13; *p>0.05*)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			EPA+DHA-Albumin 4.6+6.5% Bound	4 days	CP	Ambient	ISO (10^{-7}M)	EPA+DHA+ISO vs. N-6+ISO - Increased CR by 66% (n=7; p<0.05) - No change in CD_{20} (n=7; p>0.05) - No change in CD_{80} (n=7; p>0.05) - No change in $+C_{max}$ (n=7; p>0.05) - No change in $-C_{max}$ (n=7; p>0.05)
			EPA+DHA-Albumin 4.6+6.5% Bound	4 days	CP	Ambient	PHE (10^{-6}M)	EPA+DHA+PHE vs. N-6+PHE - Increased CR by 115% (n=6; p<0.05) - No change in CD_{20} (n=6; p>0.05) - No change in CD_{80} (n=6; p>0.05) - No change in $+C_{max}$ (n=6; p>0.05) - No change in $-C_{max}$ (n=6; p>0.05)
Ponsard, 1999	France NP	Rat Neonatal Ventricular	EPA+DHA-Albumin 4.6+6.5% Bound	4 days	CP	Normoxia-Posthypoxic Reoxy	ISO (10^{-7}M)	EPA+DHA+ISO in Hypoxia vs. EPA+DHA+ISO in Normoxia - Increased CR (% in fig) (n=6; p<0.001) - No change in CD_{20} (n=6; p>0.05) - No change in CD_{80} (n=6; p>0.05) - Increased $+C_{max}$ (%=ND) (n=6; p<0.05) - No change in $-C_{max}$ (n=6; p>0.05)
			EPA+DHA-Albumin 4.6+6.5% Bound	4 days	CP	Normoxia-Posthypoxic Reoxy	PHE (10^{-6}M)	EPA+DHA+PHE in Hypoxia vs. EPA+DHA+PHE in Normoxia - No change (n=6; p>0.05) - No change in CD_{20} (n=6; p>0.05) - No change in CD_{80} (n=6; p>0.05) - No change in $+C_{max}$ (n=6; p>0.05) - No change in $-C_{max}$ (n=6; p>0.05)
Reithman, 1996	Germany U	Rat Neonatal Cardiac	DHA 60µM Bound	3 days	BEP	Ambient	None	DHA vs. Ctrl - Increased amplitude by 20% (n=28-29; p<0.05) - No change in APR (n=14-19; p>0.05)
			DHA 60µM Bound	3 days	BEP	Ambient	NA + TIM (100µmol/L+10 µmol/L)	DHA+NA+TIM vs. Ctrl+NA+TIM - Decreased APR by 28% (n=14-19; p<0.05)
			DHA 60µM Bound	3 days	CP	Ambient	NA + TIM (100µmol/L+10 µmol/L)	DHA+NA+TIM vs. Ctrl+NA+TIM - Decreased arrhythmias by 84% (n=15-28; p<0.01)
			DHA 60µM Bound	3 days	BEP	Ambient	Isoprenaline (10 µmol/L)	DHA+Isoprenaline vs. Ctrl+Isoprenaline - Decreased APR by 26% (n=10-11; p<0.05)
			DHA 60µM Bound	3 days	BEP	Ambient	OUA (10 µmol/L)	DHA+OUA vs. Ctrl+OUA - Decreased APR by 16% (n=4 ; p<.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
Rinaldi, 2002	Italy NP	Rat Adult Ventricular	DHA 10µM Free	20 minutes (acute)	IPIM	Ambient	None	DHA vs. Ctrl - - No change in basal cytosolic Ca^{2+} levels (n=9; p>0.5)
			DHA 10µM Free	3 days (chronic)	IPIM	Ambient	None	DHA vs. Ctrl - - No change in cytosolic Ca^{2+} levels (n=9; p>0.5)
			DHA 10µM Free	20 minutes (acute)	IPIM	Ambient	ET-1 (100nM)	DHA+ET-1 vs. Ctrl - Increased ET-1 induced cytosolic Ca^{2+} levels by 128% (n=9; p<0.01)
			DHA 10µM Free	3 days (chronic)	IPIM	Ambient	ET-1 (100nM)	DHA+ET-1 vs. Ctrl - Increased ET-1 induced cytosolic Ca^{2+} by 148% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute)	IPIM	Ambient	KCl (50mM) Added after FA	DHA+KCl vs. Ctrl - Decreased Ca2+ by 71% (n=9; p<0.01)
Rinaldi, 2002	Italy NP	Rat Adult Ventricular	DHA 10µM Free	3 days (chronic)	IPIM	Ambient	KCl (50mM) Added after FA	DHA+KCl vs. Ctrl+KCl - Decreased Ca^{2+} by 48% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute) 3 days (chronic)	IPIM	Ambient	KCl (50mM) Added after FA	DHA+ET-1 (chronic) vs. DHA+ET-1 (acute) - Decreased Ca^{2+} by 17% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute)	IPIM	Anoxia	97%N_2 and 3% CO_2	DHA+Anoxic Soln vs. Ctrl - Decreased Ca^{2+} by 58% (n=9; p<0.01)
