共役ポリエン脂肪酸の特異的な生理作用とその作用機構

宮澤陽夫

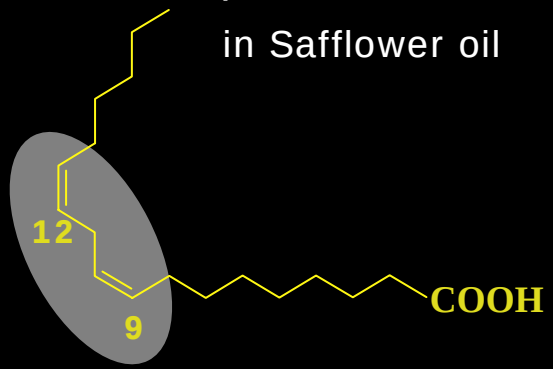
（東北大学大学院農学研究科）

Chemical structures of LA, CLA, LnA and CLnA.

Linoleic acid

(n-6, 18:2, c9c12)

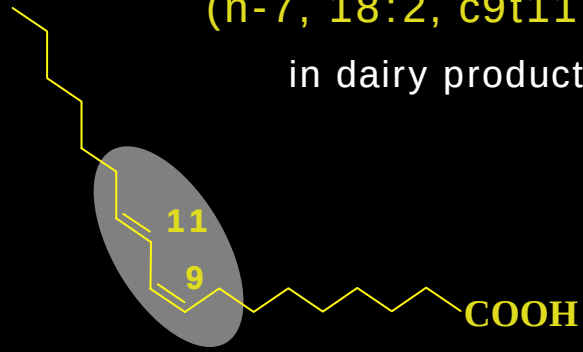
in Safflower oil



Conjugated linoleic acid

(n-7, 18:2, c9t11, CLA)

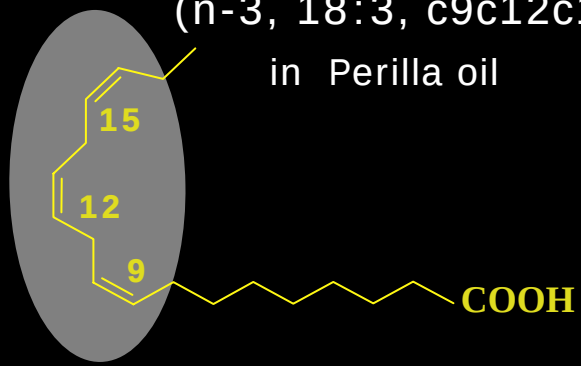
in dairy products



α-Linolenic acid

(n-3, 18:3, c9c12c15)

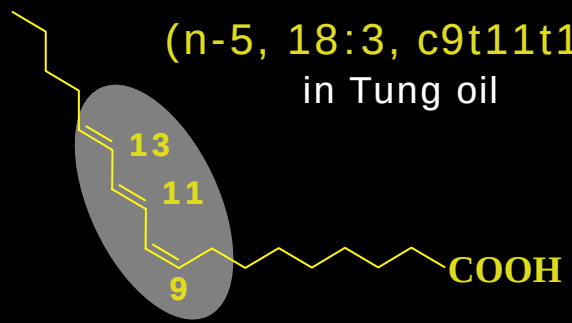
in Perilla oil



Conjugated linolenic acid α-Eleostearic acid

(n-5, 18:3, c9t11t13)

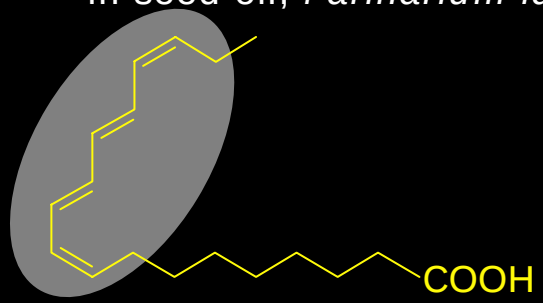
in Tung oil



Chemical structures of conjugated fatty acids found in plant seed oil and algae.

