Razones por las que es saludable consumir aceite de oliva extra virgen

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ASSUMPTIONS FOR NUTRITIONAL VALUES OF EVOO

High MUFA content, principally oleic acid

Presence of linoleic acid

High levels and variability of phenolic compounds

INTERVENTIONAL NUTRITIONAL STUDIES

Decrease lipid oxidative levels.
Better plasmatic lipid profile.
Decrease blood pressure.
Improves endothelial function.
Better postpandrial glycemic control.
Higher postpandrial insulin plasmatic levels.

25-50 ml EVOO/day 3-6 months
Healthy, SM, hypercholesterolemic, DM2

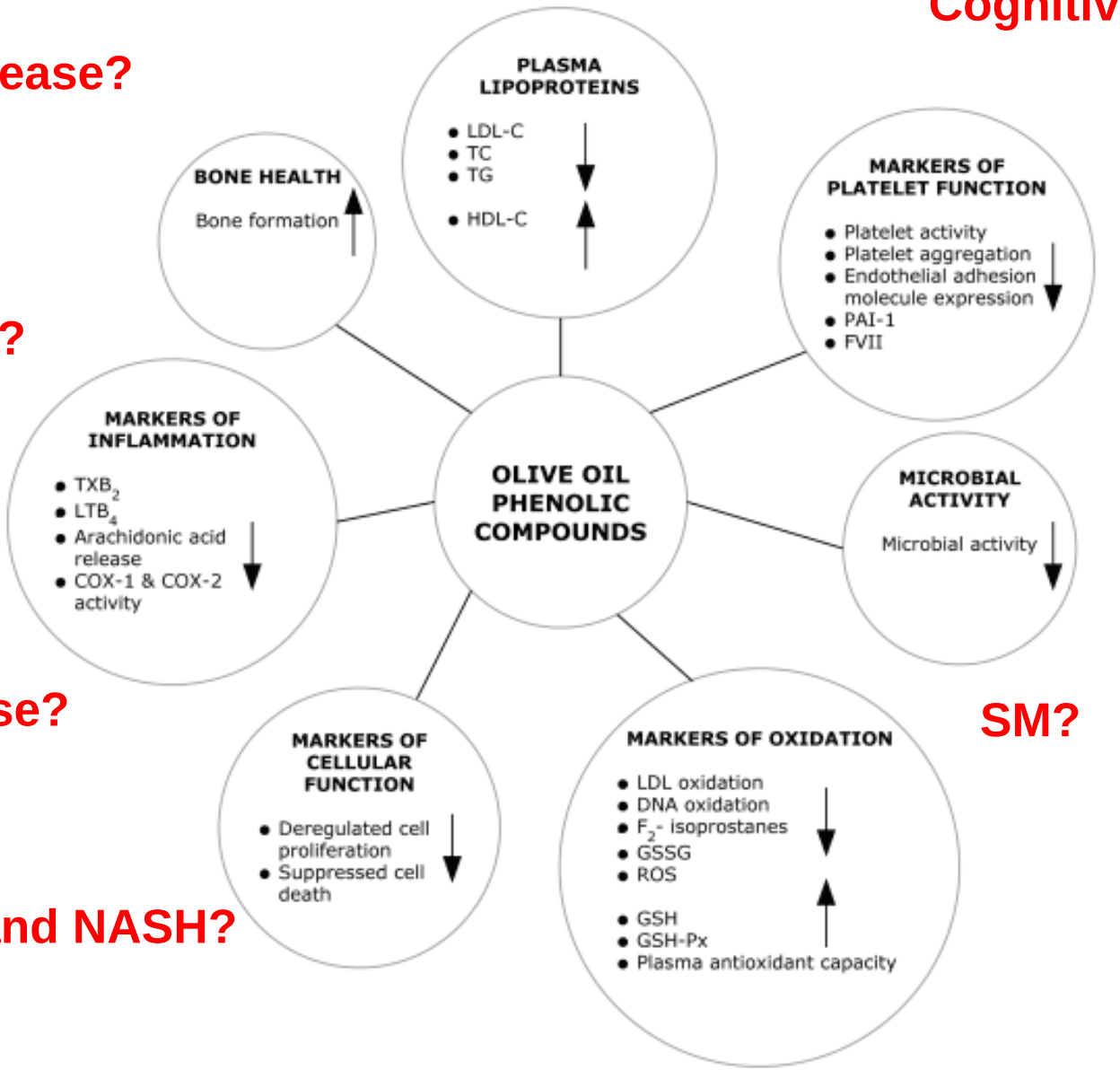
Trevisan et al., 1990
Garg et al., 1998
Gimeno et al., 2002
Grundy et al., 2004
Castañer et al., 2005
Ruano et al., 2005
Covas et al., 2006
Covas et al., 2009
Jimenez –Morales et al., 2011
Oliveras-Lopez et al., 2012
Moreno-Luna et al., 2012
Martín-Pelaez et al., 2013
Oliveras-Lopez et al., 2013
Muros et al., 2015
Violi et al., 2015

Phenolic compounds

PROPERTIES OF EVOO PHENOLIC COMPOUNDS

Cognitive diaseases?

Heart disease?



Cancer?

DM2?

CV disease?

SM?

NAFLD and NASH?

EFSA J., 2012

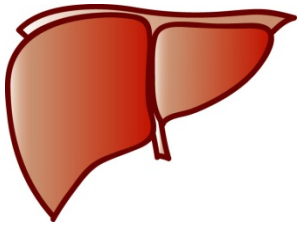
WHAT HAPPENS WITH MUFAS?

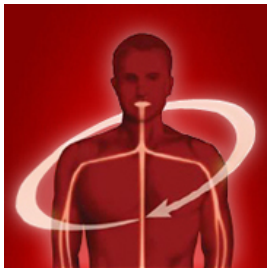
HFD are important but lipid profile makes the difference.

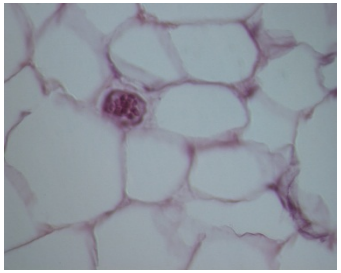
Spanish population: 42% of energy from fats (NAOS strategy)

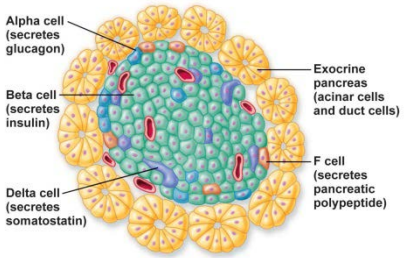
AIMS: ***HFD based on phenol-rich virgin olive oil.***

Role of minoritary compounds.
Role of monounsaturated fatty acids.



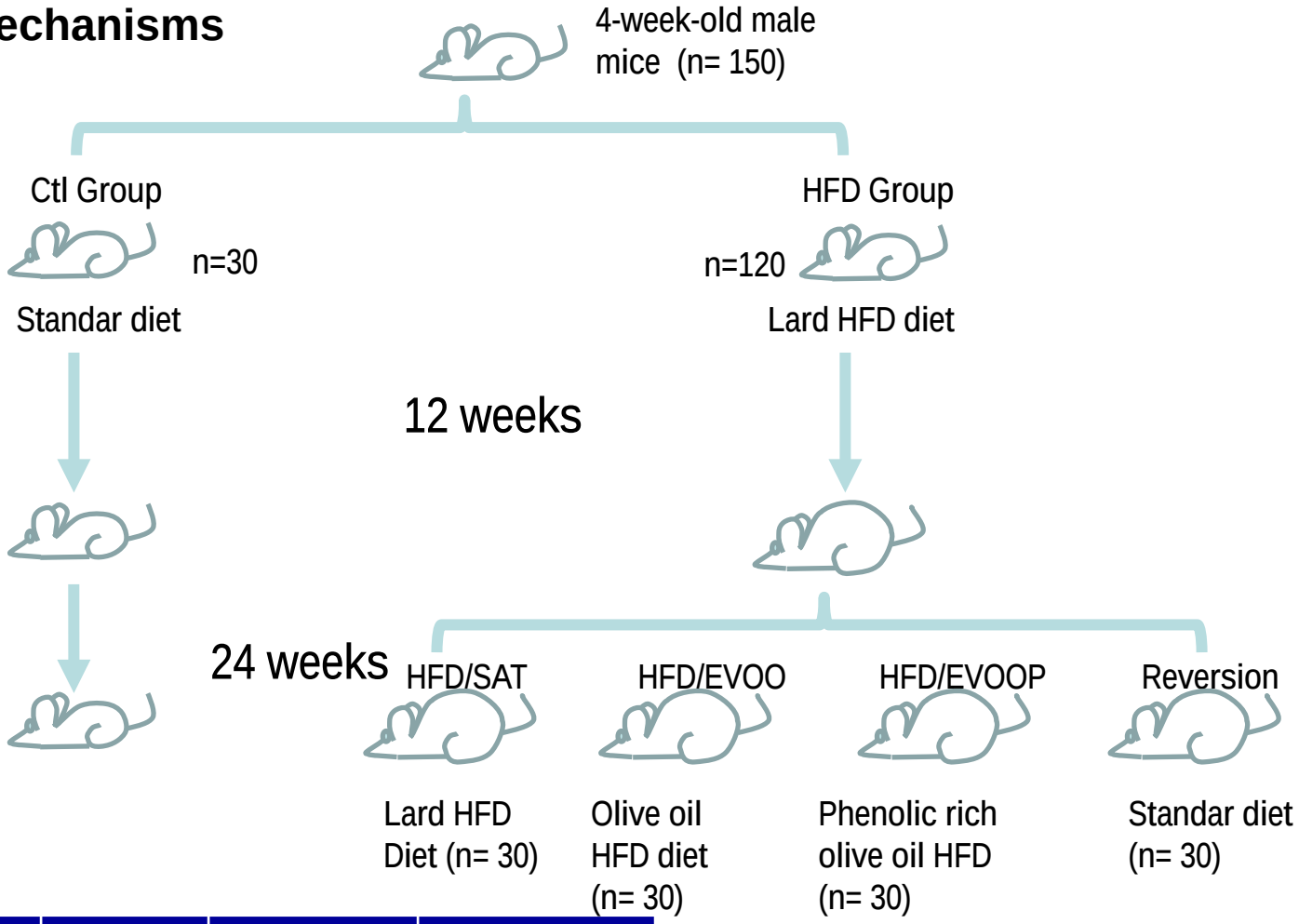






Aim and animal model: Preventive role of olive oil in steatohepatitis and DM2: its molecular mechanisms

