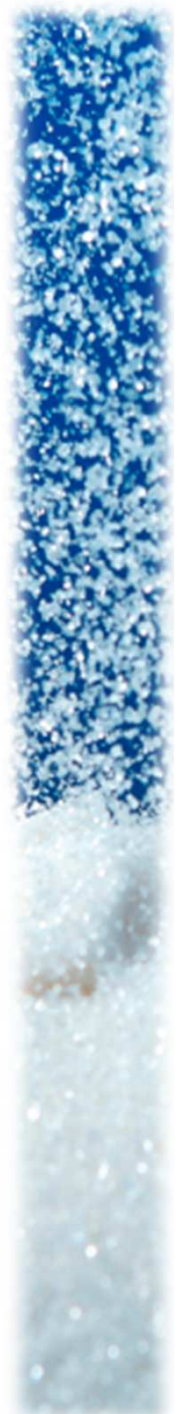
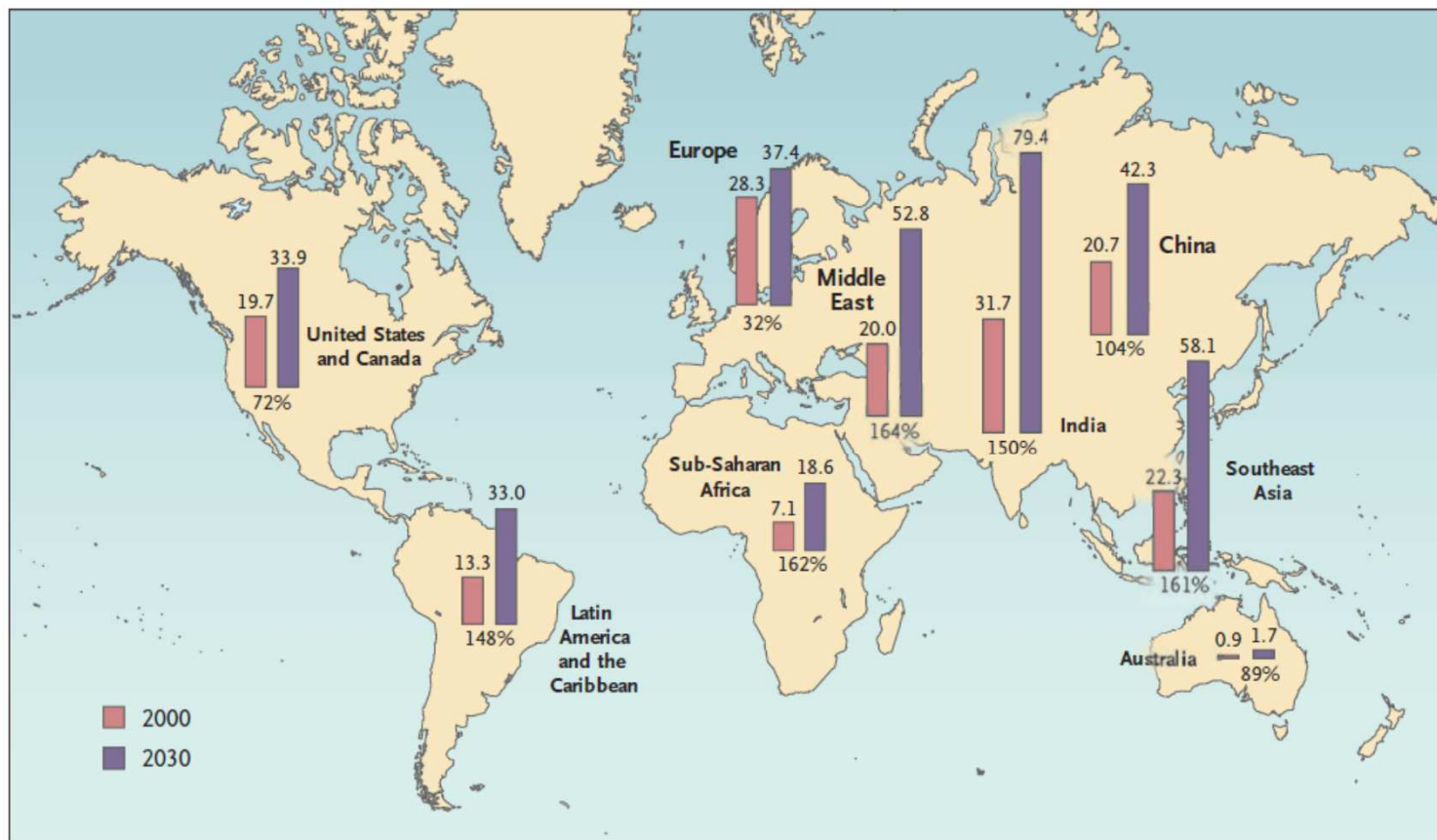