			DHA 10µM Free	3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2	DHA+Anoxic Soln vs. Ctrl - Decreased Ca^{2+} by 83% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute) 3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2	DHA+Anoxic Soln (chronic) vs. DHA+Anoxic Soln (acute) - Decreased Ca^{2+} by 59% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute)	IPIM	Anoxia	97%N_2 and 3% CO_2+ KCl (50mM)	DHA+Anoxic Soln+KCl vs. Ctrl - Decreased Ca^{2+} (%=ND) (n=9 ;p<0.01)
			DHA 10µM Free	3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2+ KCl (50mM)	DHA+Anoxic Soln+KCl vs. Ctrl - Decreased Ca^{2+} (%=ND) (n=9; p<0.01)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA 10µM Free	20 minutes (acute) 3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2+ KCl (50mM)	DHA+Anoxic Soln+KCl (chronic) vs. DHA+Anoxic Soln+KCl (acute) - Decreased Ca^{2+} by 70% (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute)	IPIM	Anoxia	97%N_2 and 3% CO_2+ ET-1 (100nM)	DHA+Anoxic Soln+ET-1 vs. Ctrl - Decreased Ca^{2+} (%=ND) (n=9; p<0.01)
			DHA 10µM Free	3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2+ ET-1 (100nM)	DHA+Anoxic Soln+ET-1 vs. Ctrl - Decreased Ca^{2+} (%=ND) (n=9; p<0.01)
			DHA 10µM Free	20 minutes (acute) 3 days (chronic)	IPIM	Anoxia	97%N_2 and 3% CO_2+ ET-1 (100nM)	DHA+Anoxic Soln+ET-1 (bound) vs. DHA+Anoxic Soln+ET-1 (free) - Decreased Ca^{2+} by 70% (n=9; p<0.01)
			ALA-Na 2mg/kg/min Free as IV	5 mins	CP	Ambient	None	ALA-Na vs. Ctrl - No change in intra-atrial conduction time (AC) (n=7; p>0.05) - No change in atrio-ventricular conductance time (AVC) (n=7; p>0.05) - No change in functional refractory period of the atrium (ARP) (n=7; p>0.05) - No change in functional refractory period of atrio-ventricular conducting system (AVRP) (n=7; p>0.05)
Rodrigo, 1999	New Zealand G/NP	Rat Adult Ventricular	EPA 5µM Free	10 mins	CP	Ambient	None	EPA vs. Ctrl - Decreased twitch contraction size by 70 (n=8; p<0.001) - Effects were reversible by BSA
			EPA 5µM Free	10 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased $I_{Ca.L}$ by 72% (n=8; p<0.001) - Effects were reversible by BSA
		Guinea Pig Adult Ventricular	EPA 5µM Free	10 mins	CP	Ambient	None	EPA vs. Ctrl - Initial increase in twitch contraction size (% cell shortening) followed by a decrease in twitch contraction strength by –88% (n=7; p<0.001) - Effects were partially reversible by BSA
		Guinea Pig Adult Ventricular	EPA 5µM Free	10 mins	ICU	Ambient	None	EPA vs. Ctrl - Decreased $I_{Ca.L}$ by 64% (n=11; p<0.001) - Effects were reversible by BSA

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Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
		Rat Adult Skinned/ Saponin Permealized Ventricular	EPA 5uM Free	10mins	CP + IPIM	Ambient	Ca^{2+} (133-267nM) Added before FA	EPA+Ca^{2+} vs. Ctrl+Ca^{2+} - Decreased frequency of spontaneous contractions (%=ND) (n=5; p<0.05) due to an inhibition of SR Ca^{2+} release - No change in degree of relaxation between spontaneous contractions (n=5; p>0.05)