C57BL6J wt



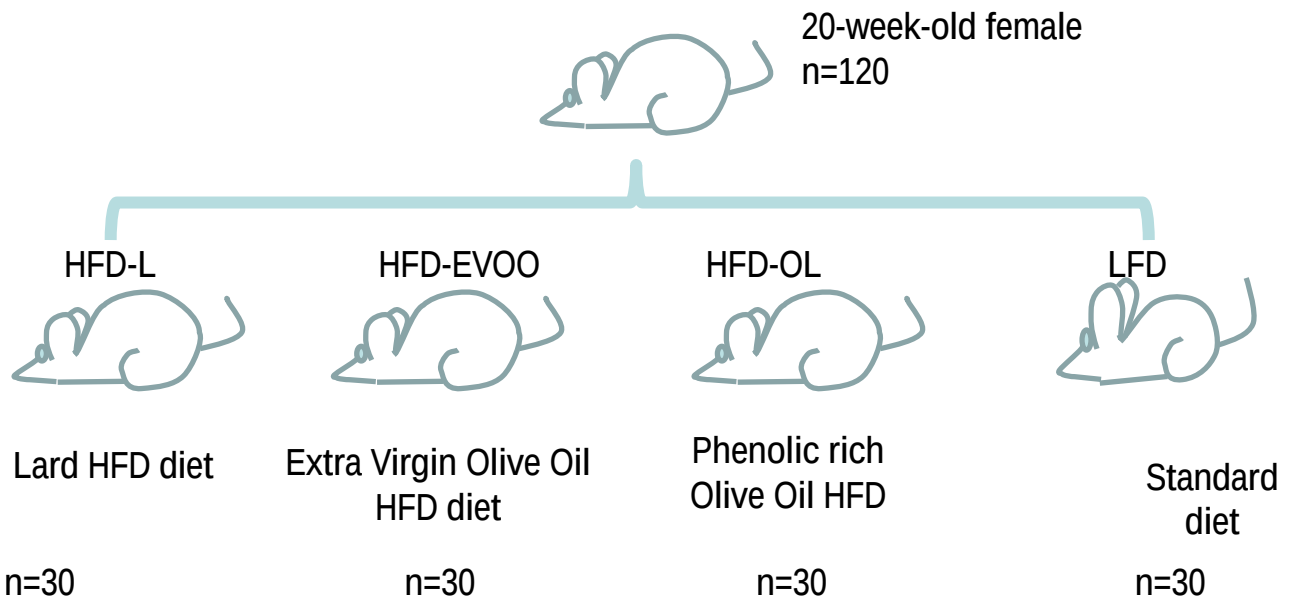
Diet (kcal%)	Ctl	HFD	HFD/EVOO	HFD/EVOOP
Carbohidrates	67	39	39	39
Proteins	20	12	12	12
Fats	13	49	49	49
%Saturates	0.6	7.5	2.2	2.7
%MUFA	0.7	9.2	15.4	15.1
%PUFA	2.1	1.8	3.6	3.5
%Oleic acid	0.7	8.9	15.3	14.9

Total polyphenols (mM/Kg)=

EVOO: 0.056
EVOOP: 0.447

Aim and animal model: Preventive role of olive oil in steatohepatitis and DM2: its molecular mechanisms

LDLR-Leiden$^{-/-}$



Fatty acid composition

Gas Chromatography

	BASAL	LARD	EVOO	OLEASTER
14:0	-	1,13	-	-
16:0	14,71	24,67	6,21	9,03
16:1 n-9	-	1,23	0,18	0,12
16:1 n-7	-	-	0,24	0,63
16:1 n-5	-	-	0,16	0,12
18:0	2,94	14,48	3,27	2,96
18:1-n9	20,59	44,88	79,58	77,66
18:1n-7	-	2,74	-	-
18:2 n-6	58,82	8,91	8,91	8,08
20:0	-	0,15	-	-
18:3 n-6	-	-	0,39	0,39
18:3 n-3	2,94	0,61	0,95	0,91
20:1 n-9	-	0,99	-	-
20:2 n-6	-	0,23	0,10	0,11
22:0	-	0,05	-	-
SFA	17,65	40,48	9,49	11,99
MFA	20,59	49,84	80,16	78,52
PFA	61,76	9,75	10,35	9,49

Triglycerides composition

GS/MS

	LARD	EVOO	OLEASTER
PPP	0,97	-	-
MOP	1,11	-	-
MLP	0,49	-	-
PPE	1,9	-	-
POP	7,77	1,13	2,36
PLP	3,51	0,33	0,80
PEE	2,59	-	-
POE	18,04	0,73	0,99
POO	24,07	15,47	21,04
PLE	7,81	0,75	1,44
POL	10	3,73	5,15
PLL	1,9	0,73	0,84
EEE	-	0,46	0,36
EOE	1,49	0,16	0,25
EOO	4,4	6,53	5,55
ELE	0,77	0,26	0,29
OOA	-	0,56	0,33
OOO	5,36	50,71	43,97
EOL	3,39	3,72	4,66
OOL	2,73	12,96	10,45
ELL	0,85	-	-
OLL	0,85	1,80	1,52

Unsaponifiable fraction

HPLC

	LARD	EVOO	OLEASTER
Colesterol (%)	100,00	0,07	0,15
Campesterol (%)	-	2,81	2,86
Stigmasterol (%)	-	0,57	0,63
Clerosterol (%)	-	0,94	0,90
β-Sitosterol (%)	-	83,19	84,29
Sitosterol (%)	-	0,42	0,68
Δ5 - Avenasterol (%)	-	10,71	9,43
Δ5,24 - Stigmadienol (%)	-	0,65	0,46
Δ7 - Stimastanol (%)	-	0,27	0,23
Δ7 - avenasterol (%)	-	0,37	0,39
Total (%)	0,53	1,48	2,37
mg/kg muestra	532	1479	2365

2x

Phenolic composition

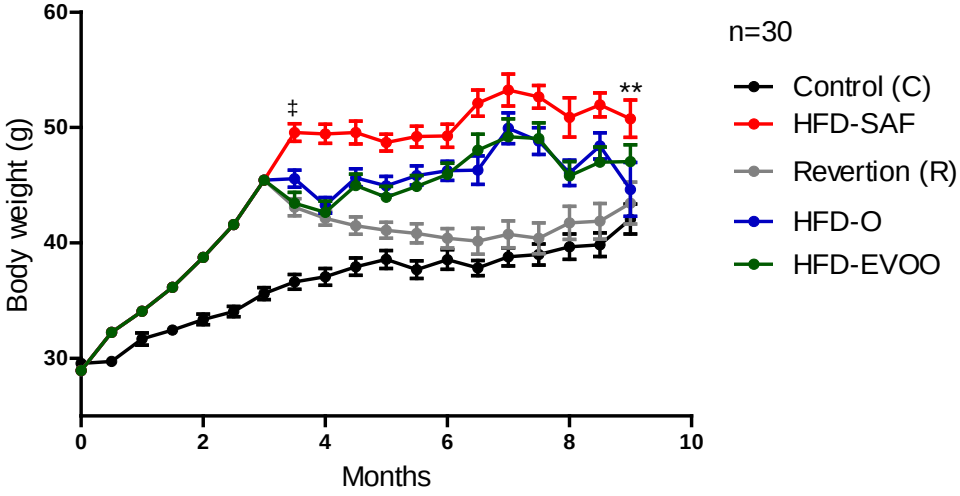
HPLC

FENOLES (ppm)	EVOO	OLEASTER
Hidroxytirosol (Hty)	6,87	219,28
Tyrosol (Ty)	4,52	70,83
Ac. Vaníllico	1,50	1,19
Vanillina	-	0,31
Acetato HTy	2,47	3,24
1ºDervHty	-	25,68
Acetato Ty	13,81	12,88
1ºDervTy	13,51	35,01
Pinoresinol	7,47	3,97
Acetoxypinoresinol	5,61	8,27
2ºDerv Hty	3,75	39,55
2ºDerv Ty	11,32	16,95
PPM		
Total ty	104	404

32x Hty

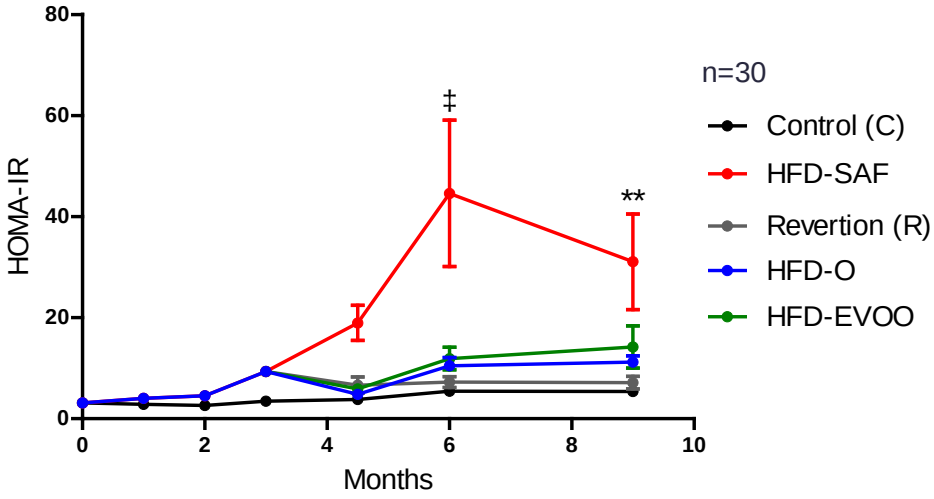
4x Σ Ty

Results: obesity, hiperglycemia and IR



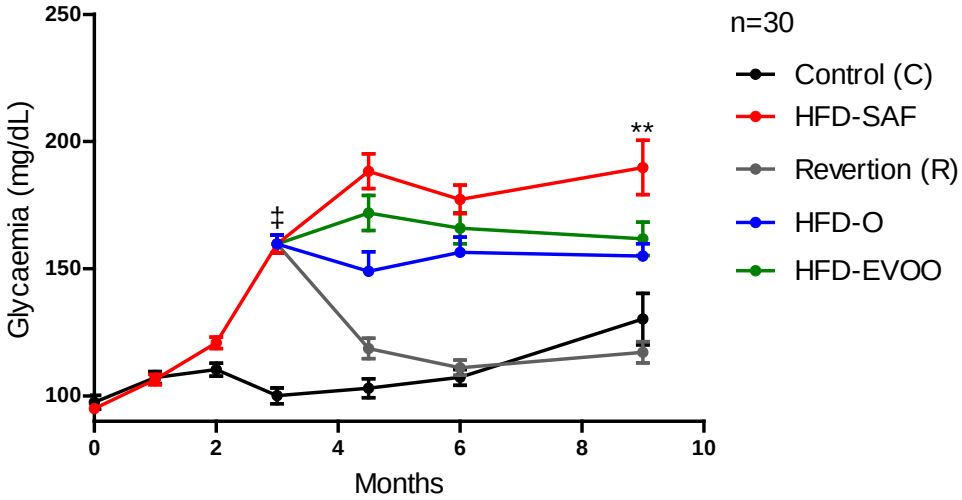
**p<0,05 HFD-SAF vs HFD-O and HFD-EVOO

‡p<0,001 C vs HFD-SAF



**p<0,0001 HFD-SAF vs HFD-O and HFD-EVOO

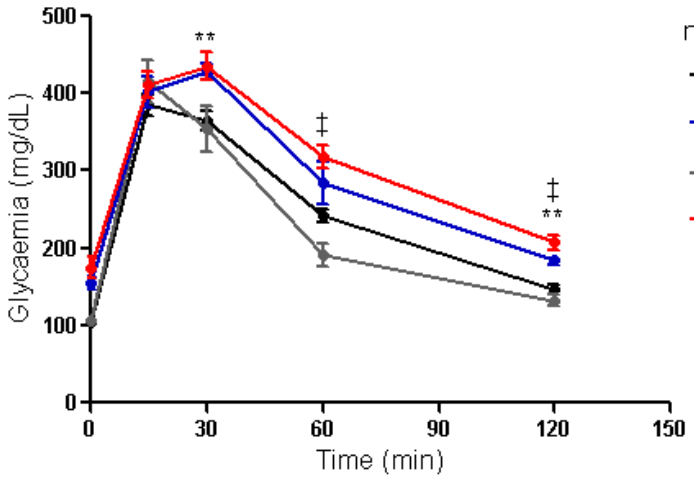
‡p<0,001 C vs HFD-SAF & HFD-VOO



**p<0,05 HFD-SAF vs HFD-O and HFD-EVOO

‡p<0,001 C vs HFD-SAF & HFD-VOO

Results: glycemic control (IPGTT and ITT)