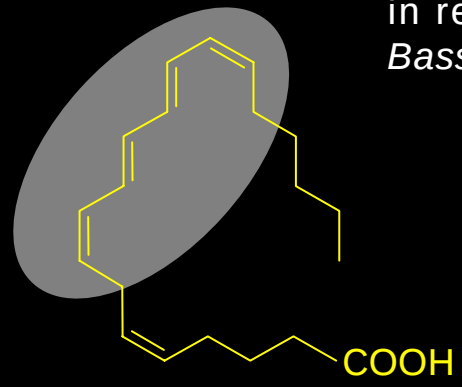
α-Parinaric acid

(n-5, 18:4, c9t11t13c15)
in seed oil, *Parinarium laurinum*



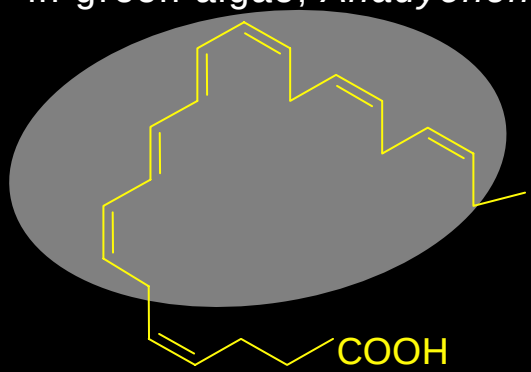
Bosseopentaenoic acid

(n-6, 20:5, c5c8t10t12c14)
in red algae,
Bassiella orbignana



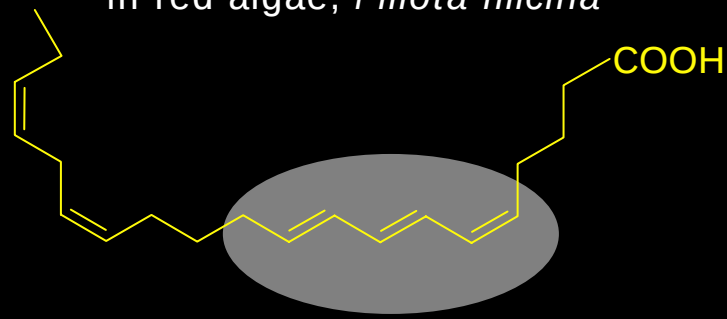
Stellaheptaenoic acid

(n-3, 22:7, c4c7t9t11c13c16c19)
in green algae, *Anadyonene stellata*



Conjugated EPA

(n-3, 20:5, c5t7t9c12c17)
in red algae, *Plilota filicina*



Conjugated Fatty Acids Found in Natural Resources

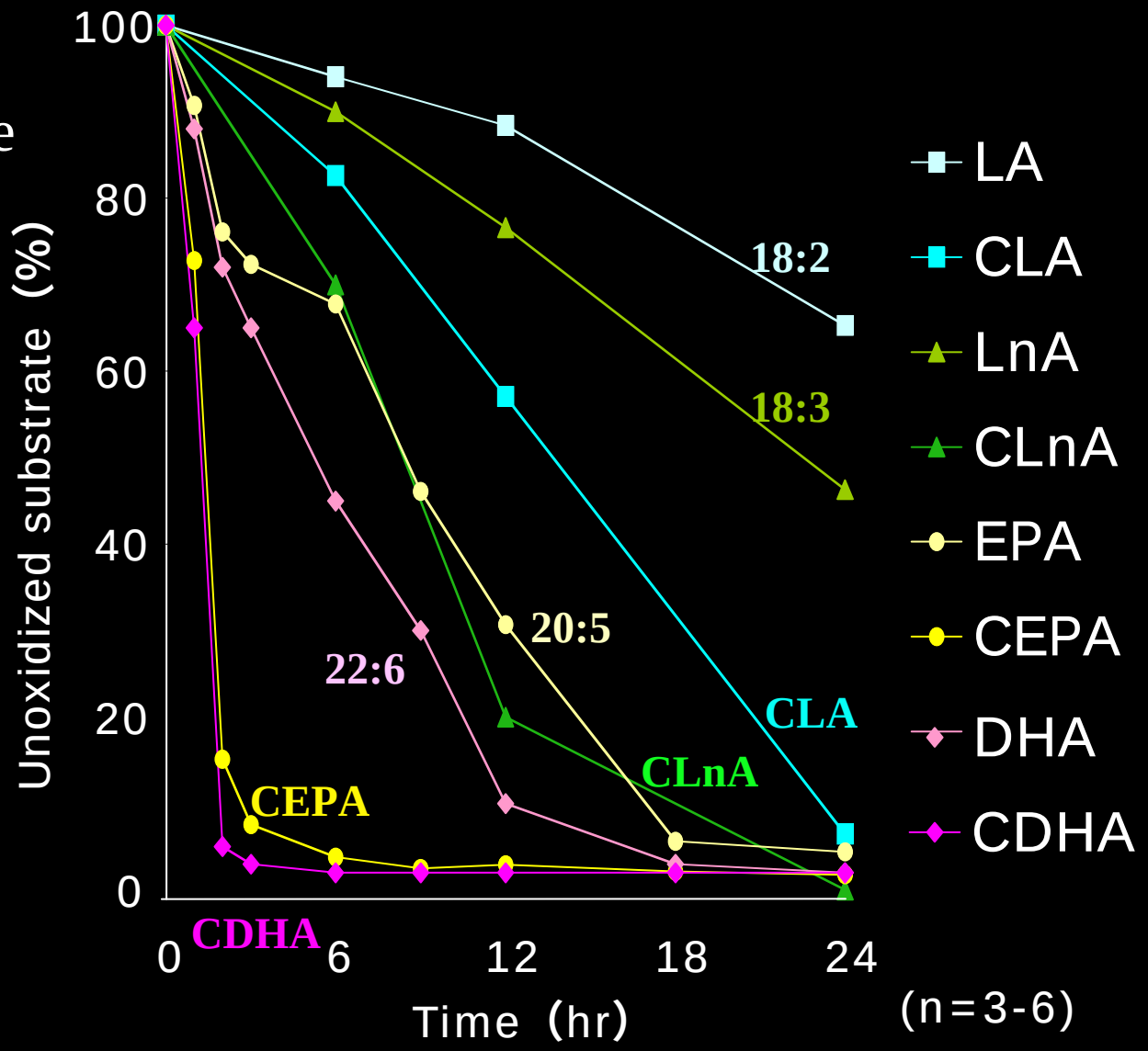
Structure	Trivial name	Location (Species)
2*t*, 4*c*-Decadienoic acid (10:2)	Stillingic acid	Seed oil (*Spapium sebiferum*)
3*t*, 5*c*-Tetradecadienoic acid (14:2)	Megatomoic acid	Female black carpet beetle (*Attagenus megatoma*)
7*t*, 9*c*-Octadecadienoic acid (18:2)		Dairy products, Human milk
9*c*, 11*t*-Octadecadienoic acid (18:2)		Dairy products
10t, 12c-Octadecadienoic acid (18:2)		Dairy products
9*t*, 11*t*-Octadecadienoic acid (18:2)		Dairy products
10*t*, 12*t*-Octadecadienoic acid (18:2)		Dairy products, Seed oil (*Chilopsis linearis*)
8*t*, 10*t*, 12*c*-Octadecatrienoic acid (18:3)	Calendic acid	Seed oil (*Calendula officinalis*)
8*c*, 10*t*, 12*c*-Octadecatrienoic acid (18:3)	Jacaric acid	Seed oil (*Jacaranda mimosifolia*)
9*c*, 11*t*, 13*t*-Octadecatrienoic acid (18:3)	α-Eleostearic acid	Tung oil (*Aleurites fordii*)
9*t*, 11*t*, 13*t*-Octadecatrienoic acid (18:3)	β-Eleostearic acid	Tung oil (*Aleurites fordii*)
9*t*, 11*t*, 13*c*-Octadecatrienoic acid (18:3)	Catalpic acid	Seed oil (*Catalpa ovata*)
9*c*, 11*t*, 13*c*-Octadecatrienoic acid (18:3)	Punica acid	Seed oil (*Punica granatum*)
9c, 11*t*, 13*t*, 15*c*-Octadecatetraenoic acid (18:4)	Parinaric acid	Seed oil (*Parinarium laurinum*)
5*c*, 8*c*, 10*t*, 12*t*, 14*c*-Eicosapentaenoic acid (20:5)	Basseopentaenoic acid	Red algae (*Bassiella orbigniana*)
5*c*, 7*t*, 9*t*, 14*c*, 17*c*-Eicosapentaenoic acid (20:5)		Red algae (*Plilota filicina*)
5*t*, 7*t*, 9*t*, 14*c*, 17*c*-Eicosapentaenoic acid (20:5)		Red algae (*Plilota filicina*)
4*c*, 7*c*, 9*t*, 11*t*, 13*c*, 16*c*, 19*c*-Docosaheptaenoic acid (22:7)	Stellaheptaenoic acid	Green alge (*Anadyomene stellata*)

Contents

1. Oxidation of conjugated fatty acids and its prevention
2. Metabolic conversion to CLA from conjugated trienoic fatty acids
3. Anti-cancer action of CEPA
4. Anti-angiogenic activity of CEPA and CDHA
5. Anti-obesity activity of conjugated PUFA

Oxidation of Conjugated and Nonconjugated PUFA.

37℃
Thin-film in test tube

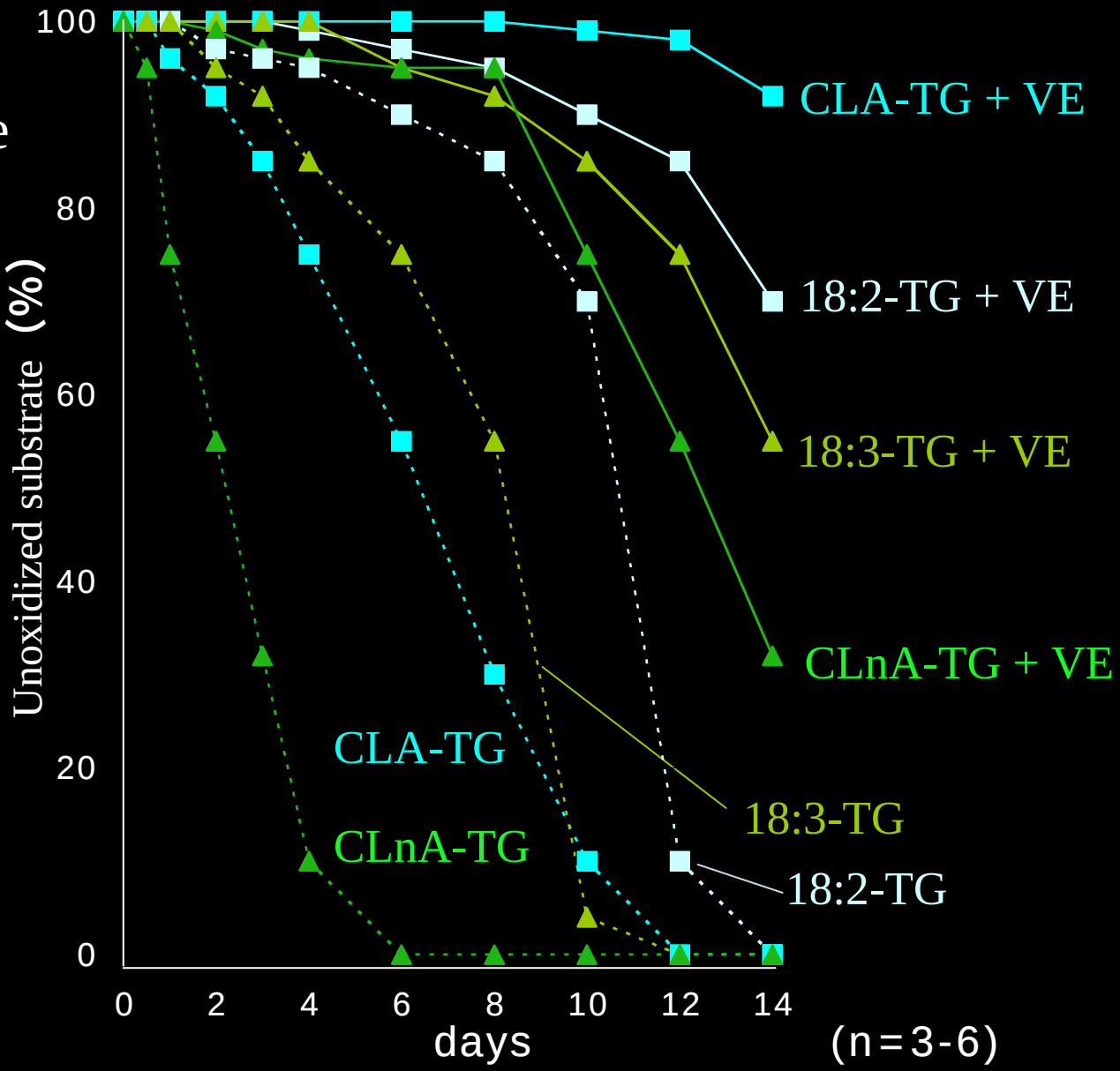


Oxidation of Conjugated and Nonconjugated PUFA.