Alteracions metabòliques induïdes per la ingesta de fructosa líquida en models animals

Marta Alegret Jordà
Seminaris de Recerca
Facultat de Farmàcia
2 d'abril de 2013



Prevalència de diabetis 2010-2030



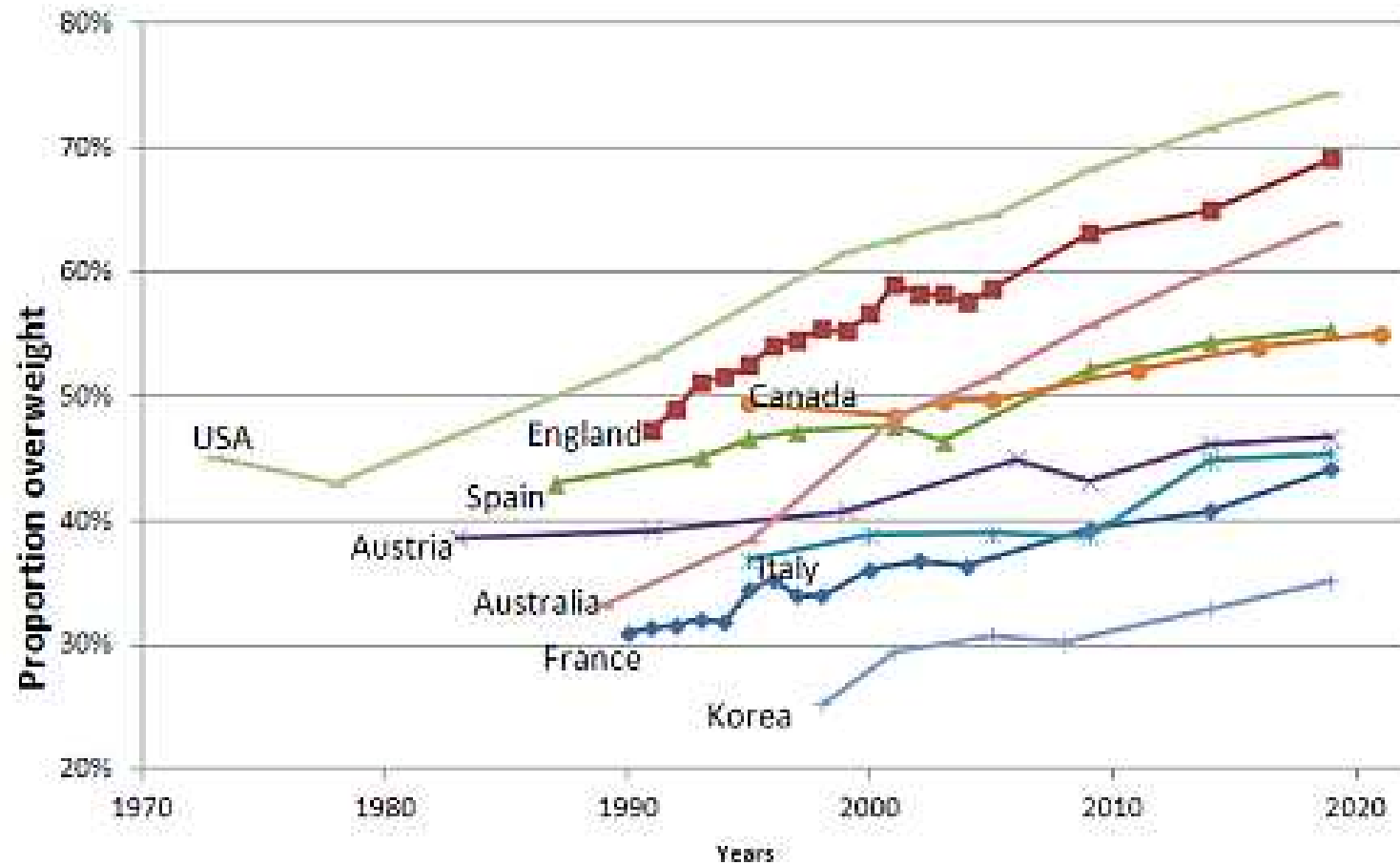
Millions of Cases of Diabetes in 2000 and Projections for 2030, with Projected Percent Changes.