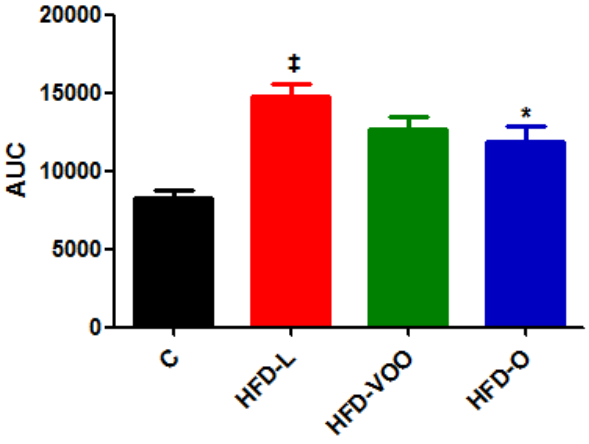


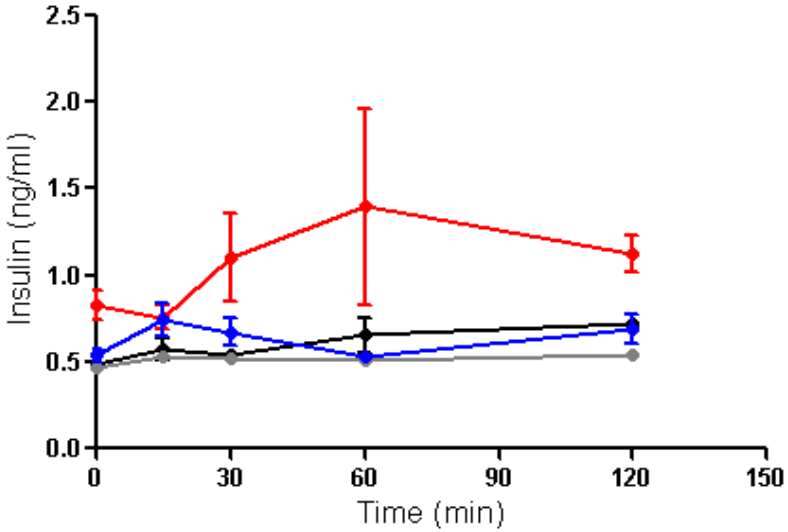
n=8

- Control (C)
- Oleaster (HFD-O)
- Revertion (R)
- High-fat diet based on lard (HFD-L)

**p<0,01 C vs HFD-L & HFD-O

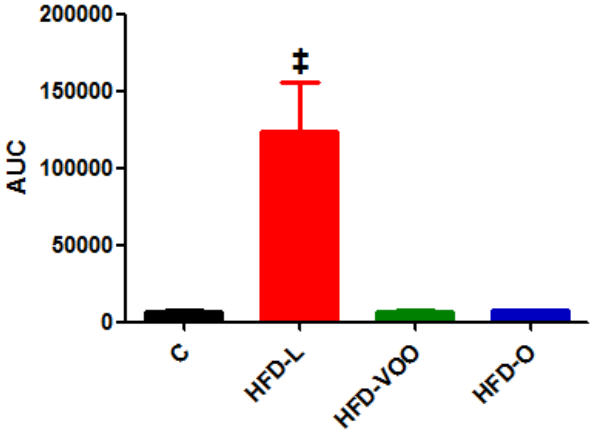
‡p<0,001 C vs HFD-L



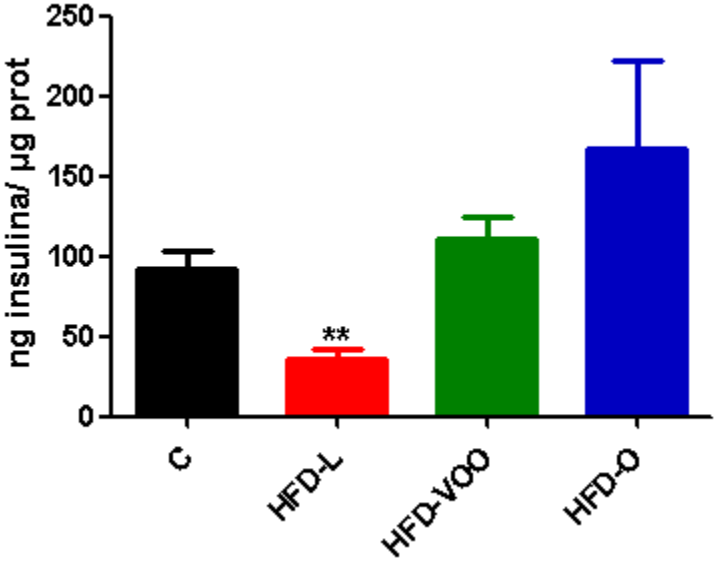


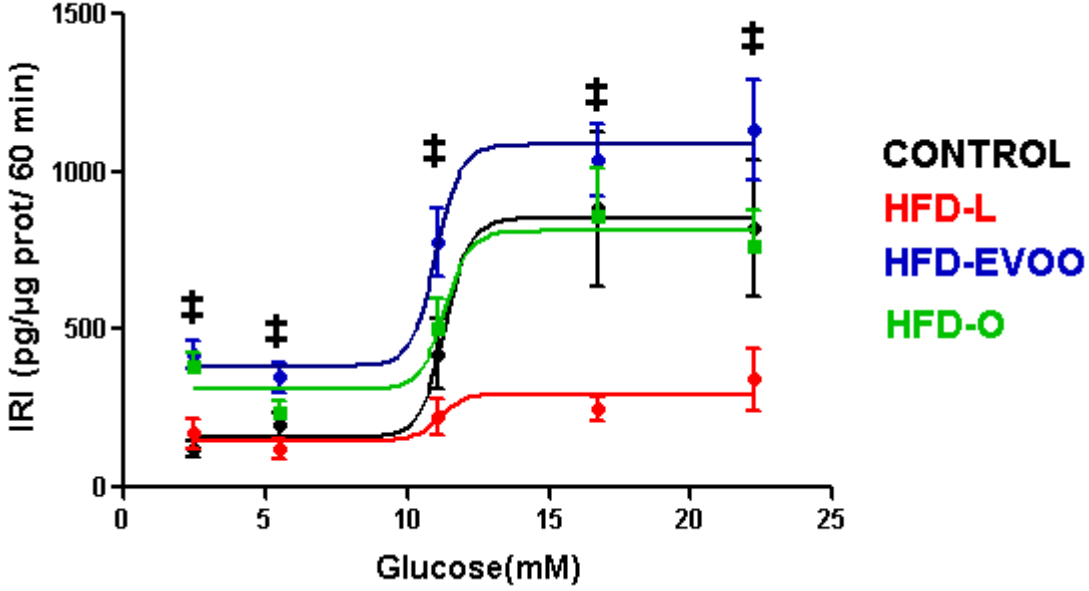
n=3

- Control (C)
- Oleaster (HFD-O)
- Revertion (R)
- High-fat diet based on lard (HFD-L)



Results: β-cell function (insulin content and release)