			EPA 10µM Free	10mins	CP+ IPIM	Ambient	Ca^{2+} (133-267nM) Added before FA	EPA+Ca^{2+} vs. Ctrl+Ca^{2+} - Decreased frequency of spontaneous contractions (%=ND) (n=5; p<0.05) due to an inhibition of SR Ca^{2+} release - No change in degree of relaxation between spontaneous contractions (n=5; p>0.05)
		Guinea Pig Adult Skinned/ Saponin Permealized Ventricular	EPA 5µM Free	10 mins	CP	Ambient	Ca^{2+} (133-267nM) Added before FA	EPA+Ca^{2+} vs. Ctrl+Ca^{2+} - Decreased frequency of spontaneous contractions (%=ND) (n=5; p<0.05) due to an inhibition of SR Ca^{2+} release - No change in degree of relaxation between spontaneous contractions (n=5; p>0.05)
Vitelli, 2002	Italy U	Rat Adult Ventricular	DHA 10µM Free	20 mins	IPIM	Ambient	Ca^{2+} free KRB (1.8mM)	DHA vs. Ctrl - No change in basal level of cytosolic Ca2+ (n=ND; p>0.01)
			DHA 10µM Free	20 mins	IPIM	Ambient	$CaCl_2$ KRB (1.8mM)	DHA vs. Ctrl - No change in basal level of cytosolic Ca2+ (n=ND; p>0.01)
Vitelli, 2002	Italy U	Rat Adult Ventricular	DHA 10µM Free	20 mins	IPIM	Ambient	DXR (100uM) Added after FA Ca^{2+} free KRB (1.8mM)	DHA+DXR vs. Ctrl+DXR - Decreased peak level of Ca^{2+} (n=ND; p<0.01) DHA+DXR vs. Ctrl - No change in peak level of Ca^{2+} (n=ND; p>0.05) DHA+DXR vs. DHA - No change in peak level of Ca^{2+} (n=ND; p>0.05)
			DHA 10µM Free	20 mins	IPIM	Ambient	DXR (100uM) Added after FA $CaCl_2$ KRB (1.8mM)	DHA+DXR vx Ctrl+DXR - Decreased peak level of Ca^{2+} (n=9; p<0.01) DHA+DXR vs. Ctrl - No change in peak level of Ca^{2+} (n=9; p>0.05) DHA+DXR vs. DHA - No change in peak level of Ca^{2+} (n=9; p>0.05)
			DHA 10µM Free	20 mins	IPIM	Ambient	Caff (10mM) Added after FA Ca^{2+} free KRB (1.8mM)	DHA+Caff vx Ctrl+Caff - Decreased peak level of Ca^{2+} (n=9; p<0.01) DHA+DXR vs. Ctrl - No change in peak level of Ca^{2+} (n=9; p>0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA 10µM Free	20 mins	IPIM	Ambient	Caff (10mM) Added after FA $CaCl_2$ KRB (1.8mM)	DHA+Caff vx Ctrl+Caff - Decreased peak level of Ca^{2+} (n=9; p<0.01) DHA+DXR vs. Ctrl - No change in peak level of Ca^{2+} (n=9; p>0.05)
Weylandt, 1996	USA G	Rat Neonatal Cardiac	EPA 15µM DHA 15µM Bound	48 hrs	CP	Ambient	ISO (3-10uM)	EPA+ISO vs. Ctrl+ISO - No change in arrhythmias (n =51-107; p=ND) EPA+ISO vs. DHA+ISO - No change in arrhythmias (n=51-107; p>0.1)
			DHA 15µM Bound	>48 hrs	CP	Ambient	ISO (3-10uM)	DHA+ISO vs. Ctrl+ISO - No change in arrhythmias (n=13 -51; p>0.1)
			EPA 15µM DHA 15µM Bound	48 hrs	CP	Ambient	Ca^{2+} (7mM)	EPA+ Ca^{2+}vs. Ctrl+ Ca^{2+} - No change in arrhythmias (n =14-20; p>0.1) EPA+ Ca^{2+}vs. DHA+ Ca^{2+} - No change in arrhythmias (n=6-14; p>0.1)
			DHA 15µM Bound	48 hrs	CP	Ambient	Ca^{2+} (7mM)	DHA+Ca^{2+} vs. Ctrl+Ca^{2+} - No change in arrhythmias (n=6-20; p>0.1)
			DHA 15µM Free	3-12mins	CP	Ambient	ISO (3-10uM) Added before FA	DHA+ISO vs. Ctrl+ISO - Terminated arrhythmias (n=8; p<0.05)
			EPA 15µM Free	3-12mins	CP	Ambient	ISO (3-10uM) Added before FA	EPA +ISO vs. Ctrl+ISO - Terminated arrhythmias (n=8; p<0.05)
Weylandt, 1996	USA G	Rat Neonatal Cardiac	DHA 15µM Bound EPA 15µM Free	3-12mins 48 hrs	CP	Ambient	ISO (3-10uM) Added before FA	DHA vs. DHA+ISO - Terminated arrhythmias (n=23; p<0.05) EPA vs. EPA+ISO - Terminated arrhythmias (n=23; p<0.05)
