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Christine Feillet Coudray, Gilles Fouret, Evanthia Tolika, Jérôme Lecomte, Manar Aoun, et al.. Effects of high fat diet intake and a mitochondrial antioxidant (MitoQ) on liver mitochondrial activity and cardiolipin content in rats. *Cardiolipin as Key Lipid of Mitochondria in Health and Disease*, Sep 2015, Florence, Italy. 1 p. hal-01837638

HAL Id: hal-01837638

<https://hal.science/hal-01837638v1>

Submitted on 5 Jun 2020

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Effects of high fat diet intake and a mitochondrial antioxidant (MitoQ) on liver mitochondrial activity and cardiolipin content in rats



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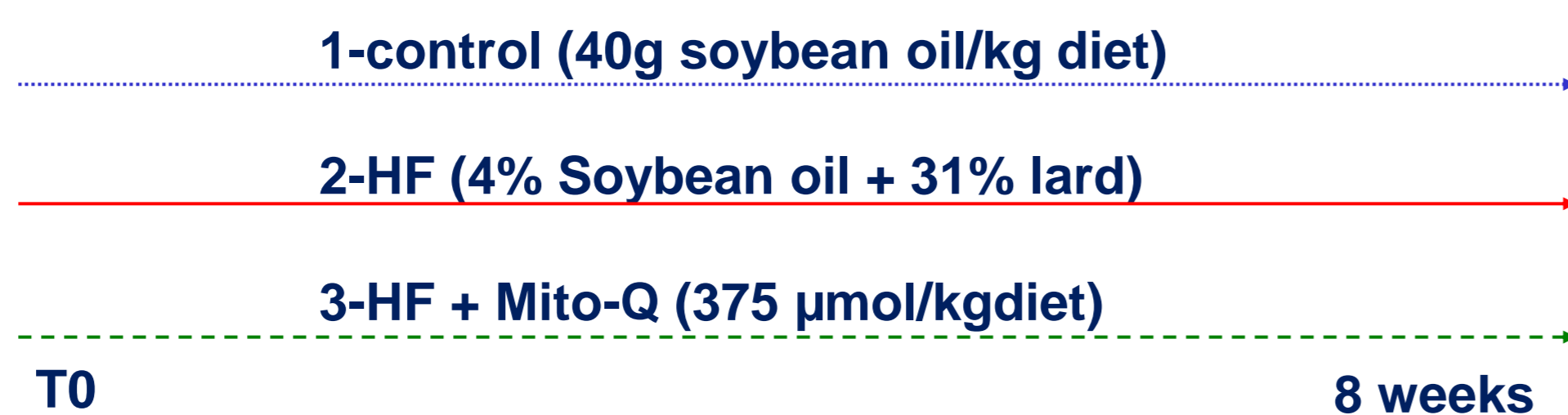
A-Introduction

Excessive intake of dietary fat is one of the major cause of appearance and progression of metabolic syndrome features, such as liver steatosis. These features are associated with structural and functional alterations of mitochondria. Recent studies indicate that some of these alterations are related to the content and quality of cardiolipin (CL), a phospholipid that occurs mainly in the inner membrane of mitochondria and is involved in the organization and functioning of the mitochondrial respiratory chain complexes [1]

B-Protocol and methods



24 rats
Sprague Dawley



1-Characterisation of rats

- Oral glucose tolerance test (OGTT) was completed 4 days before rat sacrifice.
- Plasma insulin was quantified with ELISA kits (Merck Millipore, Allemagne).
- Liver TG levels were quantified by enzymatic methods (TG PAP kit, Biomerieux, Fr)