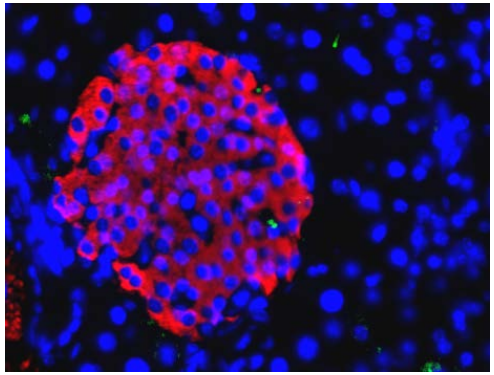


n= 7

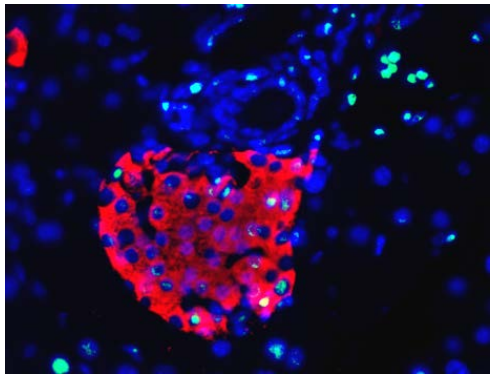
Results: β-cell mass and apoptosis

n= 5

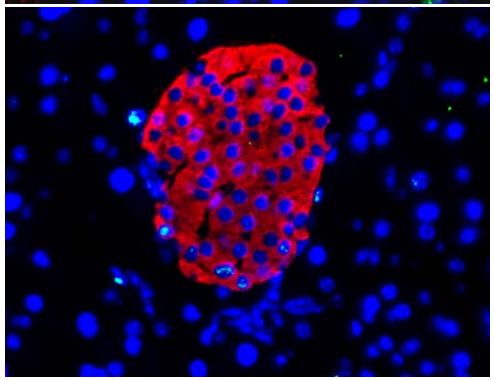
Control



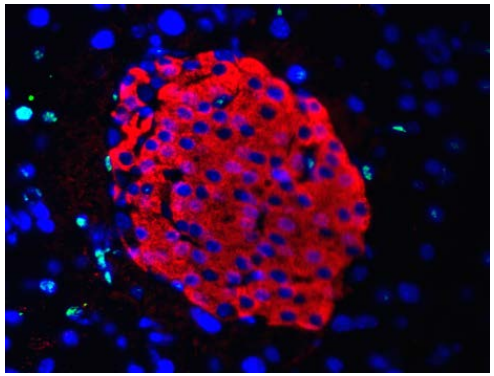
HFD-SAF



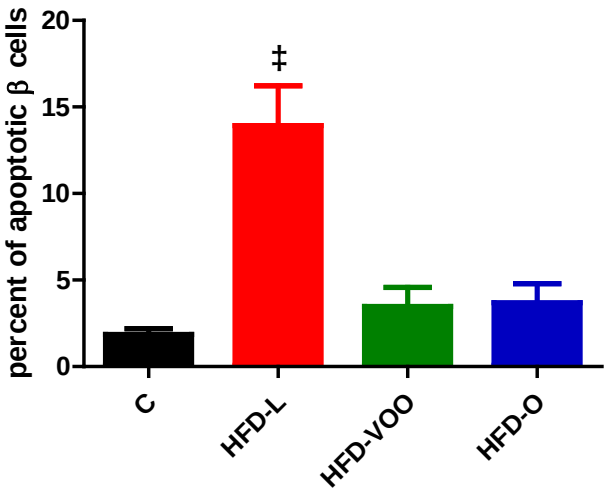
HFD-EVOO

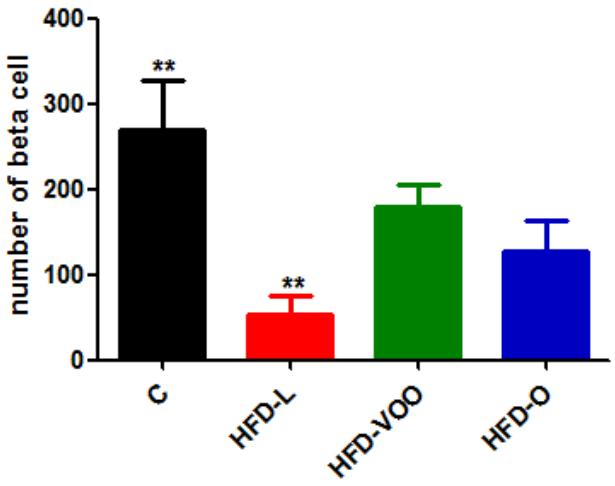


HFD-O



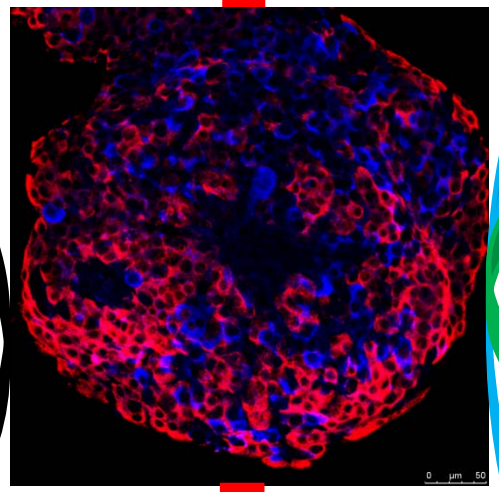
Tunnel assay





Results: β-cell gene expression

n= 3



↓ OXPHOS

↓ Cat, Gpx1, Prdx4-5

↑ Pdx-1, MafA, Nkx6.1, Pax6, Cdkn1b

↑ Pcsk1-2, tSNAREs

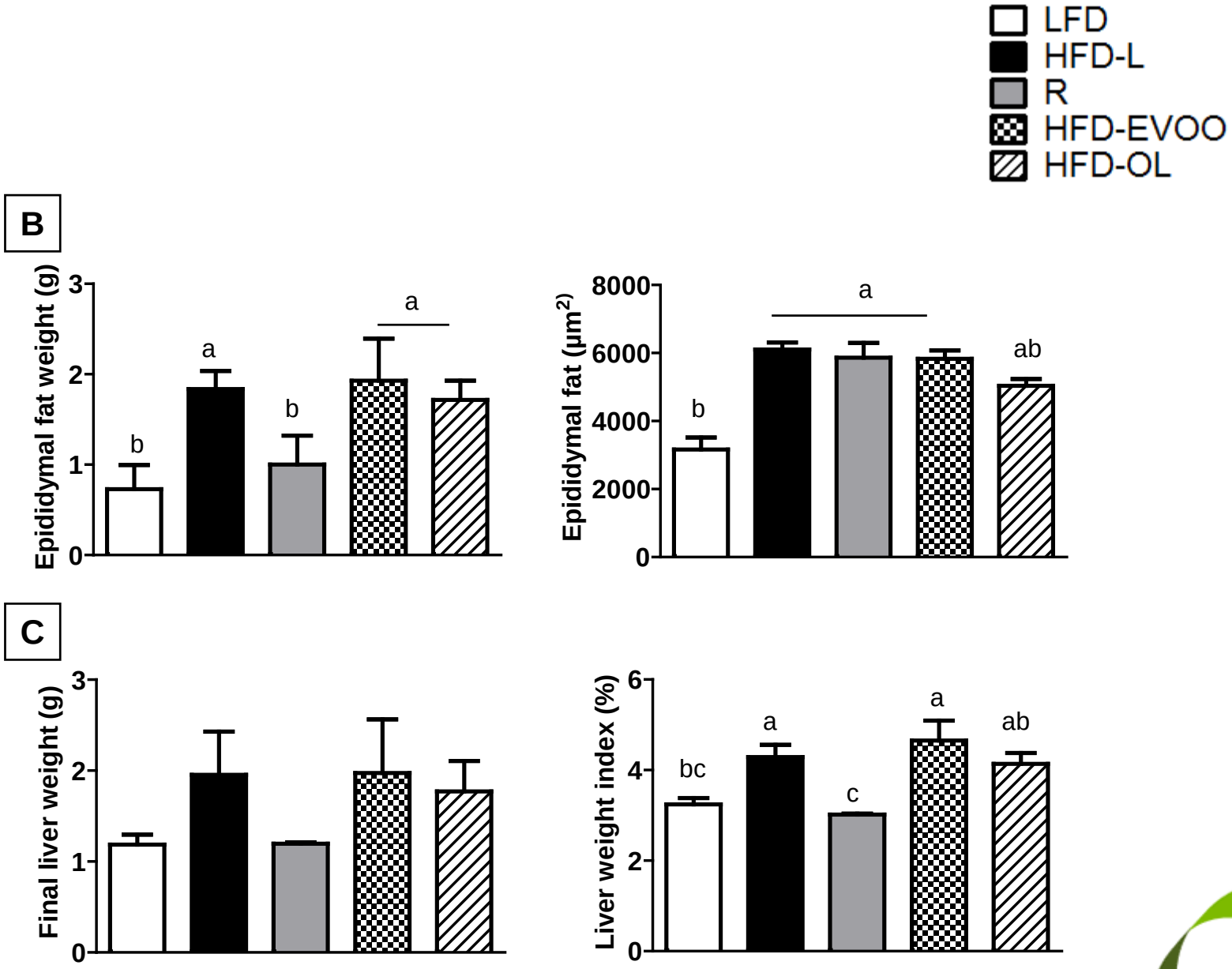
↑ Insulin exocytosis

↑ Phenotype, development and proliferation
↑ Insulin synthesis
↑ GSIS