			DHA or EPA 15µM Free	3-12mins	CP	Ambient	Ca^{2+} (7mM))	DHA+Ca^{2+} vs. Ctrl+Ca^{2+} - Decreased arrhythmias by -83% (n=12; p<0.05) EPA vs. Ctrl+Ca^{2+} - Decreased arrhythmias by -83% (n=12; p<0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			DHA or EPA 15µM Bound DHA or EPA 15µM Free	3-12mins 48 hrs	CP	Ambient	Ca^{2+} (7mM)	DHA (free) vs. DHA (bound)+Ca^{2+} - Decrease in arrhythmias by -90% (n=10; p<0.05) EPA (free) vs. EPA (bound)+Ca^{2+} - Decrease in arrhythmias by -90% (n=10; p<0.05)
Xiao, 1995	USA G	Rat Neonatal Ventricular	EPA 5-10µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Suppressed voltage activated Na^+ currents within 2mins which was reversible by BSA (n=6; p<0.05) - No change in current-voltage relations or in the activation and inactivation time constants of Na^+ current (n=10; p>0.05)
			EPA 10-40µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Suppressed Na^+ current by 68% to 99% with 10um and 40um EPA respectively indicating a dose dependent effect (n=4-10; p<0.05)
			EPA 10µM Free	ND	ICU	Ambient	None	EPA vs..Ctrl - Modified the voltage dependence of the steady state inactivation of I_{Na} (n=7; p<0.001). Inhibition of 83% at –80mV and 29% at –150mV indicating a voltage dependent effect. Application of a train of stimulating pulses at freq.l of 1.0, 0.2, 0.1, or 0.03 Hz had no effect on time required to attain same level of inhibition of I_{Na} independent of concentration (n=5; p>0.05) (time and dose but not use dependent effect)
			EPA 5µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Inhibition of I_{Na} by 51% (n=10; p<0.01)
			DHA 5µM Free					DHA vs. Ctrl - Inhibition of I_{Na} by 52% (n=7; p<0.01)
			EPA 10µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Inhibition of I_{Na} by 64% (n=21; p<0.001)
Xiao, 1995	USA G	Rat Neonatal Ventricular	DHA 10µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Inhibition of I_{Na} by 66% (n=7; p<0.05)
			ALA 10µM Free	ND	ICU	Ambient	None	ALA vs. Ctrl - Inhibition of I_{Na} by 71% (n=5; p<0.05)

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Evidence Table 3. Isolated Organ And Cell Culture Studies

Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
			EPA 1.5µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased $I_{Ca,L}$ by 50% (n=11; p<0.05) and effects were partially reversible by BSA - No change in shape of current voltage relationship (n=11; p>0.05) - Negative shift (3.33+/-0.4 mV) of the $I_{Ca,L}$ inactivation curve (n=11;p<0.05) and effects were reversible by BSA
Xiao, 1997	USA G	Rat Neonatal Ventricular	EPA 0.1-40µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Time and dose dependant decrease in $I_{Ca,L}$ within seconds (n=6; p<0.05) - $I_{Ca,L}$ was almost completely inhibited when the concentration of EPA was above 5 uM
			EPA 1µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased $I_{Ca,L}$ by 33% when elicited from the holding potential –40 to 0mV than from -80 to 0mV indicating a voltage dependent effect (n=6; p<0.05) - Effect was also time but not frequency or use-dependent (n=4; p>0.05)