2-Liver mitochondrial lipid content

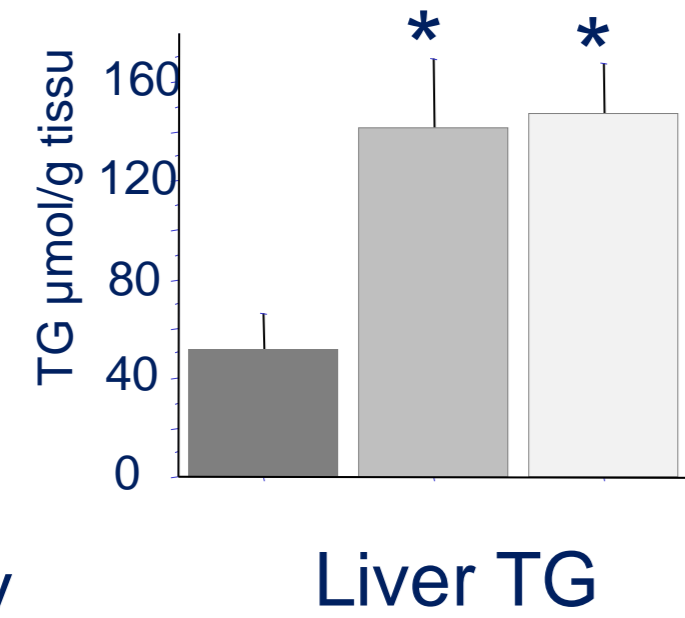
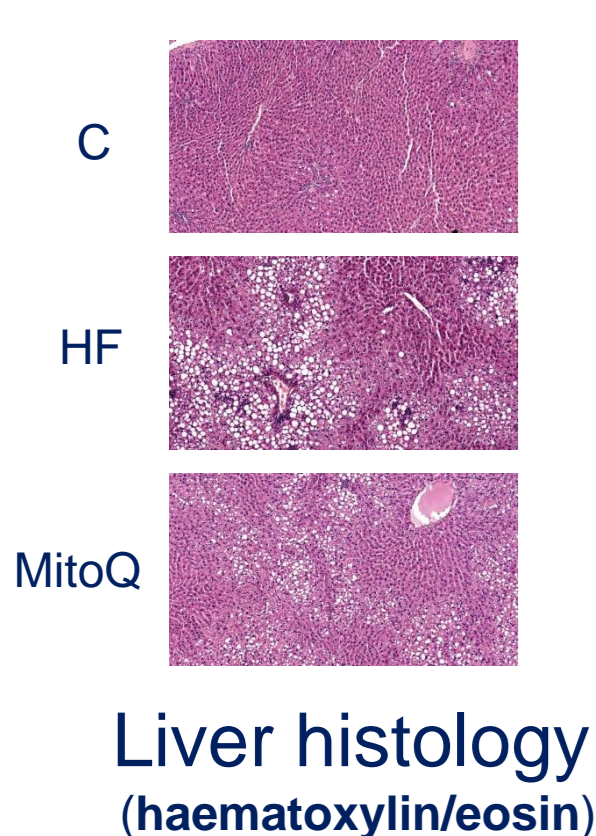
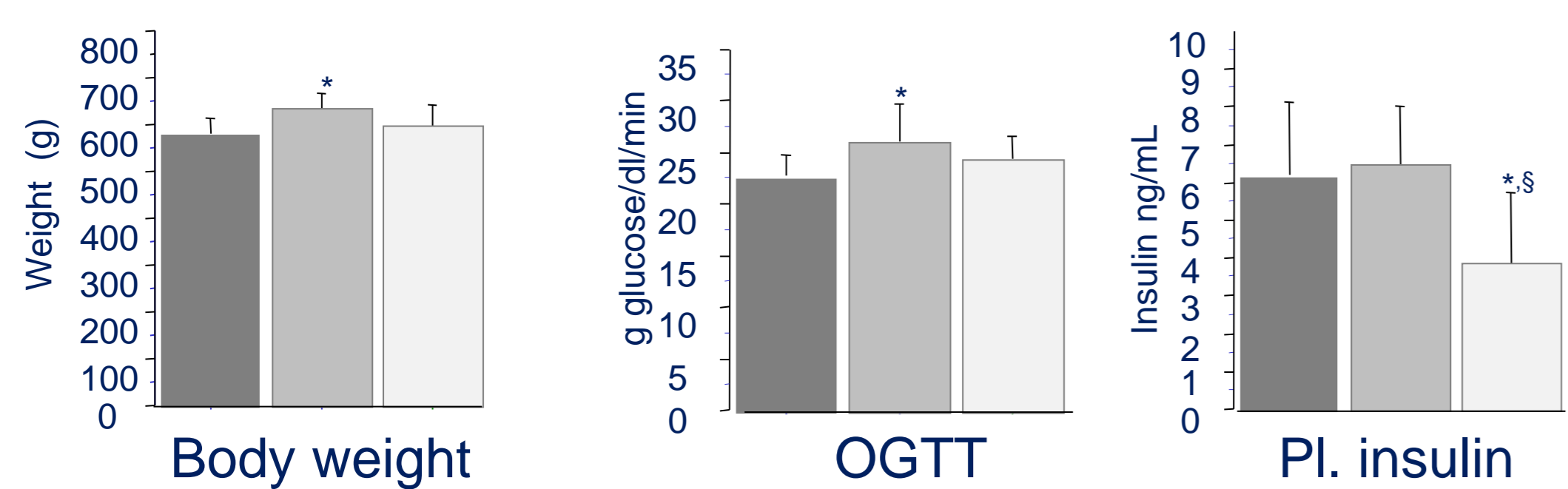
- Mitochondrial PL, including CL, were separated by TLC (Merck plates) revealed with Mb blue spray and quantified using Scanner 3 CAMAG [3]
- Fatty acid content of mitochondrial PL was determined by GC after separation of the PL fraction by TLC
- Reverse transcription q-PCR analyses were performed to evaluate gene expression of enzymes involved in CL synthesis and remodeling