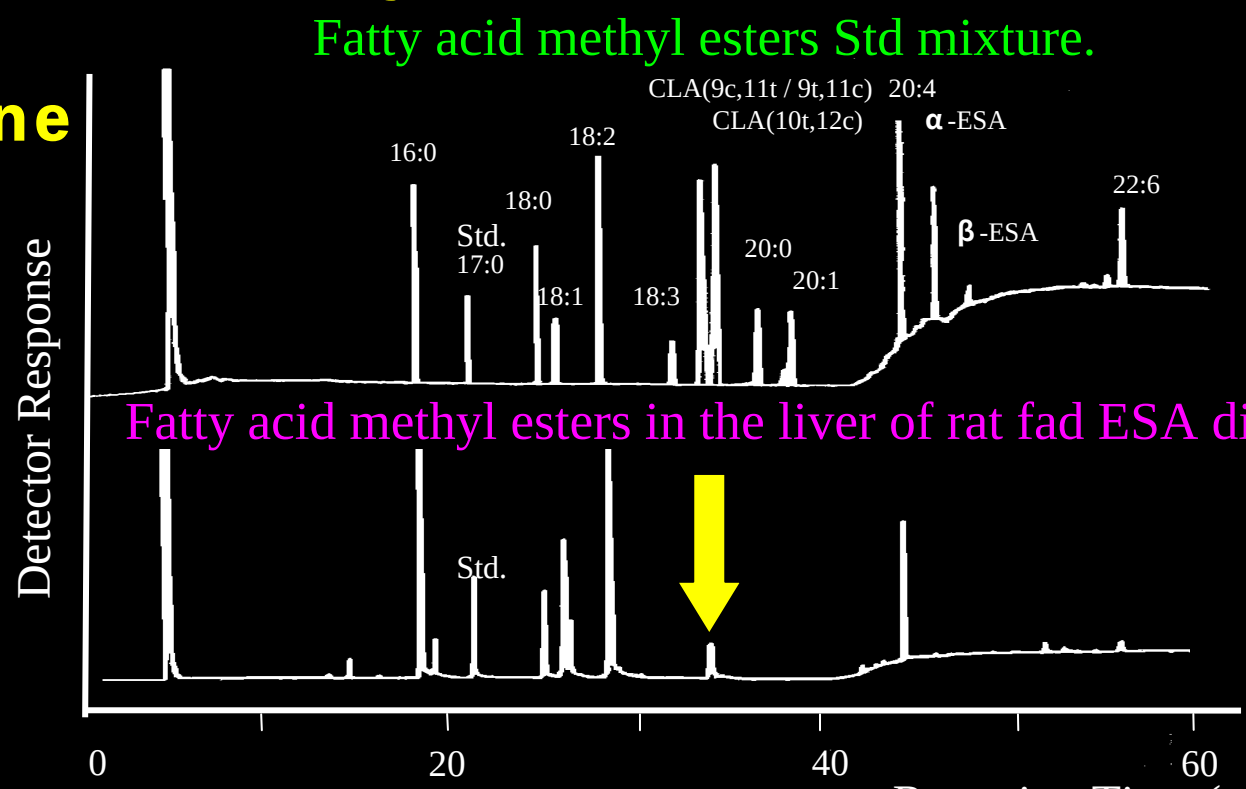
37℃
Thin-film in test tube

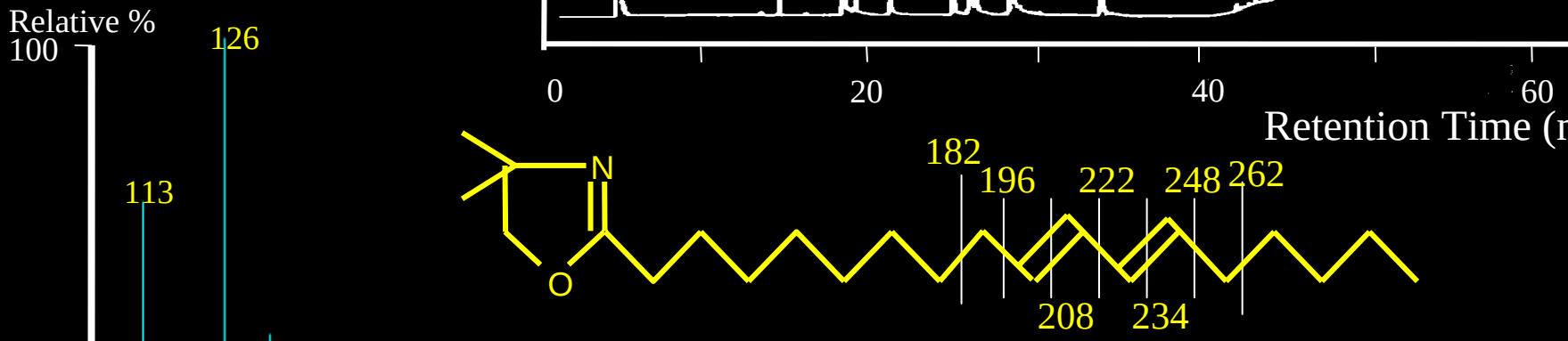
18:2-TG = Safflower oil
18:3-TG = Perilla oil
CLnA-TG = Tung oil