			EPA 5µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Inhibition of $I_{Ca,L}$ by 83% (n=5; p<0.01) - EPA, DHA and ALA had similar effects on the steady -state inactivation of the calcium cannel (approx 3 to 5 mV shift to negative potentials a the V1/2 point)
			DHA 5µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Inhibition of $I_{Ca,L}$ by 62% (n=6; p<0.01)
			ALA 5µM Free	ND	ICU	Ambient	None	ALA vs. Ctrl - Inhibition of $I_{Ca,L}$ by 77% (n=5; p<0.01)
			EPA 1µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Suppression of $I_{Ca,L}$ by 57% (n=5; p<0.01)
			EPA 5µM Free	ND	ICU	Ambient	None	EPA vs.. Ctrl - Suppression of $I_{Ca,L}$ by 47% (n=8; p<0.01)
			EPA 1.5µM Free	ND	IPIM	Ambient	None	EPA vs. Ctrl - Decreased the calcium transients induced by $I_{Ca,L}$ (n=ND;p<0.01)
			EPA 15µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased the calcium transients induced by $I_{Ca,L}$ (n=ND; p<0.01) - Decreased SR Ca^{2+}release (n=ND; p<0.05) - No change in time constant of decay (tau) or temporal and spatial spread of the calcium sparks (n 33-46; p>0.05) indicating no direct action of EPA on SR Ca^{2+} release or re-uptake
Xiao, 2002	USA G/NP	Ferret Adult Atrial	DHA 10µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_k by 62% -69% (n=7-12; p<0.05)

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Author, yr	Study Characteristics [Country: Funding:]	Cells [Animal: Age: Type:]	Fatty Acid [N3: Dose: Form:]	Incubation/ Exposure Duration	Outcome Category	Experimental Condition	Agent [Amt]	Results
		Ferret Adult VentrIcular	DHA 0.2-50µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Dose dependant decrease in I_k (% in fig) (n=6; p<0.05)
			DHA 5µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_k by 31% (n=12; p<0.05) - No change in I_{KI} (n=6; p>0.05)
			DHA 10µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_k by 42% regardless of holding potential (n=8; p<0.05) - Decreased I_{to} by 57% (n=7; p<0.001) - No change in I_{KI} (n=5; p>0.05)
			DHA 20µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_k by 50% (n=6; p<0.01) - No change in I_{KI} (n=2; p>0.05)
			DHA 50µM Free	ND	ICU	Ambient	None	DHA vs. Ctrl - Decreased I_k by 61% (n=11; p<0.001)
			EPA 5µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_k by 26% (n=6; p<0.05)
			EPA 10µM Free	ND	ICU	Ambient	None	EPA vs. Ctrl - Decreased I_k by 40% (n=8; p<0.001) - Decreased I_{to} by 67% (n=4; p<0.01) - No change in I_{KI} (n=ND; p>0.05)
			ALA 5µM Free	ND	ICU	Ambient	None	ALA vs. Ctrl - Decreased I_k by 22% (n=7; p<0.01)
			ALA 10µM Free	ND	ICU	Ambient	None	ALA vs. Ctrl - Decreased I_k by 46% (n=8; p<0.001) - Decreased I_{to} by 49% (n=4; p<0.05) - No change in I_{KI} (n=ND; p>0.05)
			DHA 10µM Free	ND	ICU	Ambient	Sta (0.1µmol/L) Added before FA	DHA+Sta vs. Ctrl+Sta - Decreased I_k by 65% (n=5; p<0.05)

APPENDIX D. Peer Reviewers

We gratefully acknowledge the following individuals who reviewed the initial draft of this Report and provided us with constructive feedback. Acknowledgments are made with the explicit statement that this does not constitute endorsement of the report.

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