3-Liver mitochondrial characteristics

- Membrane fluidity was assessed by ESR using 16-NS [2]
- Membrane potential and ROS production were monitored using respectively Rhodamine (RH-123) and 2',7'-Dichlorofluorescein diacetate
- Respiration was monitored in thermo-stated chambers of high resolution Oxygraph (Oroboros Oxygraph2k, Autriche)
- ATPase activity was determined spectrophotometrically

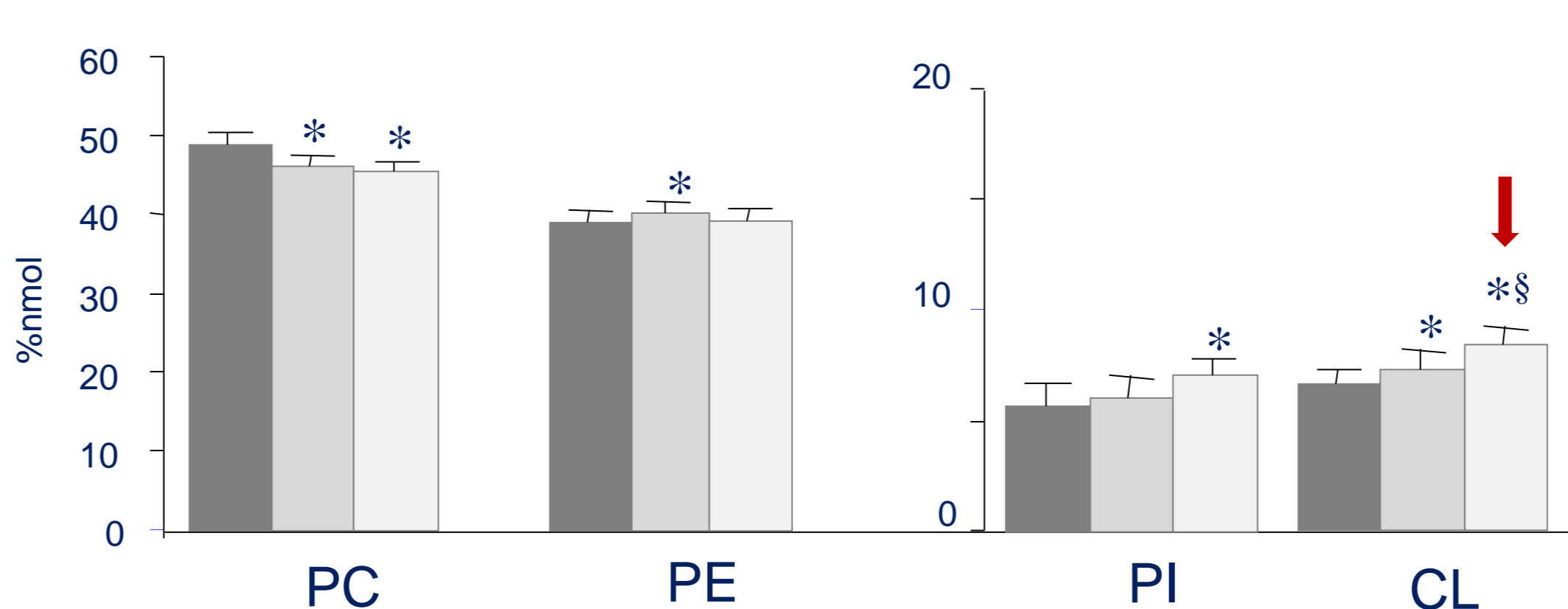
C-Results

1-Characteristics of the rats

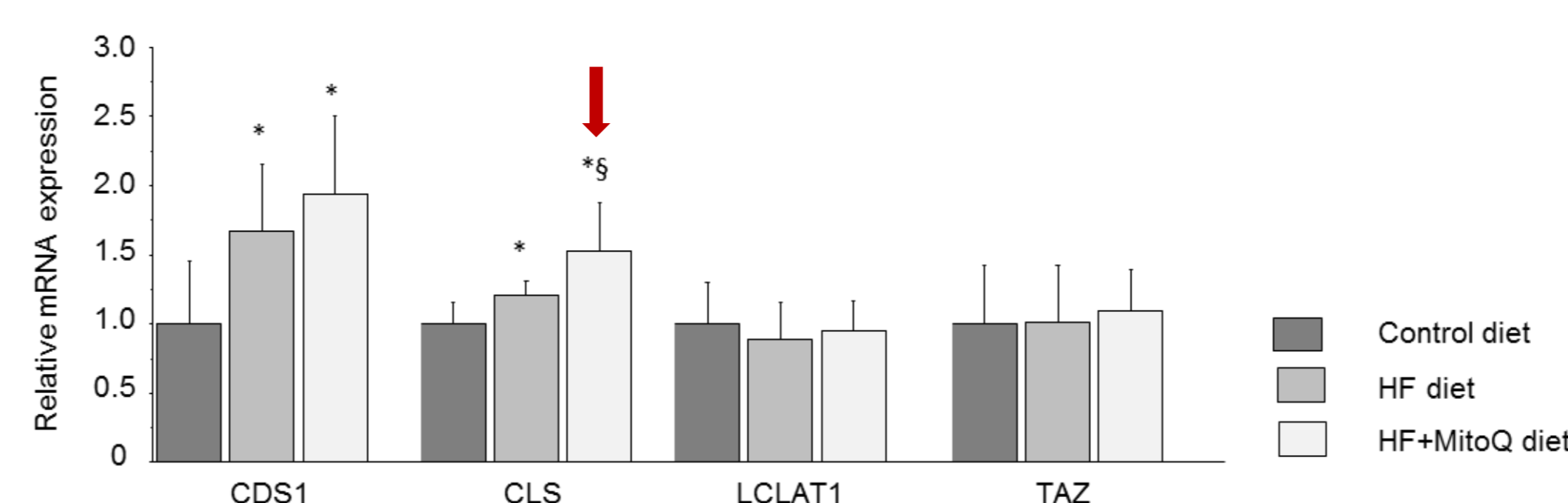
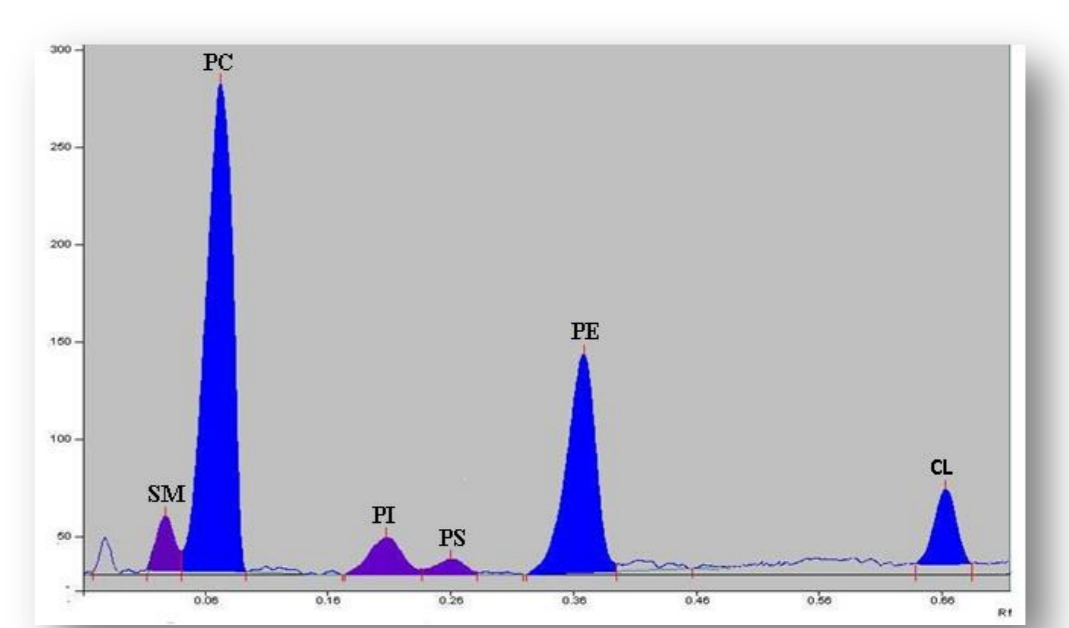