+0.1% VE

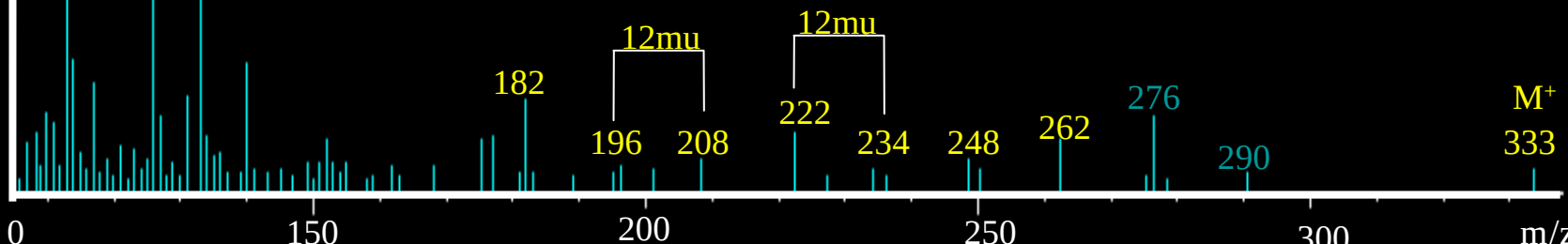


GC of Liver Fatty Acid Methyl Esters & GC-MS 0f CLA Dimethyloxazoline Derivative

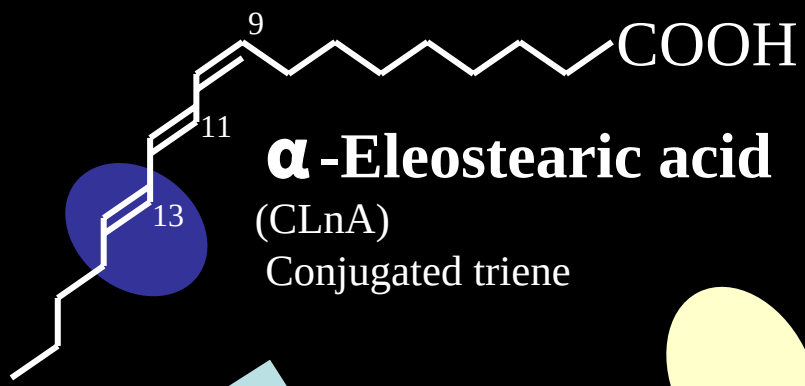




9, 11-Octadecadienoic acid (CLA) M+=333

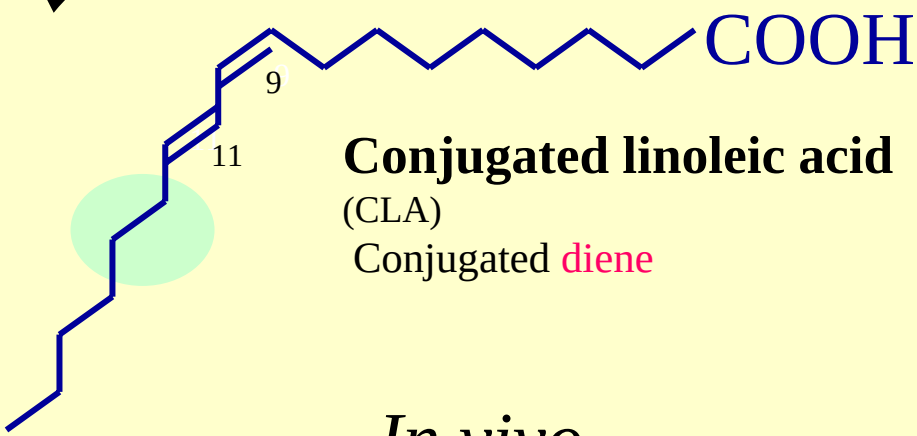


Conclusion



α-Eleostearic acid
(CLnA)
Conjugated triene

Δ13 saturation reaction

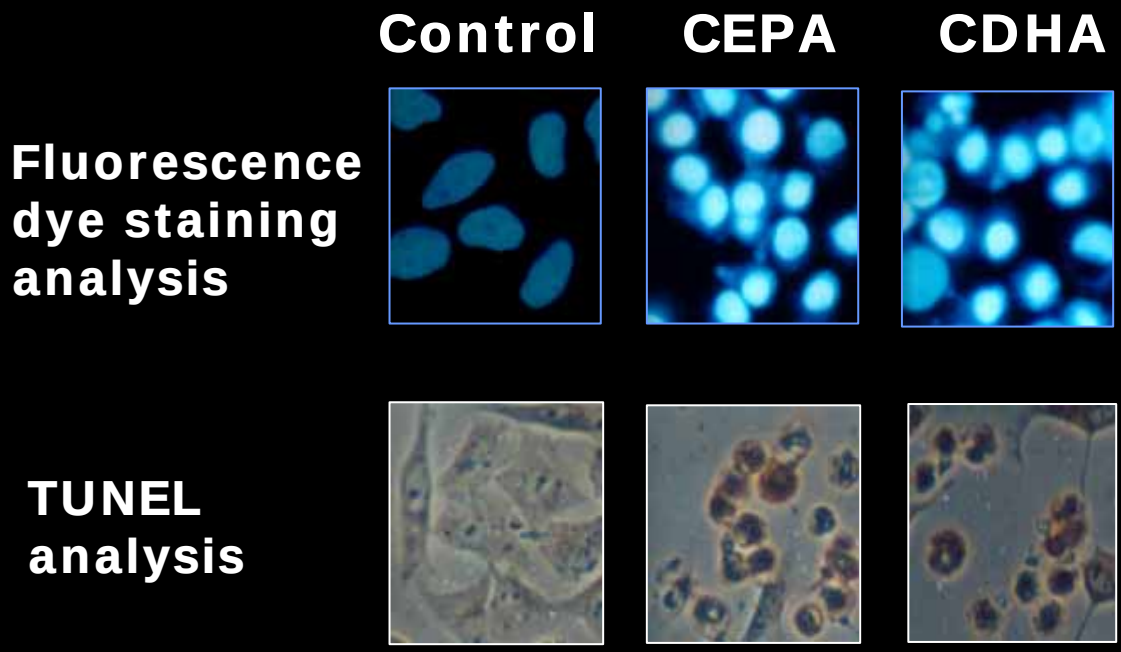


Conjugated linoleic acid
(CLA)
Conjugated diene

In vivo

These data suggested the existence of delta 13 saturation reaction to form CLA from alpha-eleostearic acid in rodents.

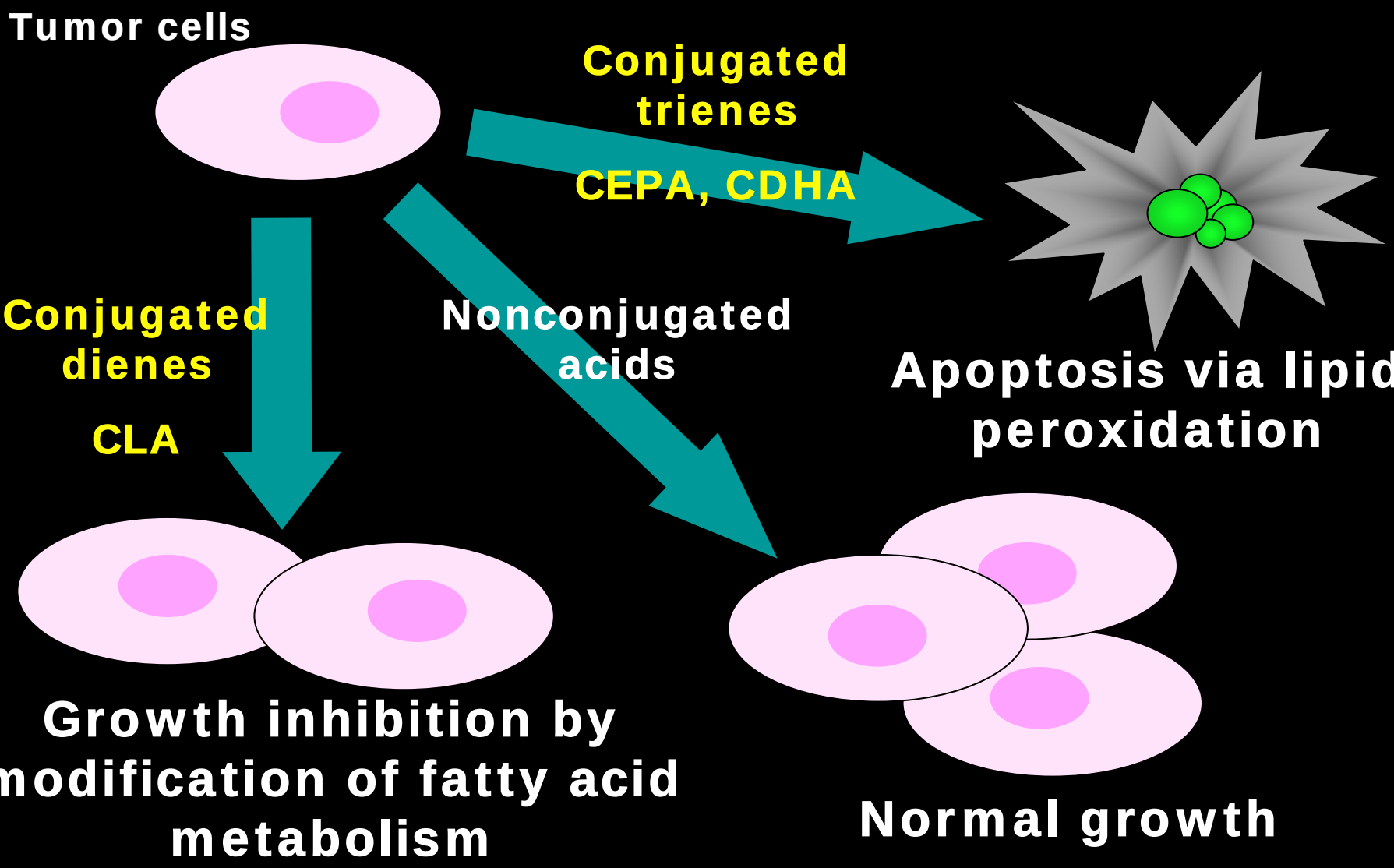
Fluorescence Dye Staining and TUNEL Analysis of DLD-1 Cells Supplemented with CEPA and CDHA



The cells added with CEPA and CDHA showed nuclea condensation and DNA fragmentation, which are characteristic for the apoptosis.

BBRC
2000

Anticarcinogenic action of conjugated PUFA



M. Igarashi & T. Miyazawa. (2000) *Biochem. Biophys. Res. Commun.*, **270**, 649-656.

CEPA privents the growth of transplanted DLD-1 cells in nude mice.