↓ Oxidative metabolism

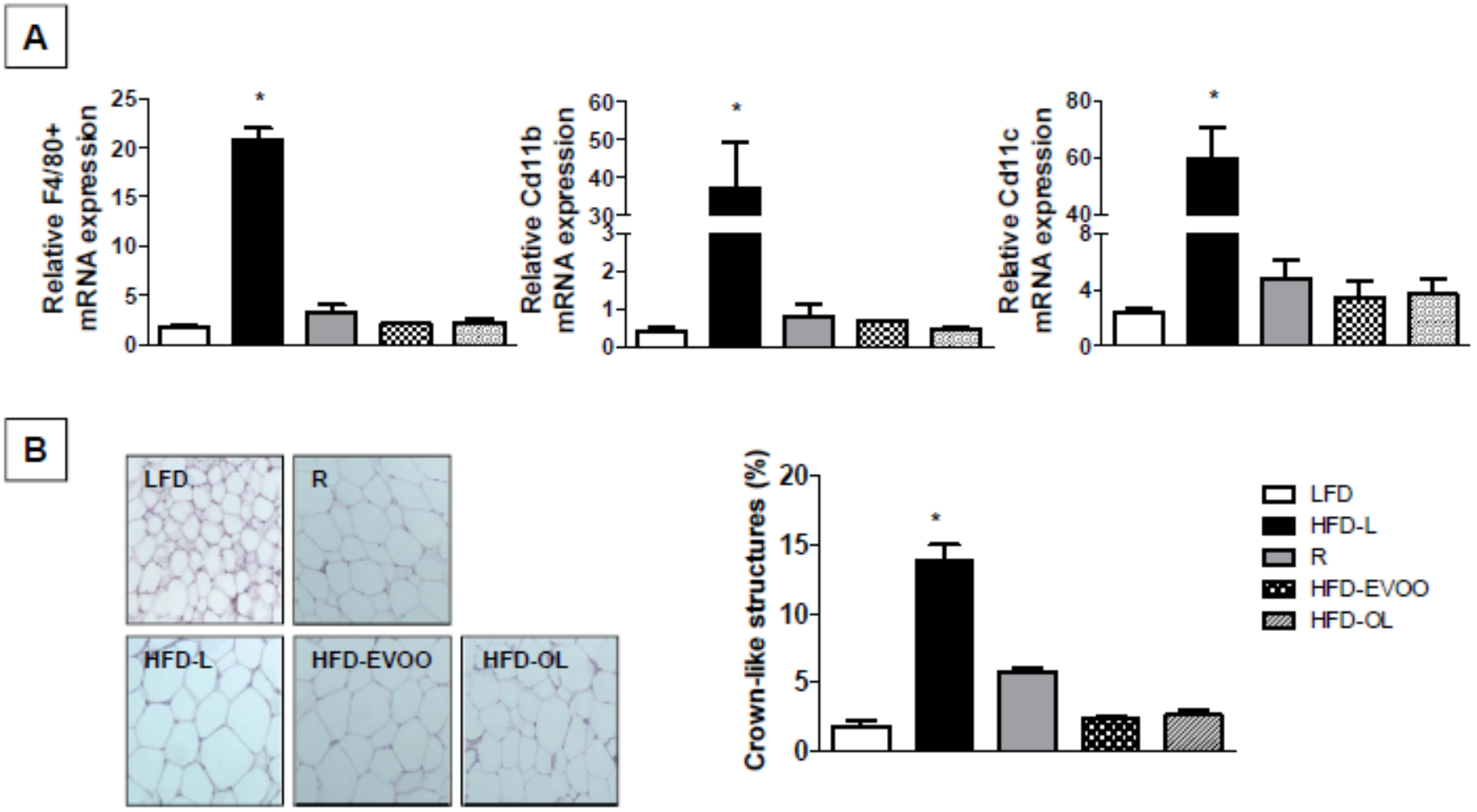
↓ Oxidative stress

Results: fat and liver weight index increase



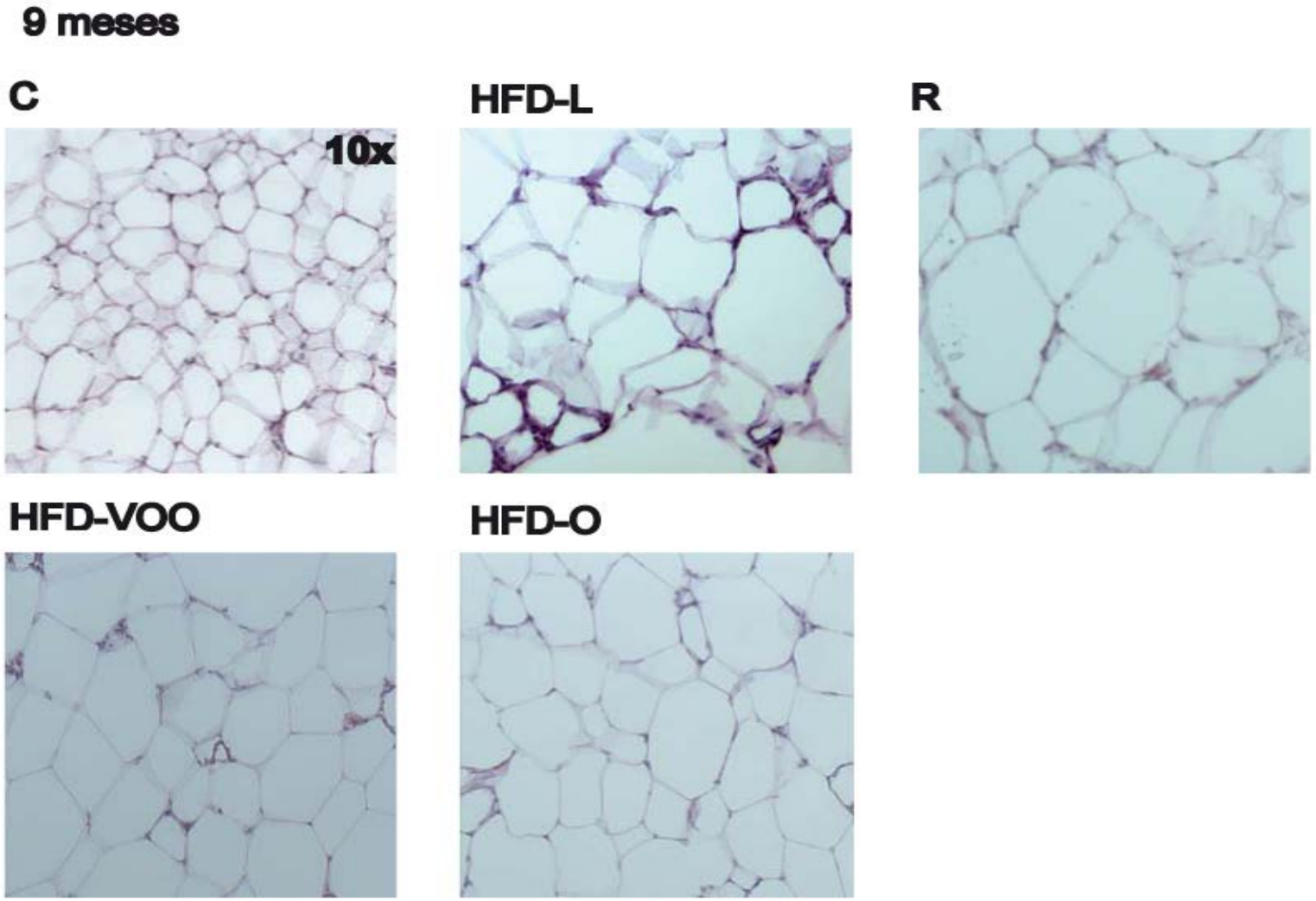
N= 10

Results: fat inflammation



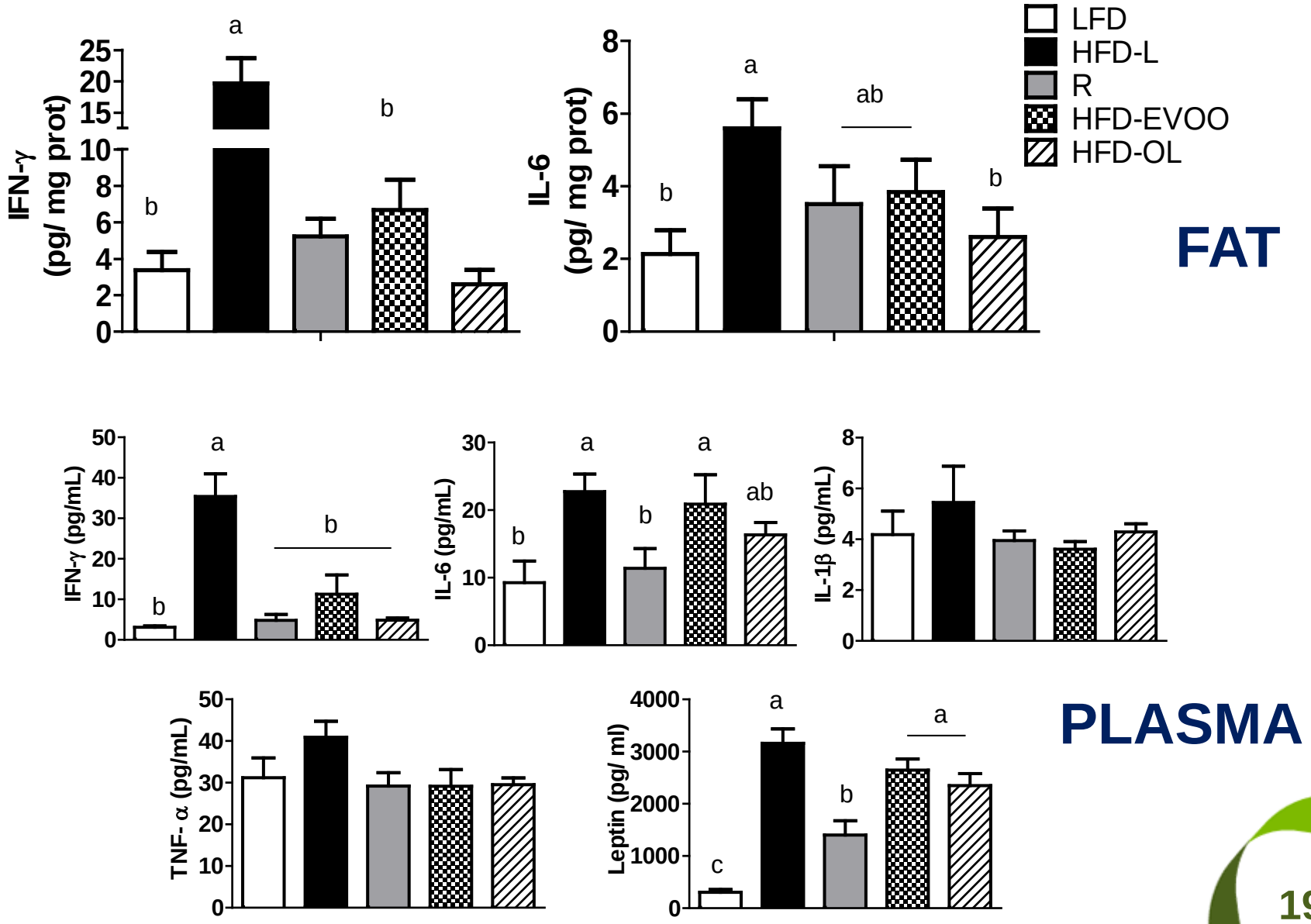
N= 10

Results: fat inflammation



N= 10

Results: fat and plasma inflammation



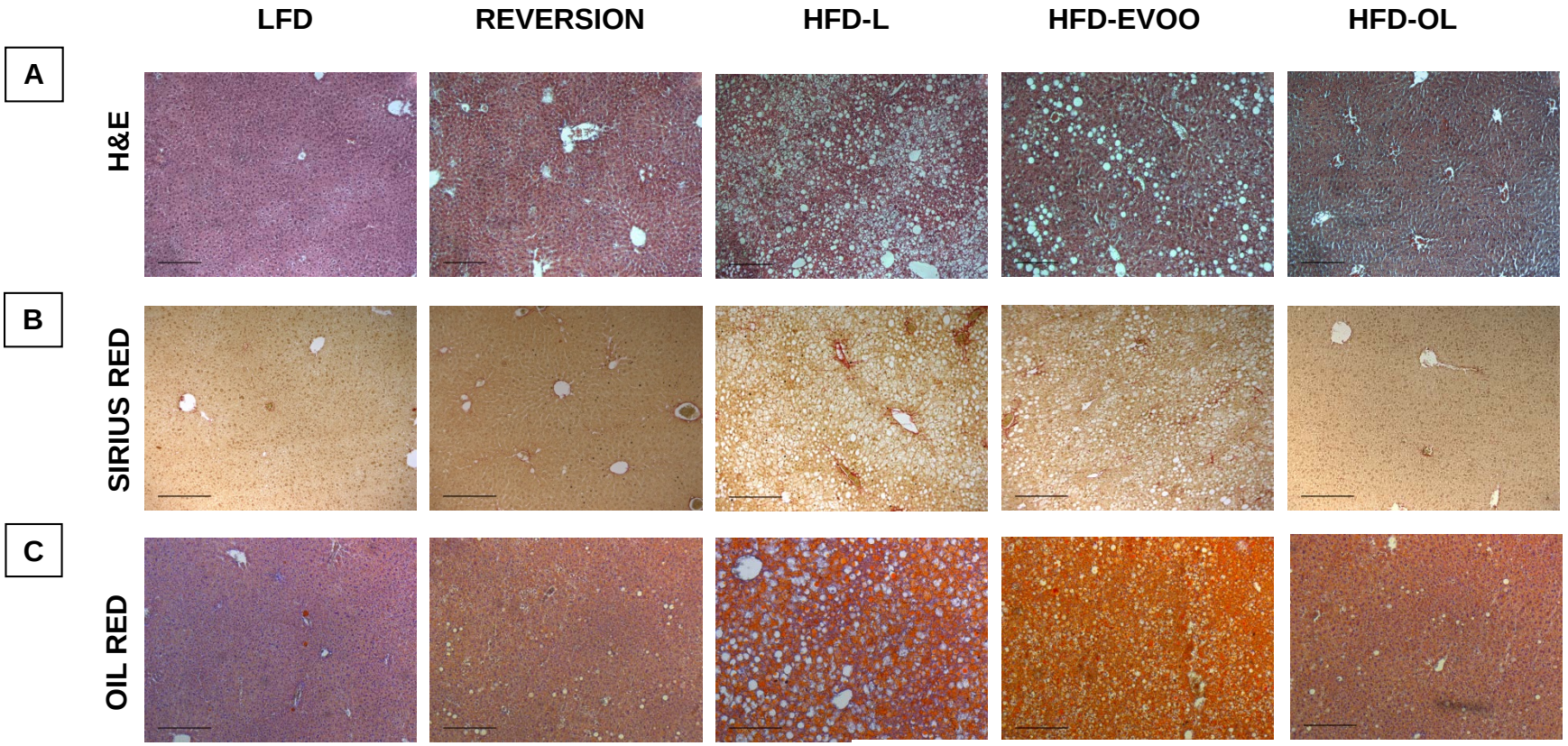
N= 10

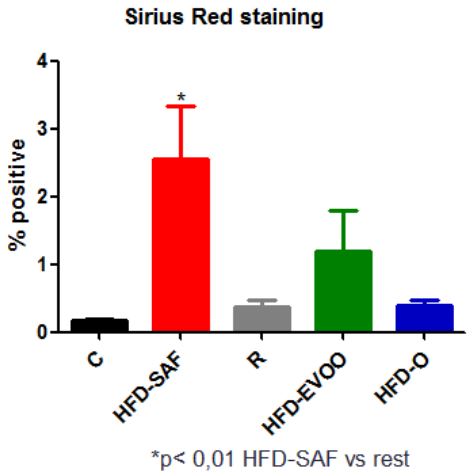
Results: dyslipidemia

mg/dL	C	HFD-SAF	HFD-EVOO	HFD-O	R
T-Cho	122 ± 4	194 ± 7	168 ± 12*	135 ± 5*	127 ± 3
LDL-Cho	72 ± 8	140 ± 11	110 ± 15	62 ± 11†	76 ± 8
HDL-Cho	37 ± 3	39 ± 4	45 ± 8	50 ± 9**	33 ± 6
Triglyceride	64 ± 2	88 ±10	65 ± 5*	68 ± 4*	61 ± 5