High-fat diet induced major features of the metabolic syndrome, and MitoQ intake ameliorated the associated weight gain and glucose intolerance.

2-Liver mitochondrial cardiolipin content



Scan of TLC plate



Results are mean ± SD; n=8. Unpaired t-test. Significance was set at p<0.05.* vs control; §vs HF

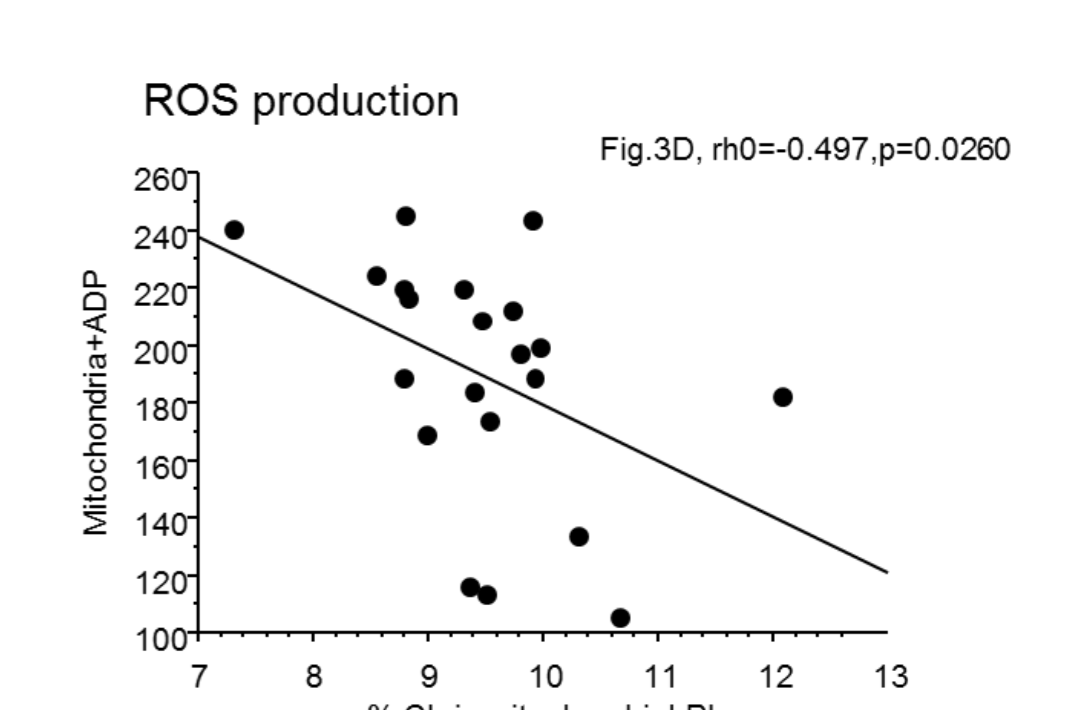
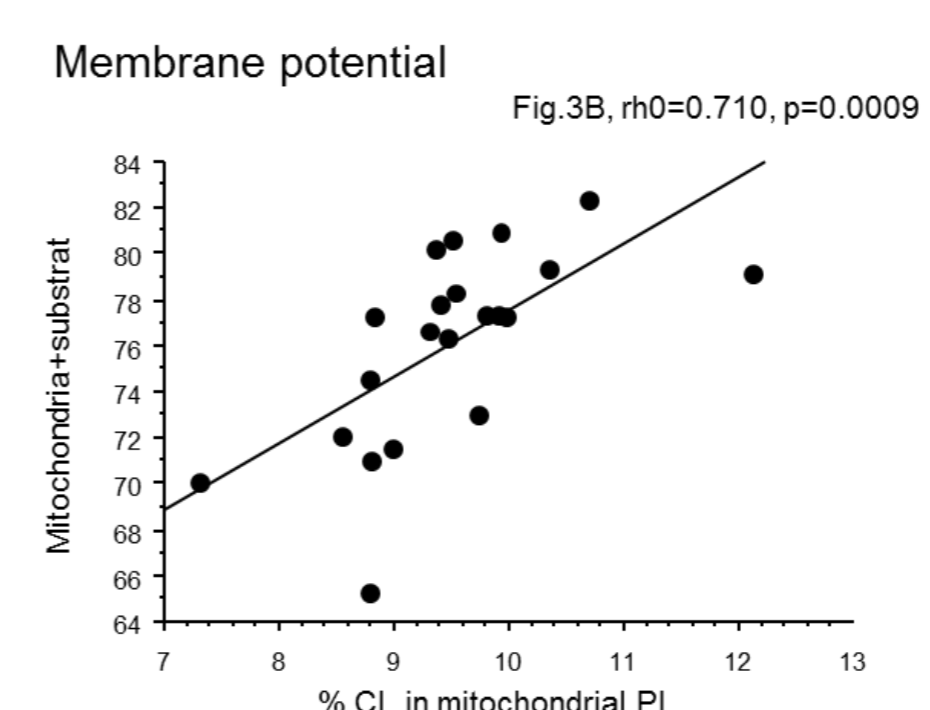
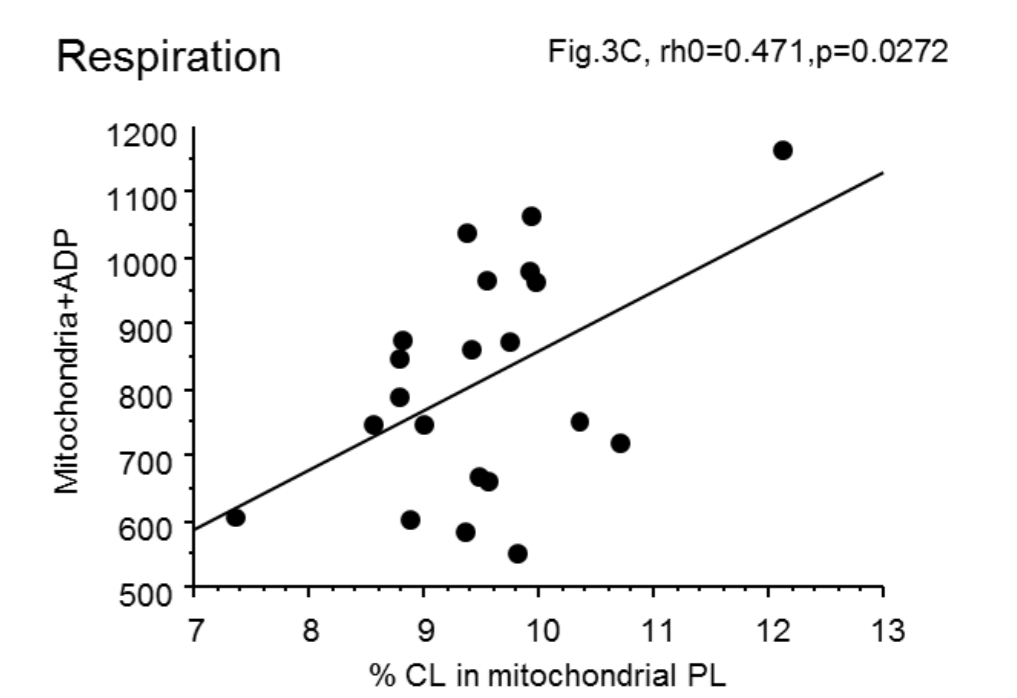