Before

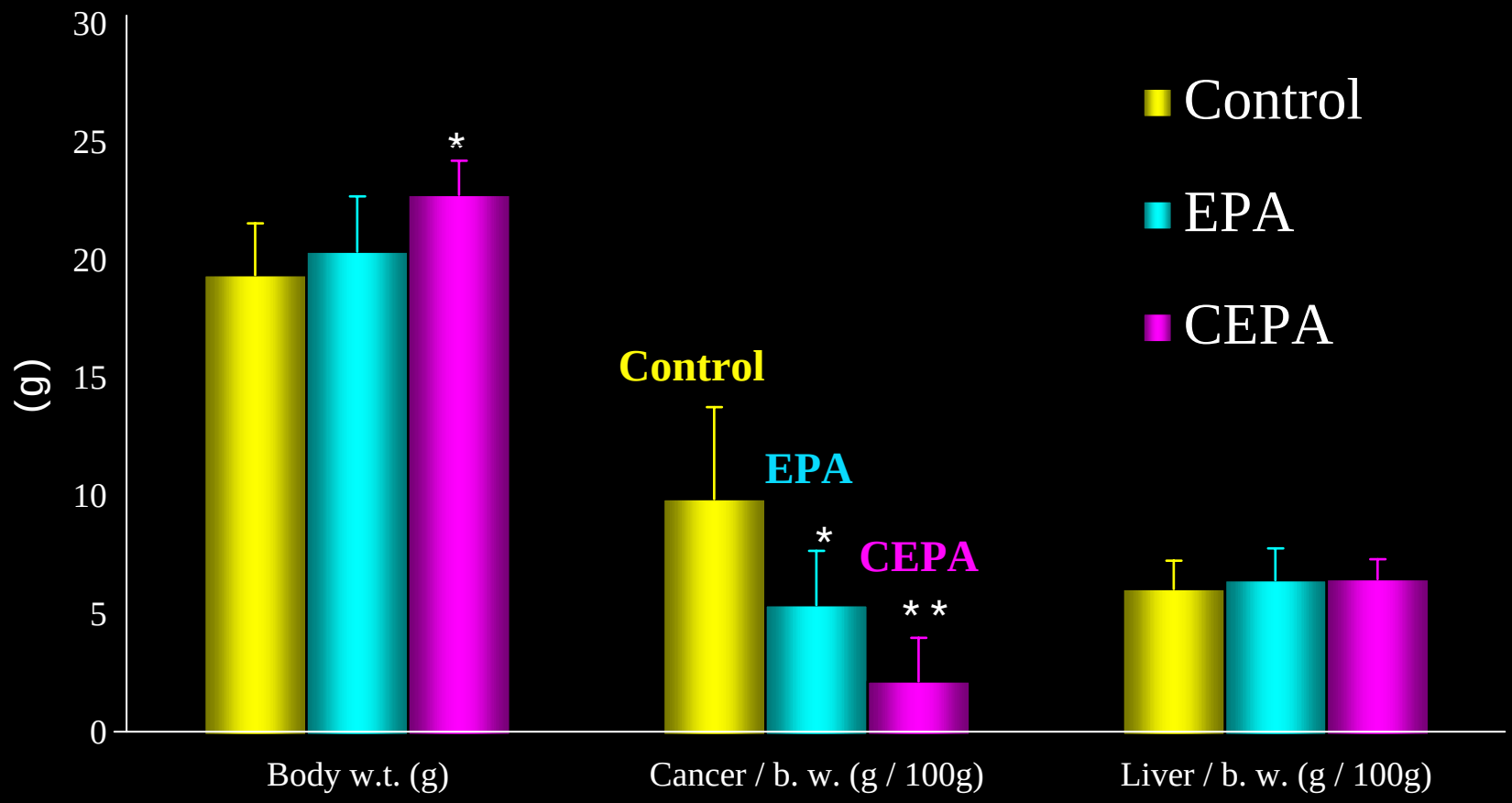
After 4 weeks

Control

EPA

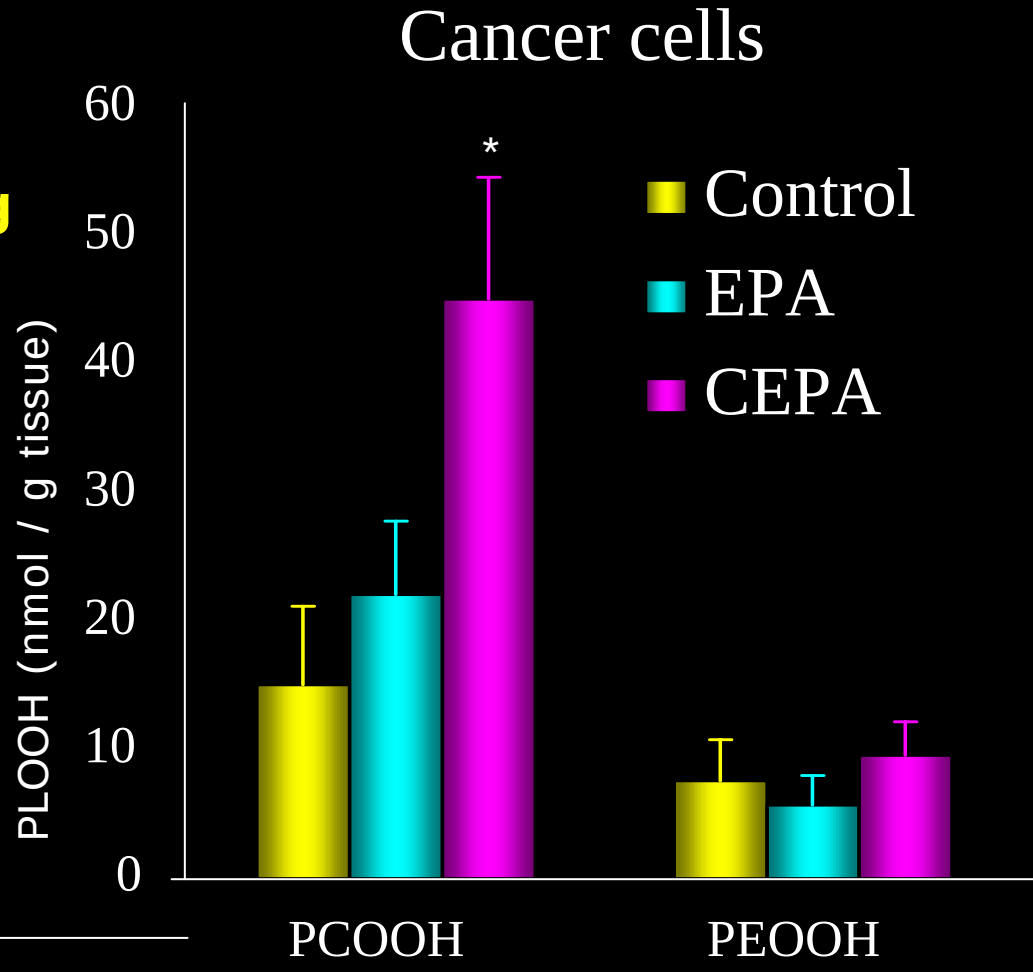
CEPA

CEPA privents the growth of colon cancer cells in nude mice.



*P<0.05 from Control. **P<0.01 from Control. Mean ±SD (n=5)