Data are from Wild et al.³

N Eng J Med 356, 213-6

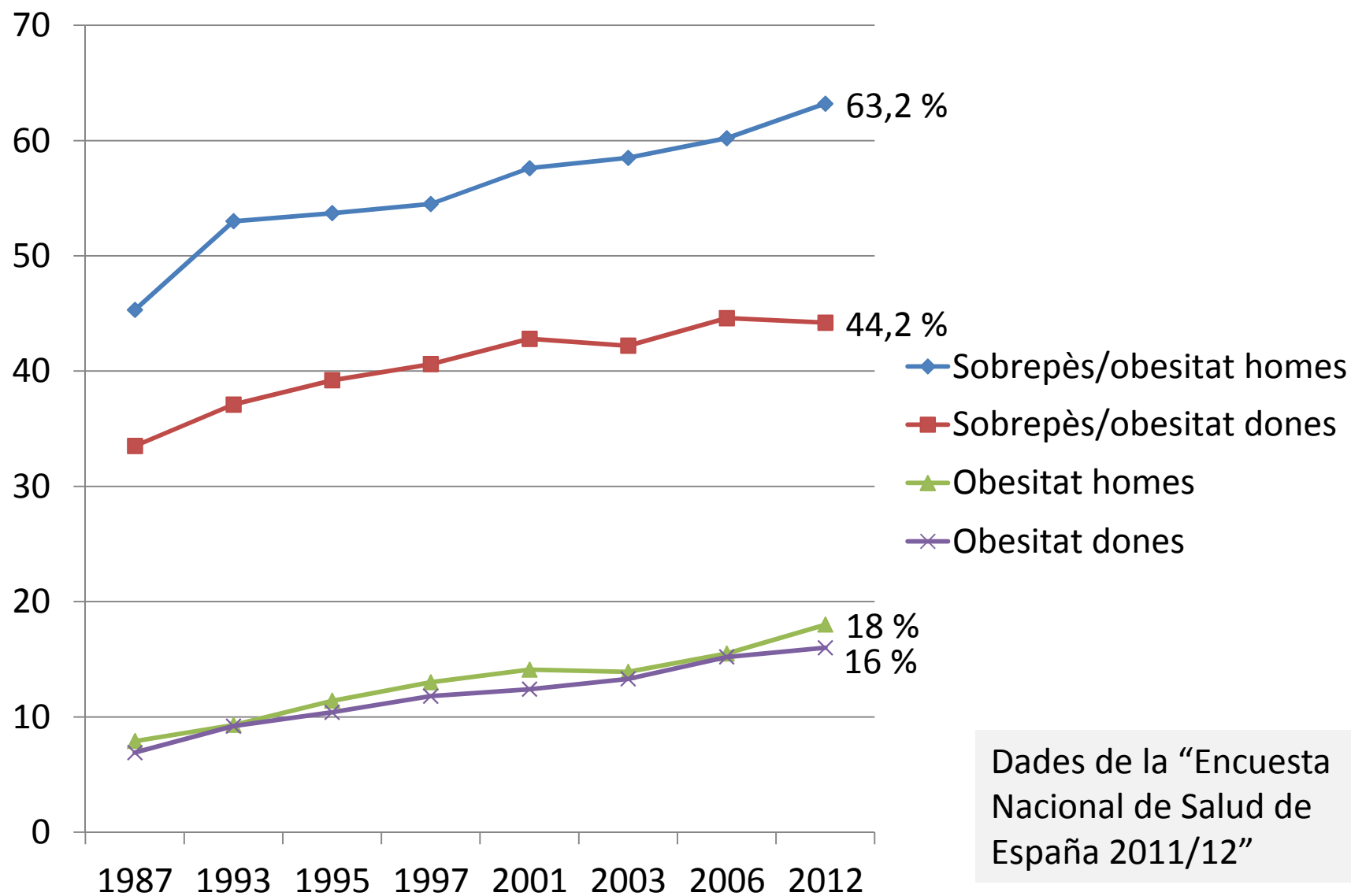
Prevalència de sobrepès

Past and projected future overweight rates in selected OECD countries

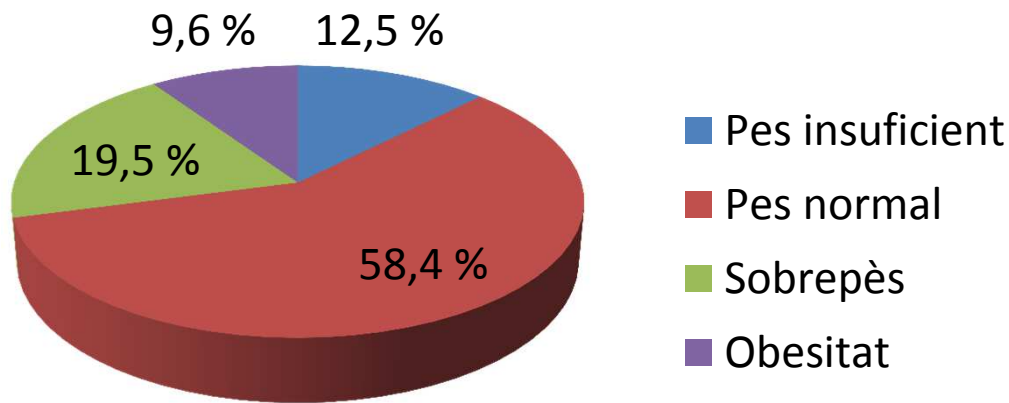