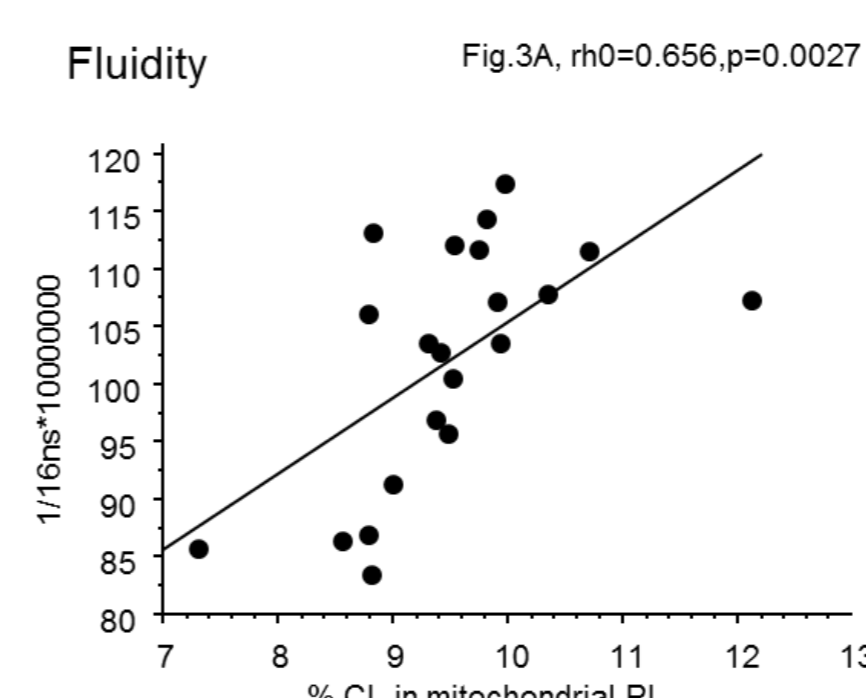
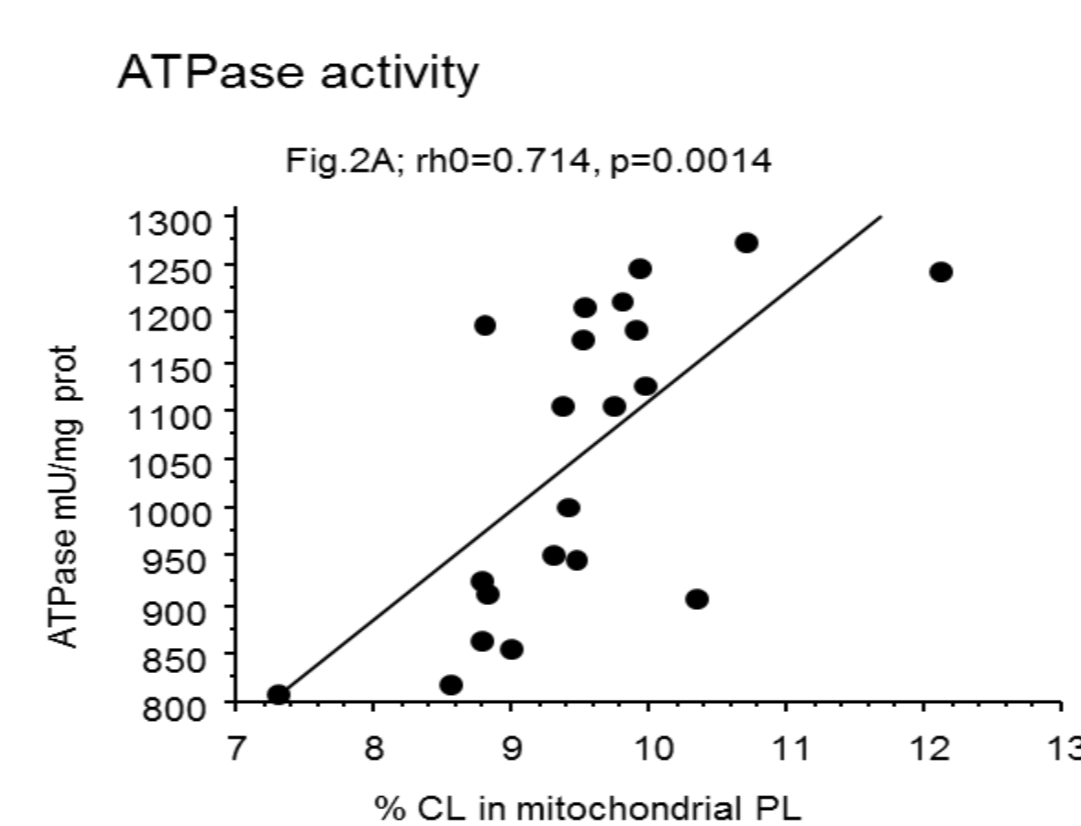
MitoQ both increased CL content of liver mitochondria in the mitochondrial phospholipids and CL synthase gene expression by comparison to the HFD.