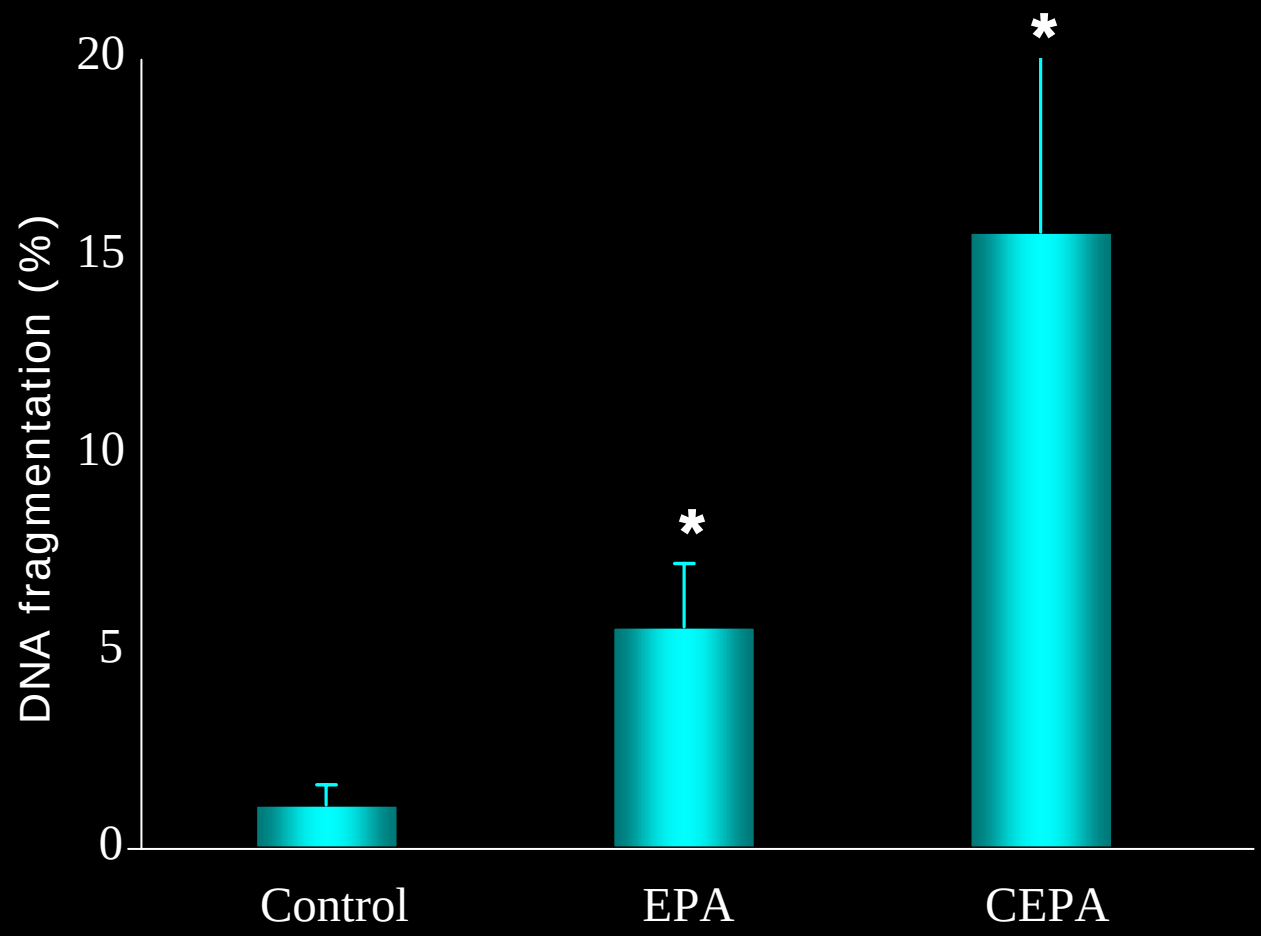
CEPA Intake Causes Membrane Phospholipid Hydroperoxidation Leading to Apoptosis of Cancer Cells, Serum and Liver in Mice.



Group	Serum PCOOH	Serum PEOOH	Liver PCOOH	Liver PEOOH
	nmol/ml		nmol/g tissue	
Control	0.30±0.03	0.01±0.01	16.1±1.9	11.6±2.1
EPA	0.29±0.09	0.05±0.01	17.7±3.4	12.8±3.2
CEPA	0.32±0.04	0.09±0.01	16.1±3.2	13.7±5.8

Mean ±SD (n=5) *$P<0.05$

Stimulated DNA fragmentation of cancer cells in mice supplemented with CEPA.



Mean ±SD (n=5)

*P<0.05 compared with Control group.