*p< 0,01 HFD-EVOO & HFD-O vs HFD-SAF; **p< 0,01 HFD-O vs rest (n= 30)
†p<0,01 HFD-O vs HFD-SAF

Results: liver damage



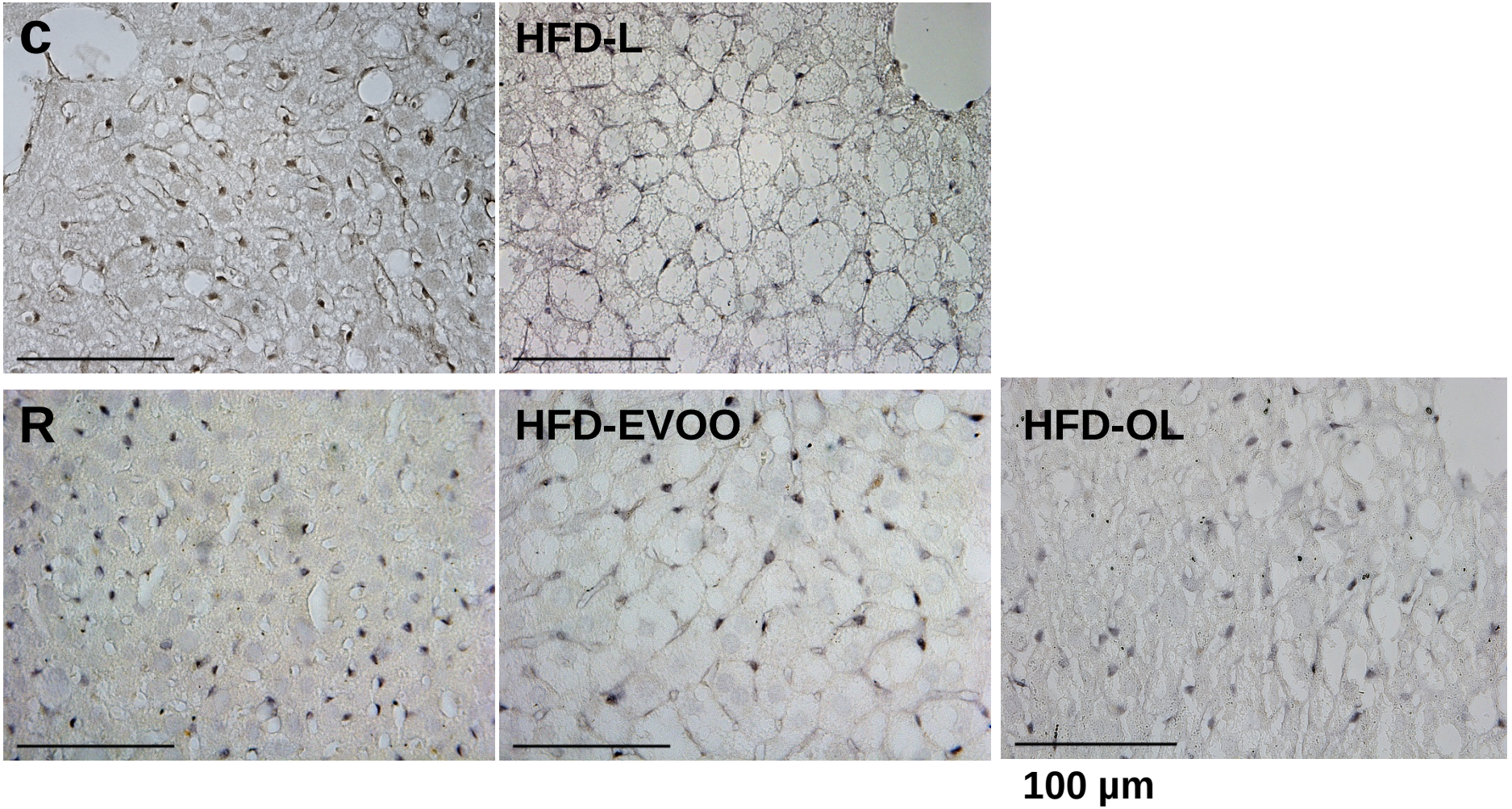


N= 5

Scale bars: 200 µm

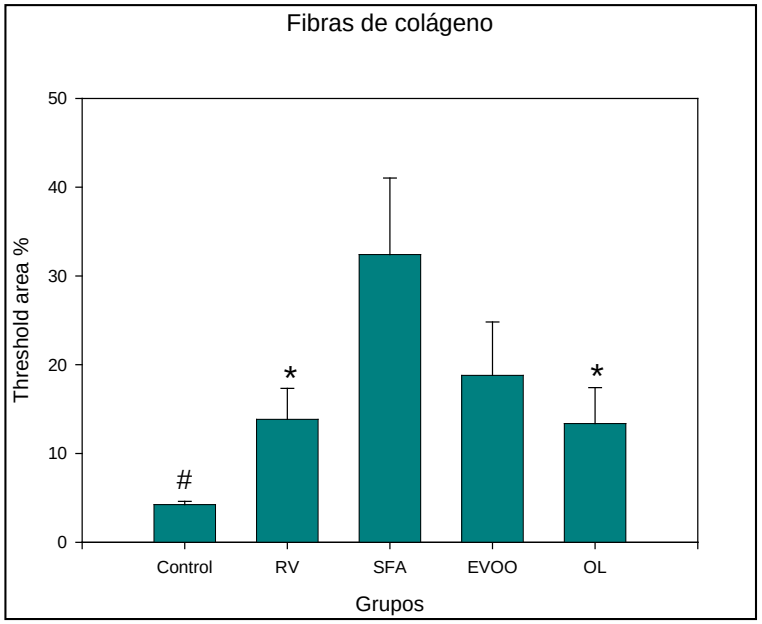
Results: liver damage

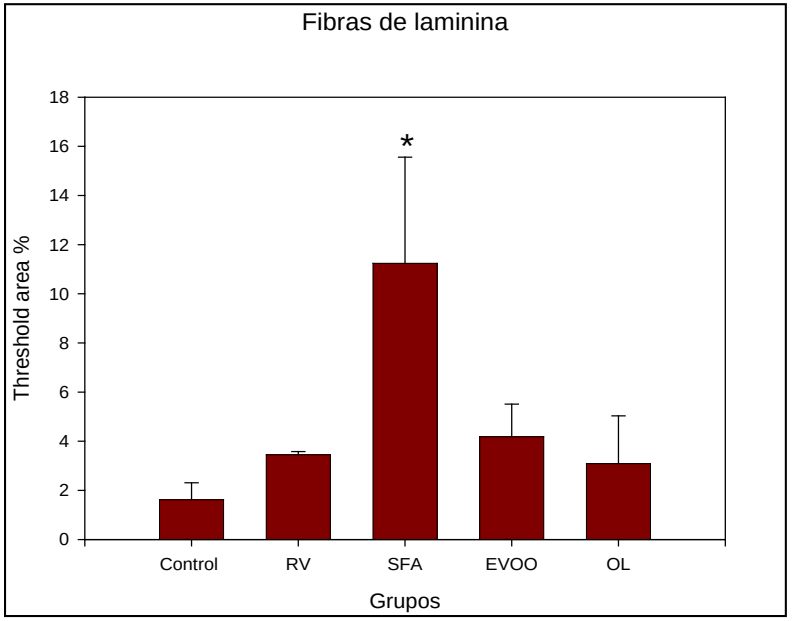
GATA4 expression in stellate cells

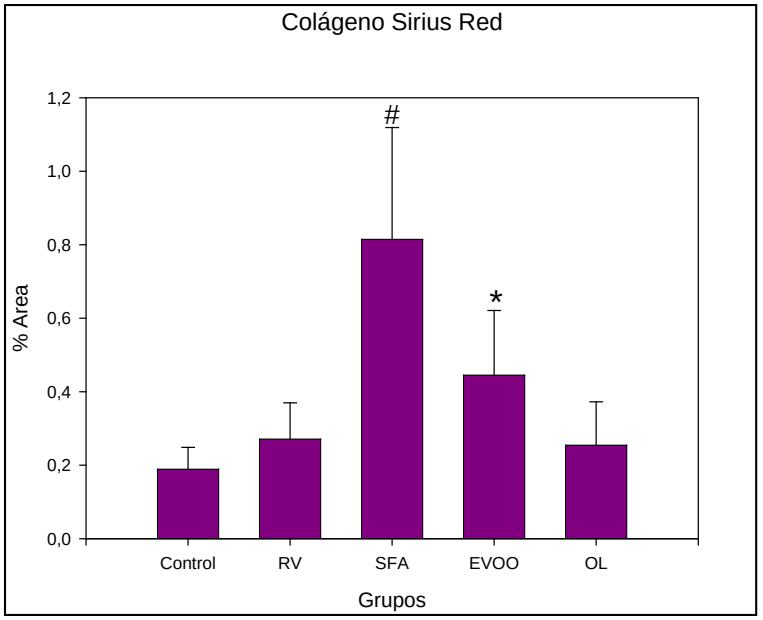


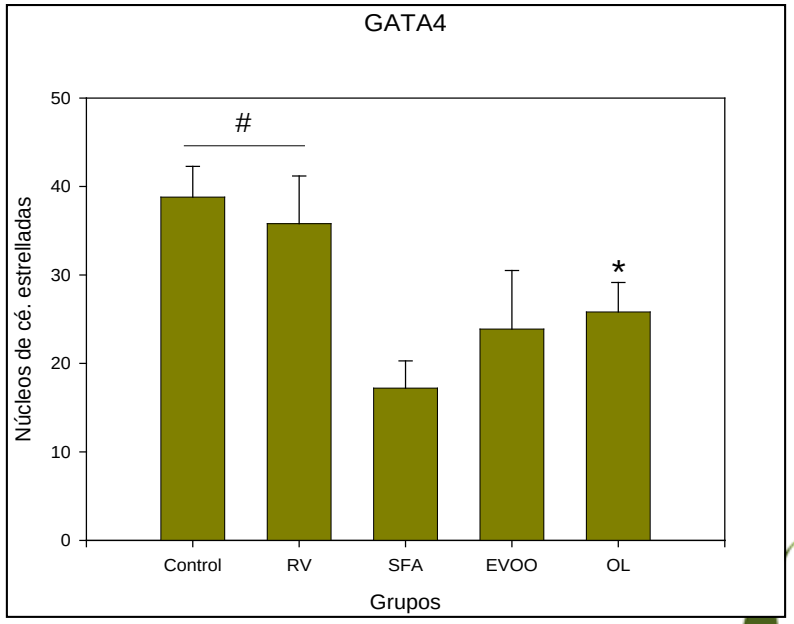
N= 5

Results: liver damage







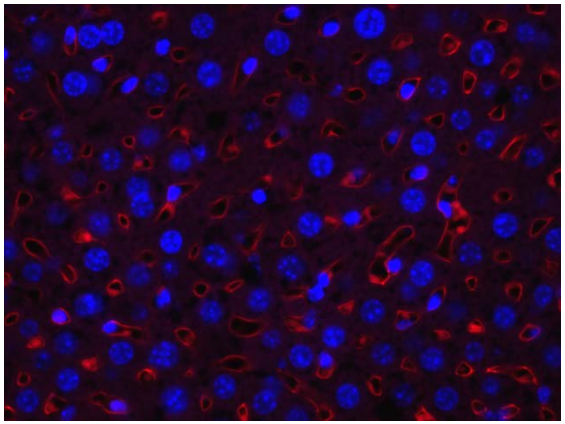


N= 5

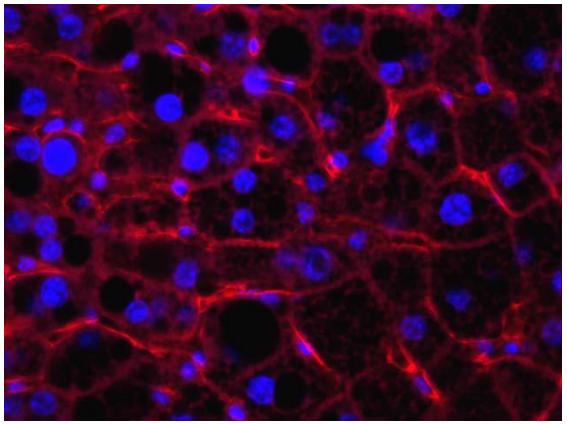
Results: liver damage

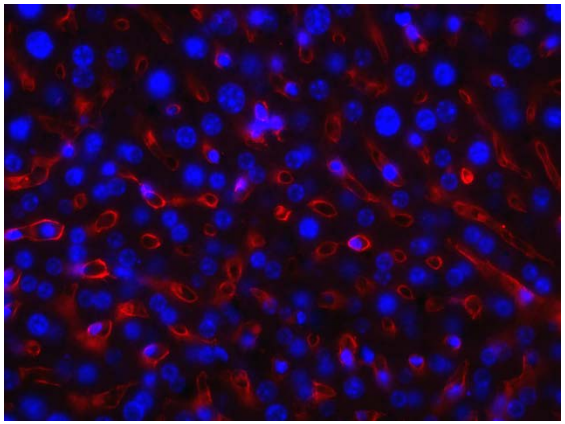
Immunostaining for laminin

CONTROL

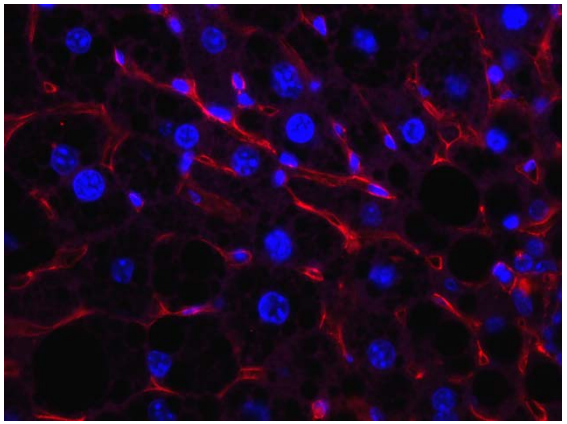


HFD-L

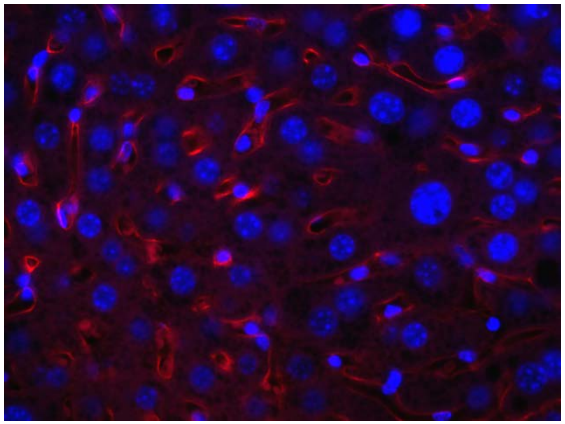




REVERSION



HFD-EVOO



HFD-OL

N= 5
40x

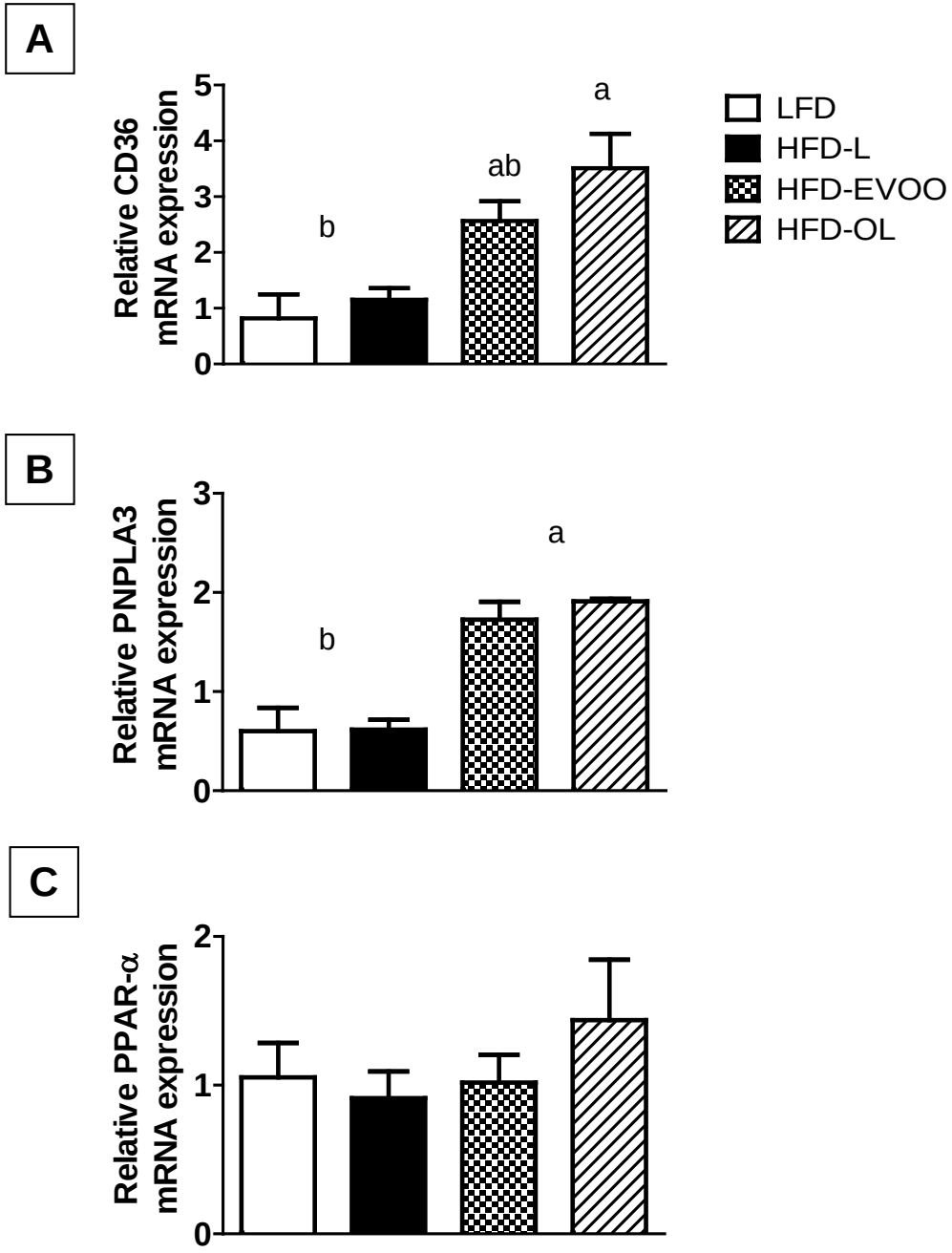
Results: liver damage (NAS score)