3-Fatty acid composition of mitochondrial PL

MitoQ increased 18:2n-6 (linoleic acid) percent in the mitochondrial phospholipids.

	Control diet	HF diet	HF-MitoQ diet
Total SFA	41.0±1.64	42.7±0.9	41.7±1.8
16:0	18.3 ± 0.6	17.0 ± 0.9*	16.2 ± 0.6*
18:0	22.7 ± 2.1	25.7 ± 1.0*	25.5 ± 1.8*
Total MUFA	8.39±0.82	6.37±0.76*	5.96±0.44*
16:1 n-7	1.28 ± 0.17	0.33 ± 0.05*	0.22 ± 0.04*§
18:1 n-9	2.99 ± 0.28	4.00 ± 0.60*	3.87 ± 0.30*
18:1 n-7	3.98 ± 0.79	1.92 ± 0.18*	1.75 ± 0.16*
Total PUFA	50.6±1.05	50.9±1.16	52.3±1.68
18:2 n-6	9.94 ± 1.53	11.5 ± 1.16	12.8 ± 0.81*
18:3 n-6	0.106 ± 0.044	0.047 ± 0.023*	0.054 ± 0.023*
18:3 n-3	1.021 ± 1.541	0.426 ± 0.198	0.314 ± 0.102
20:3 n-6	0.881 ± 0.304	0.892 ± 0.119	0.865 ± 0.184
20:4 n-6	27.4 ± 1.3	28.0 ± 0.5	28.6 ± 1.11
20:5 n-3	0.114 ± 0.037	0.099 ± 0.058	0.082 ± 0.015
22:5 n-3	0.761 ± 0.044	0.954 ± 0.047*	0.975 ± 0.199*
22:6 n-3	9.75 ± 1.21	8.56 ± 0.57*	8.36 ± 0.41*

4-Liver mitochondrial characteristics



CL content is positively correlated with ATP synthase activity, mitochondrial membrane fluidity, membrane potential, respiration and negatively correlated with mitochondrial ROS production.

Correlations were performed with the Spearman method.

D-Conclusion

Our studies show that the high fat diets impair liver mitochondrial functions and modify membrane structure and characteristics. MitoQ ameliorates some metabolic syndrome features, and in particular increases mitochondrial cardiolipin content. Antioxidant-independent mechanisms of MitoQ may be involved in addition to its own antioxidant action.

Acknowledgments

The support and sponsorship of the COST Action CM1201 "Biomimetic Radical Chemistry" to Manar Aoun and Eva Tolika is gratefully acknowledged. The authors acknowledge the financial support of the French Lipid Nutrition Group and the National Institute for Agronomic Research and in particular the Human nutrition Department (Alim-H department).