Fluorescence method

Control

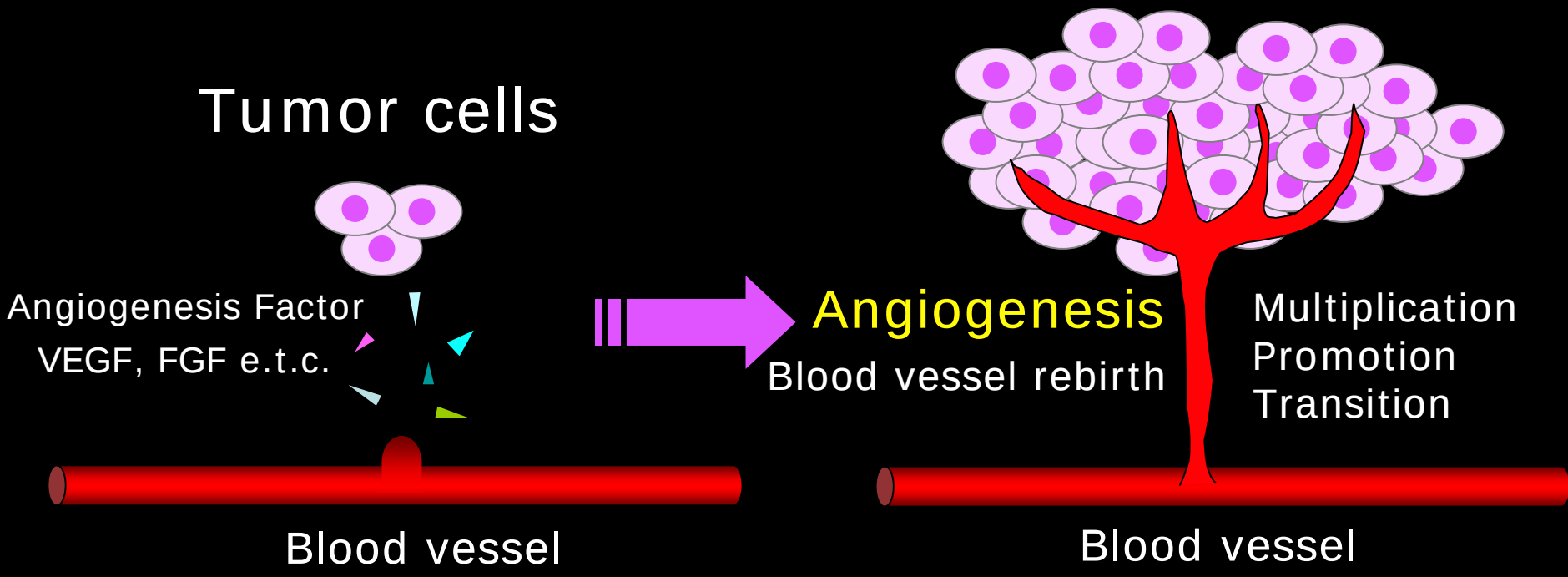
After 6 weeks

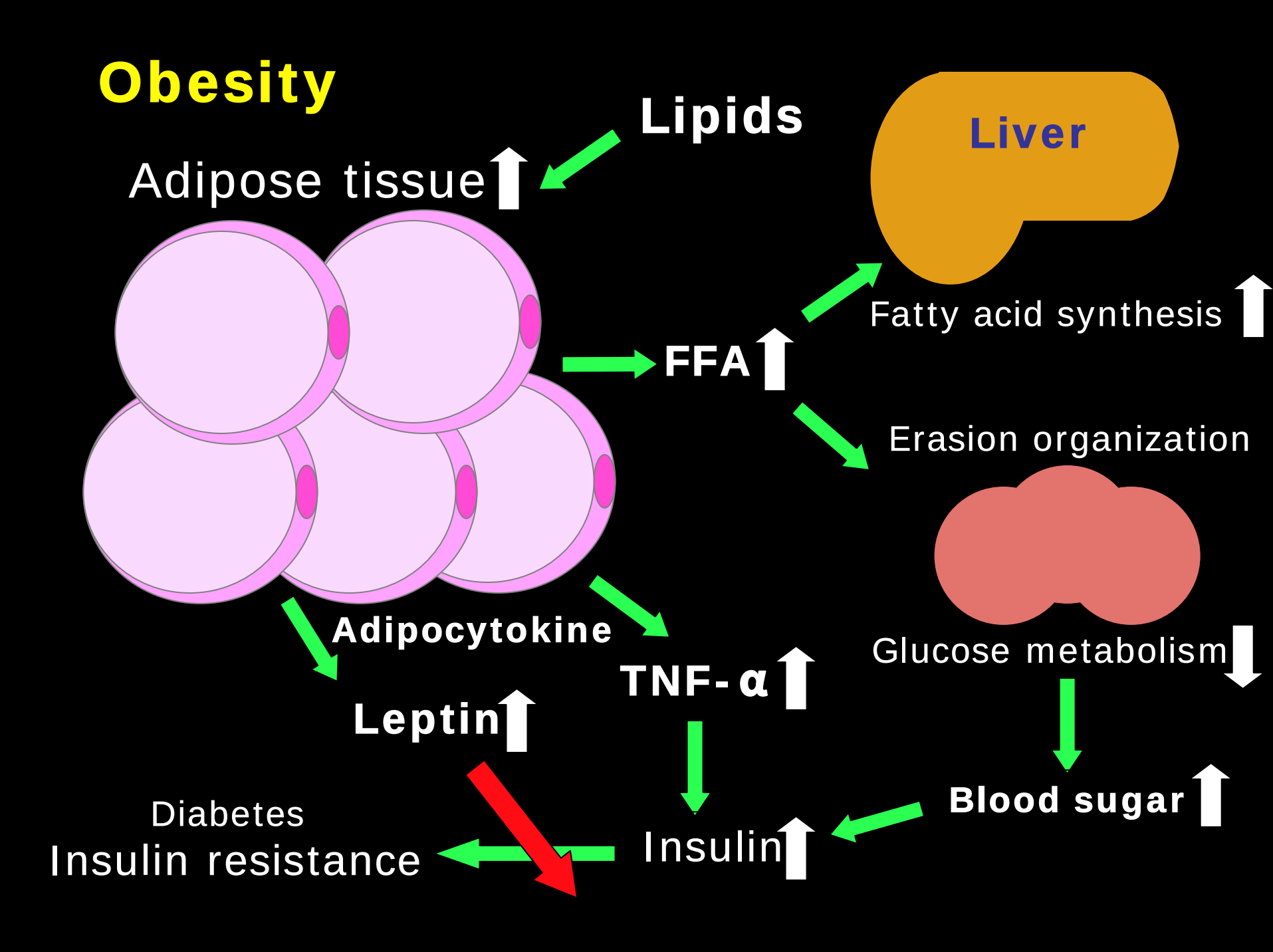
CEPA

Angiogenesis

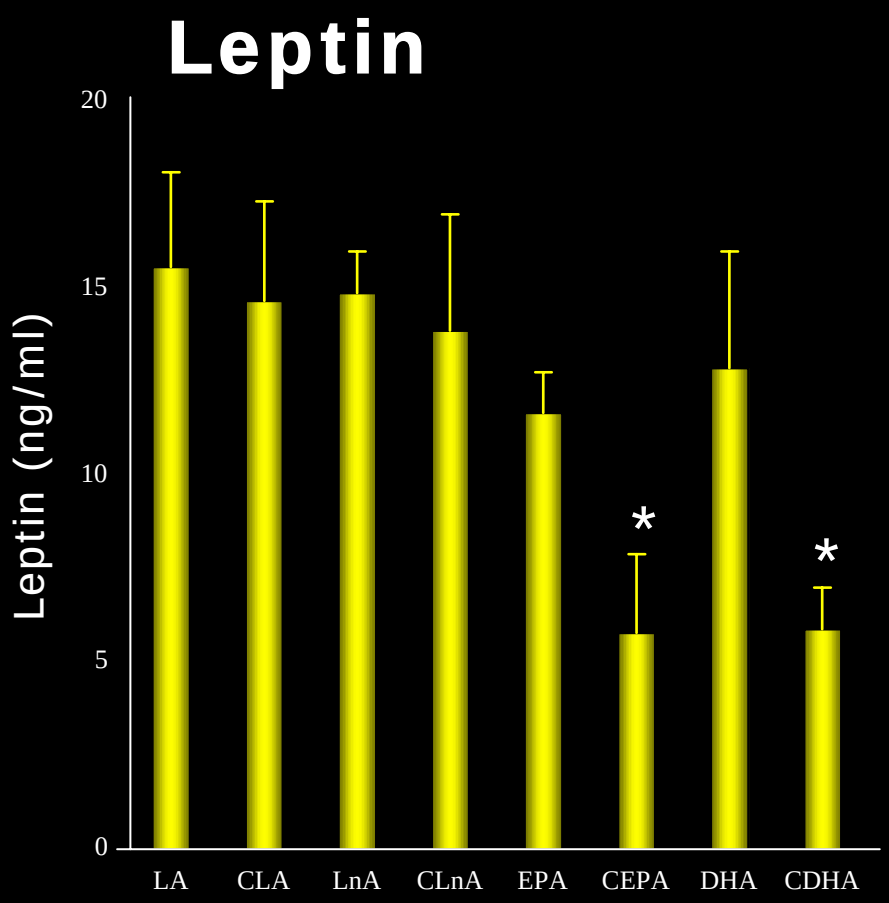
Anti-Angiogenesis with CEPA?

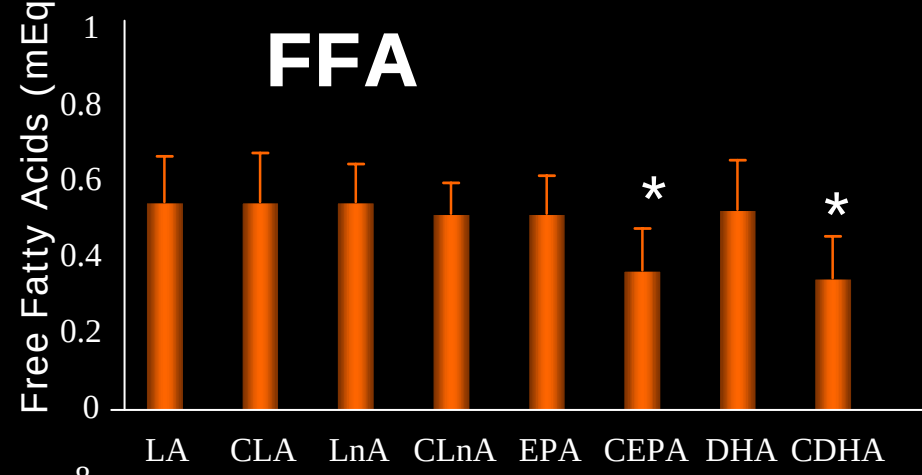
Cancer and Angiogenesis

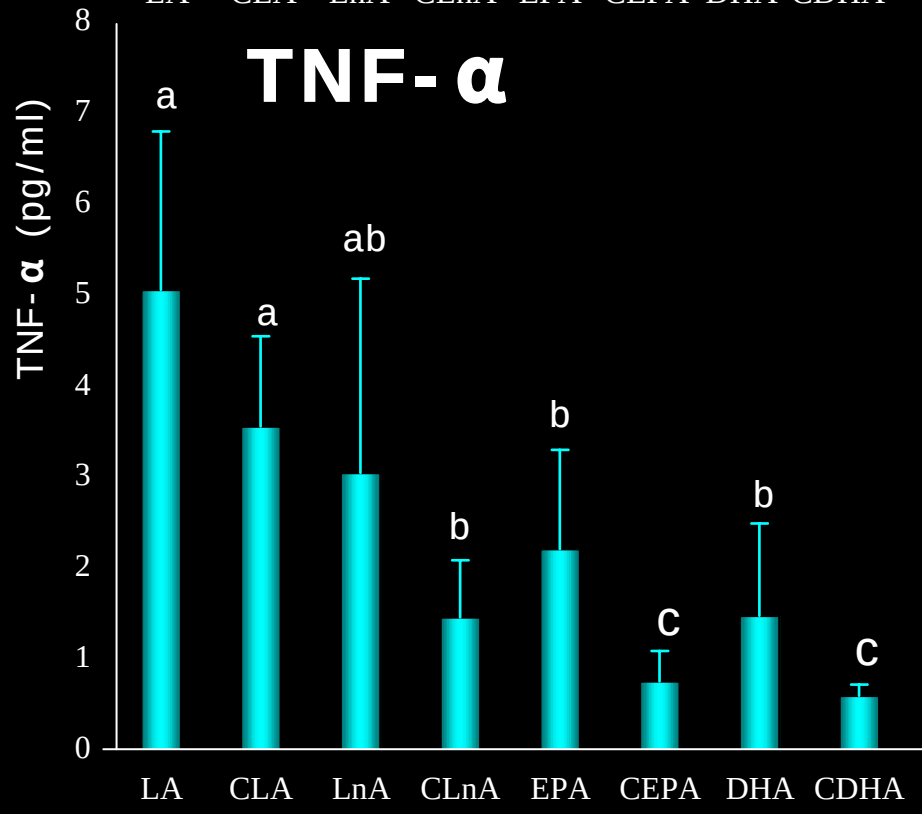



Obesity
Lipids
Adipose tissue
Liver
Fatty acid synthesis
FFA
Erasion organization
Adipocytokine
TNF-α
Glucose metabolism
Leptin
Blood sugar
Diabetes
Insulin resistance
Insulin