Histological features	LFD	R	HFD-L	HFD-EVOO	HFD-OL
Steatosis (0-3)	0	0	3 ± 0	3 ± 0	1.33 ± 0.44*
Lobular inflammation (0-3)	0	0	1.67 ± 0.44	0.33 ± 0.44	0.67 ± 0.44
Ballooning (0-2)	0	0	0	0	0
NAS	0	0	4.67 ± 0.44	3.33 ± 0.44*	2 ± 0.1*
Fibrosis (0-4)	0	0	0	0	0

*$P < 0.05$ *vs.* HFD-L and HFD-EVOO. **$P < 0.05$ *vs* HFD-L.

N= 5

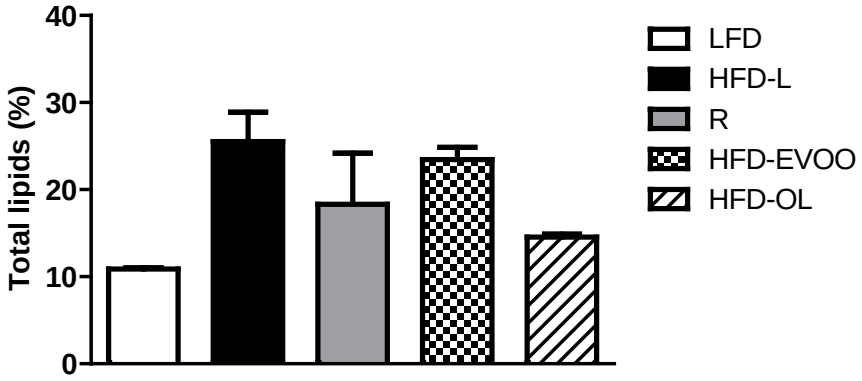
Results: liver damage (gene expression)



N= 4

Results: liver lipids profile changes

N= 5



Liver FFA and triglycerides content (GS/MS and Gas Chromatography)

g/100g liver	C	HFD-SAF	HFD-EVOO	HFD-O	R
SFA	25 ± 1	27 ± 2	23 ± 1	22 ± 3	ND
MUFA	38 ± 2	53 ± 2	66 ± 2*	61 ± 1*	ND
PUFA	36 ± 2	19 ± 1	12 ± 0.7	14 ± 1	ND
C18:1n-9	25 ± 1	42 ± 2	50 ± 1*	51 ± 1*	ND
OOO	3,2 ± 0,5	6,7 ± 0,2	12,5 ± 2*	12,8 ± 1*	ND
OOX	25 ± 2	43 ± 3	56 ± 4*	55 ± 3*	ND

*p< 0,01 HFD-EVOO & HFD-O vs HFD-SAF (n= 5)