Plasma adipocytokine concentration

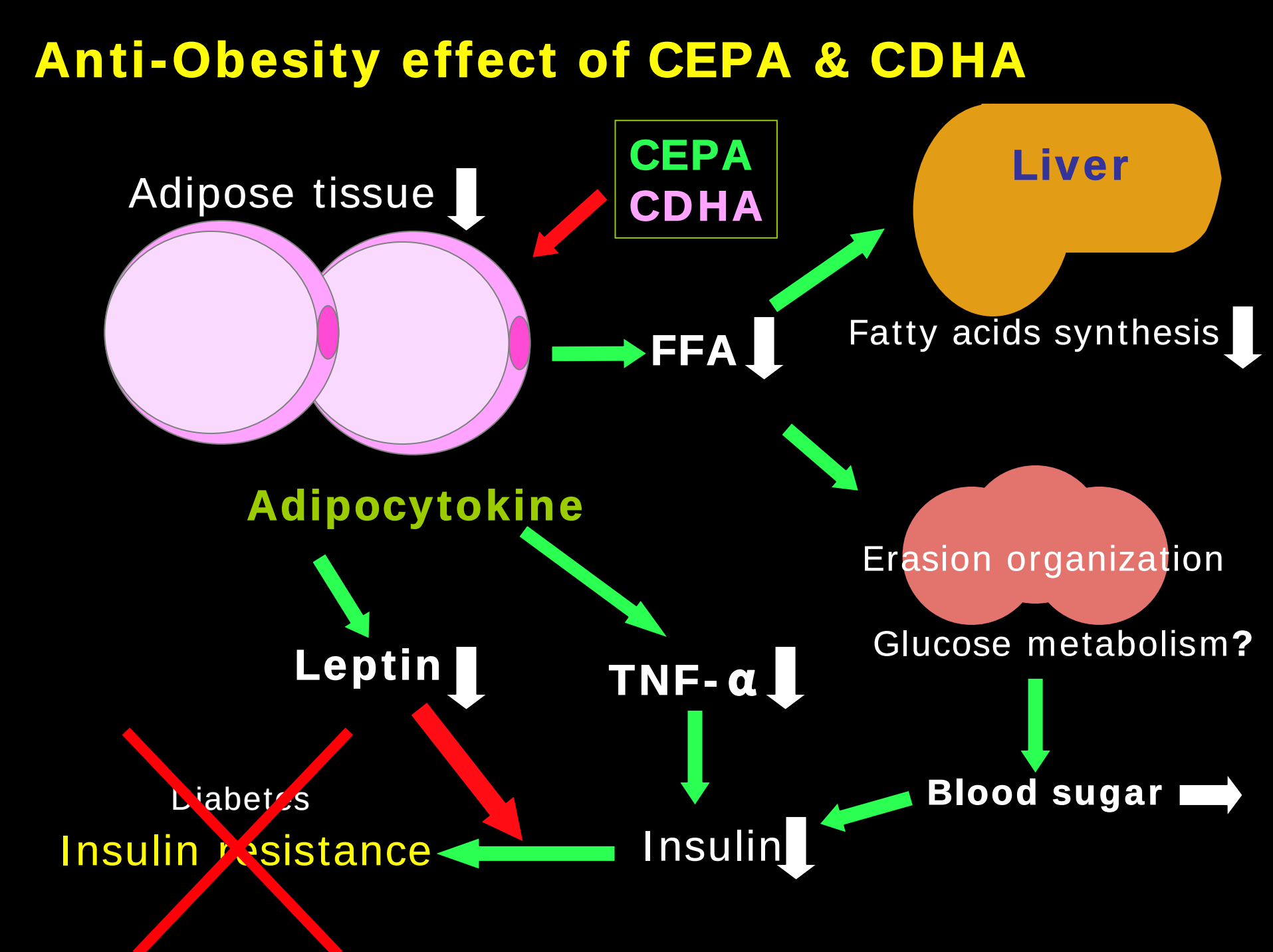




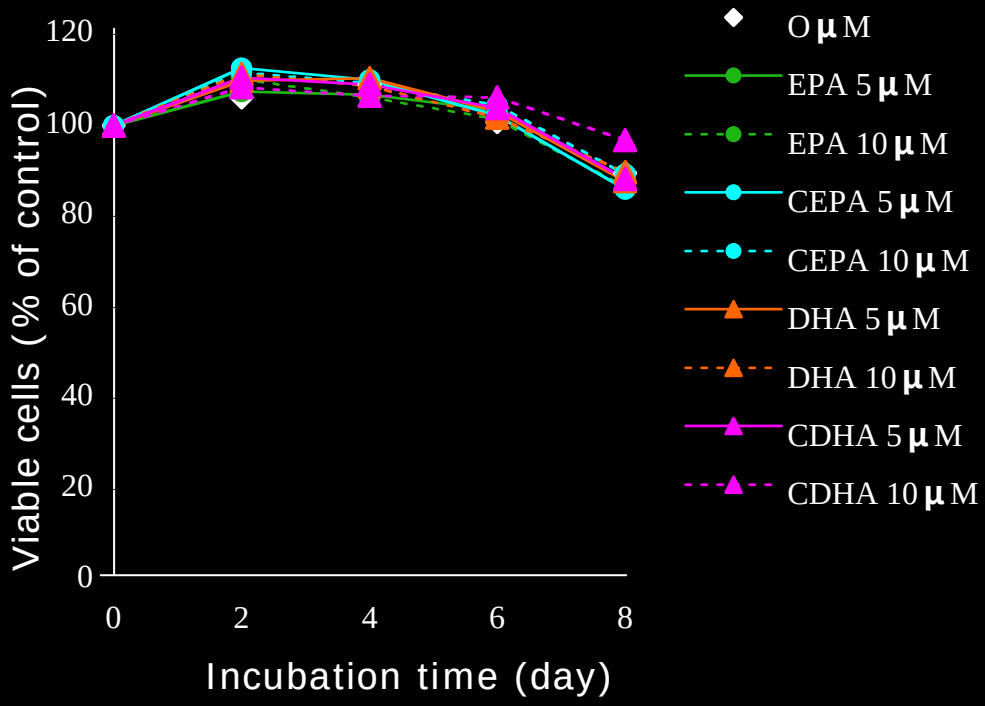


Mean±S.D.(n=6-8)
*P < 0.05 from other groups.
a,b,c, P < 0.05.

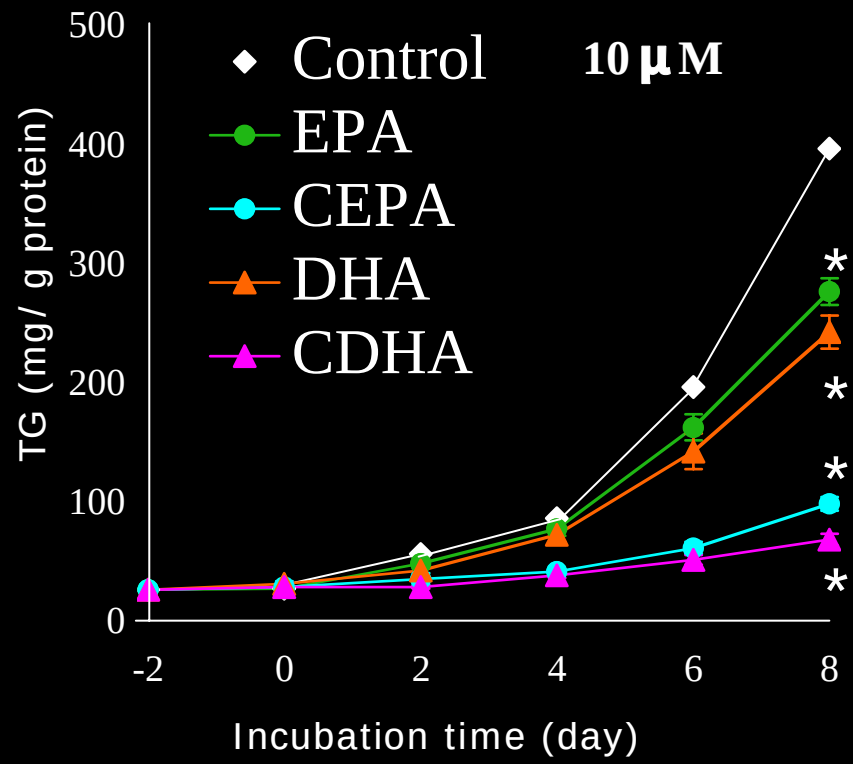
Anti-Obesity effect of CEPA & CDHA



Triacylglycerol concentration in 3T3-L1 cells.



Mean ±SD (n=10).



Mean ±SD (n=10).
*P < 0.05 from Control.

総括

- 共役PUFA (共役EPA) の生物機能

1. In vitroで酸化されやすい。ビタミンEで効果的に抑制。
2. 共役PUFA (共役トリエン) は癌細胞の脂質過酸化を誘発。
3. 共役EPAは癌細胞にアポトーシスを誘発。
4. 共役EPAは担癌マウスの癌組織を退縮。
5. 共役トリエンの一部は動物体内で共役ジエンに代謝。
6. 共役トリエンに血管新生抑制作用。
7. 共役トリエンに抗肥満作用。