Results: liver proteomic expression changes

A

Top Networks: HFD-EVOO Associated Network Functions	Score
1. Lipid Metabolism, Small Molecule Biochemistry, Vitamin and Mineral Metabolism	36
2. Nucleic Acid Metabolism, Small Molecule Biochemistry, Cell Signaling	15
3. Cellular Assemby and Organization, Cellular Function and Maintenance, Infectious Disease	3
4. Carbohydrate Metabolism, Cancer, Gastrointestinal Disease	3

Top Bio Functions	p-Value	Molecules
Catabolism of lipid	3.85E-04	AMACR,CES1,NUDT7
Concentration of fatty acid	5.91E-03	AMACR,CES1,IDH1
Concentration of cholesterol	6.63E-03	AMACR,CES1,IDH1
Concentration of triacylglycerol	7.74E-03	AMACR,CES1,IDH1
Fatty acid metabolism	8.01E-03	ACSM1,CES1,MDH1,NUDT7

B

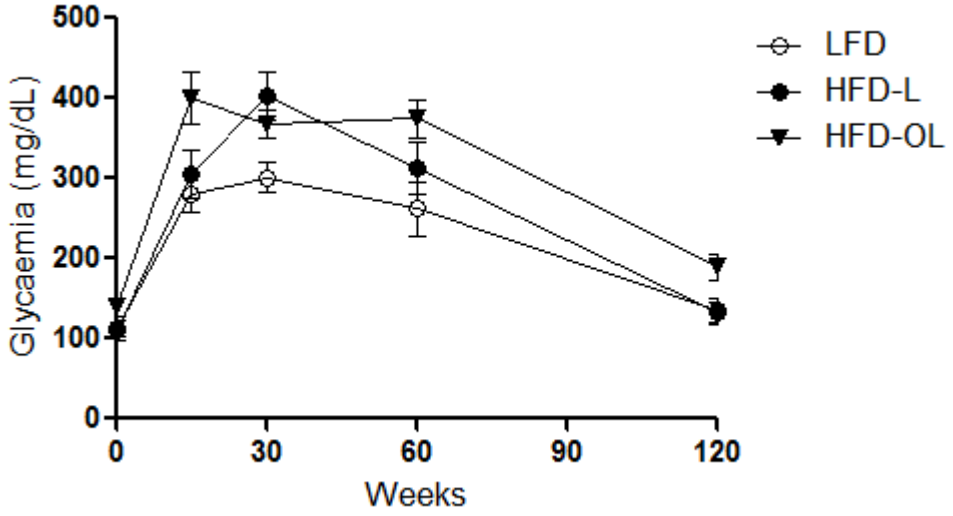
Top Networks: HFD-OL Associated Network Functions	Score
1. Cell Morphology, Cellular Compromise, Gastrointestinal Disease	36
2. Nucleic Acid Metabolism, Small Molecule Biochemistry, Cell Signaling	15
3. Cellular Assemby and Organization, Cellular Function and Maintenance, Infectious Disease	3
4. Carbohydrate Metabolism, Cancer, Gastrointestinal Disease	3

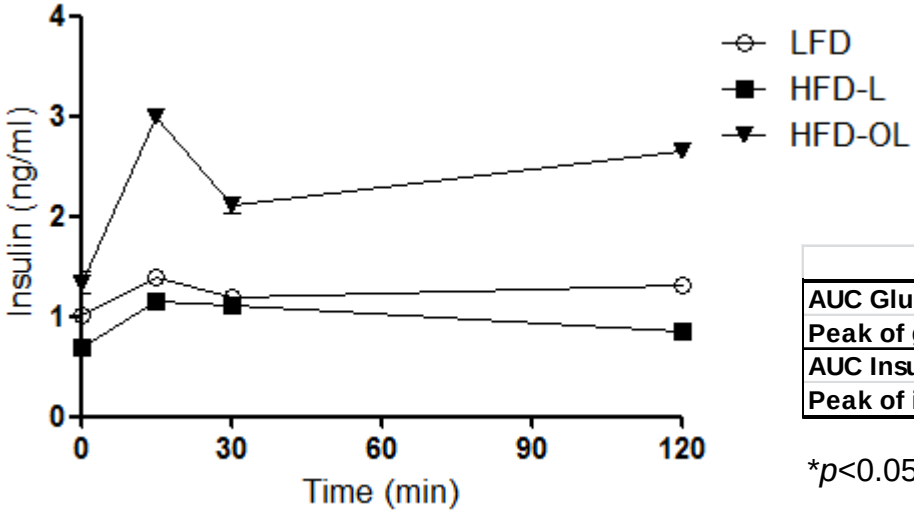
Top Bio Functions	p-Value	Molecules
Inborn error of amino acid metabolism	2.33E-03	AHCY, ARG1, HGD
Hydrolysis of amino acids	3.42E-03	AHCY, ARG1
G2 phase	3.58E-03	AMACR,ARG1
Metabolism of nucleid acid component or derivative	5.69E-03	AHCY, CES1, MDH1, NUDT7
Interphase	1.96E-02	AMACR, ARG1, Calm1, IDH1, TF

C

Top Tox Functions	p-Value	Molecules
Hepatomegaly	3.58E-03	AMACR,ARG1
Proliferation of hepatic stellate cells	5.51E-02	TF

Results: too much polyphenolic compounds or a different composition seems to be worst: a double-edge sword

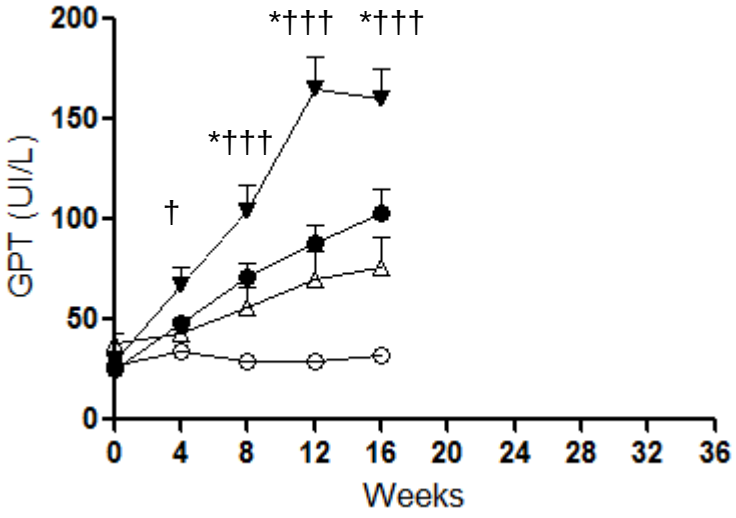




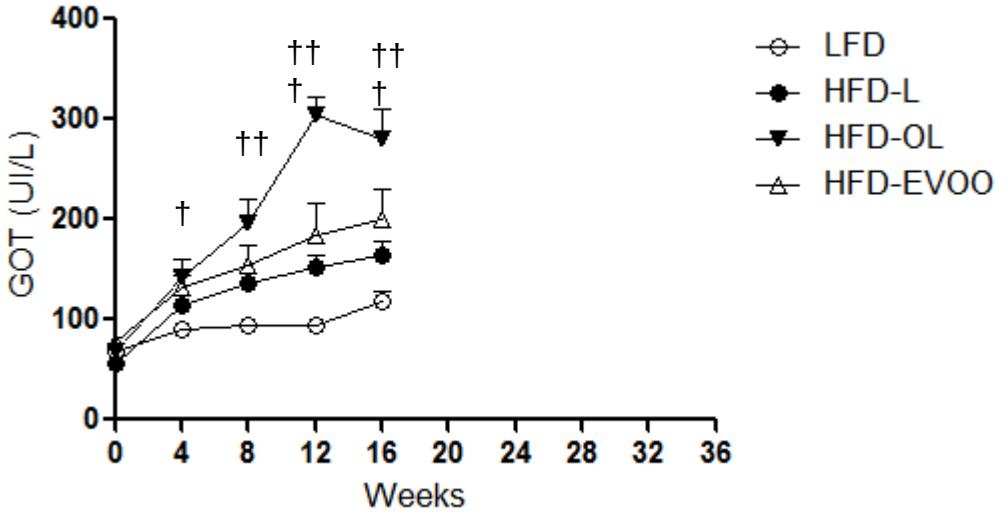
	LFD	HFD-L	HFD-OL
AUC Glucose	27691	32491	37844*
Peak of glucose (min)	30	30	15
AUC Insulin	149,7	119,0	285,7†
Peak of insulin (min)	15	15	15

*p<0.05 LFD vs HFD-OL; †p<0.05 HFD-L vs HFD-OL

Results: too much polyphenolic compounds or a different composition seems to be worst: a double-edge sword



***p*<0.05 LFD vs HFD-L; †*p*<0.05 LFD vs HFD-OL; †††*p*<0.001 LFD vs HFD-OL; *n*=16**



†*p*<0.05; ††*p*<0.01; †††*p*<0.001 LFD vs HFD-OL; *n*=16

Results: too much polyphenolic compounds or a different composition seems to be worst: a double-edge sword

	AOVG 2016	AOVG 2012	OL 2016	OL 2012
FENOLES, *280 nm*	PPM	PPM	PPM	PM
Hty	**1,22**	6,87	**4,00**	219,28
Ty	6,01	4,52	**15,29**	70,83
Ac. Vaníllico	**0,78**	1,50	**2,09**	1,19
Vanillina	0,21		0,35	0,31
Ac. p-Cumárico	0,00		0,52	0,00
Acetato HTy	1,89	2,47	**8,48**	3,24
1ºDervHty	**7,95**	0,00	**9,66**	25,68
Acetato Ty	0,00	13,81	**0,00**	12,88
1ºDervTy	6,40	13,51	**4,73**	35,01
Pinoresinol	**2,64**	7,47	3,50	3,97
Ac. Cinámico	0,00	0,00	0,00	0,00
Acetoxypinoresinol	**1,69**	5,61	**3,46**	8,27
2ºDerv Hty	**14,71**	3,75	**13,86**	39,55
2ºDerv Ty	**68,07**	11,32	**33,10**	16,95
FLAVONAS, *335 nm*				
Ac. Ferúlico	**58,79**	8,41	**253,56**	7,17
LUTEOLINA	1,10	0,00	0,59	0,00
APIGENINA	0,53	0,00	0,43	0,00
SUMA TOTAL POLIFENOLES	**171,99**	79,24	353,60	444,33
SUMA ORTODIFENOLES	**26,87**	13,09	**36,59**	287,74
SUMA DERIVADOS SECOIRIDOIDEOS	**97,12**	28,58	**61,35**	117,19

HFD are important but lipid profile makes the difference.

Mediterranean obese mice:

1.- Reduced obesity.
2.- Better lipid profile.
3.- Better glucose homeostasis and lower IR.
4.- Better β-cell function and survival.
5.- Lower subcutaneous fat.
6.- Lower adiponectin levels.
7.- Lower liver and adipose tissue macrophage infiltration.
8.- Lower systemic and adipose tissue inflammation.
9.- Lower liver damage.
10.- Better liver repair.

A healthier metabolic syndrome and consequences