OECD Health Data 2010 Report

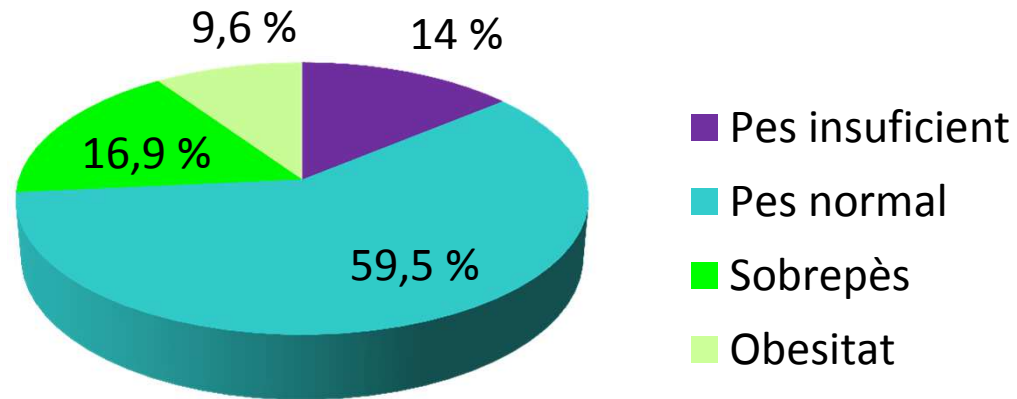
Evolució sobrepès-obesitat a Espanya



Sobrepès-obesitat 2-17 anys a Espanya (2012)

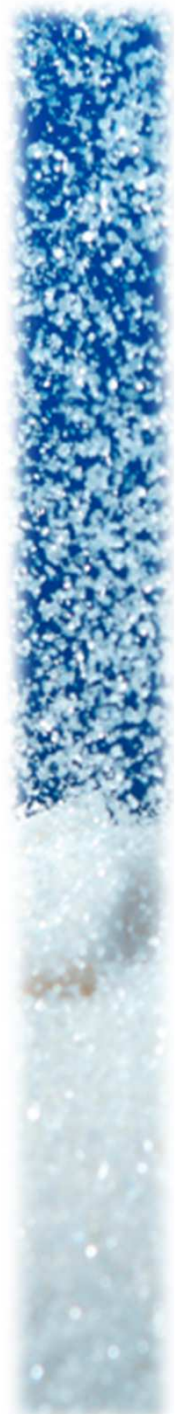


Nens

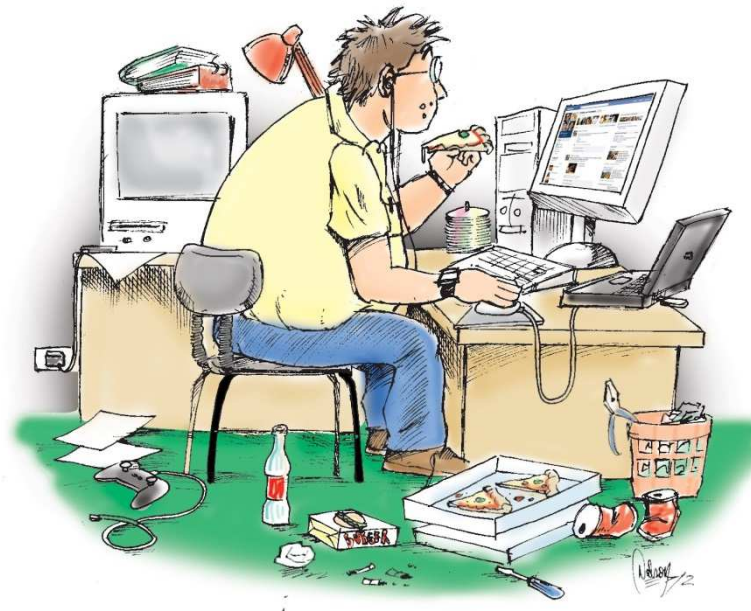


Nenes

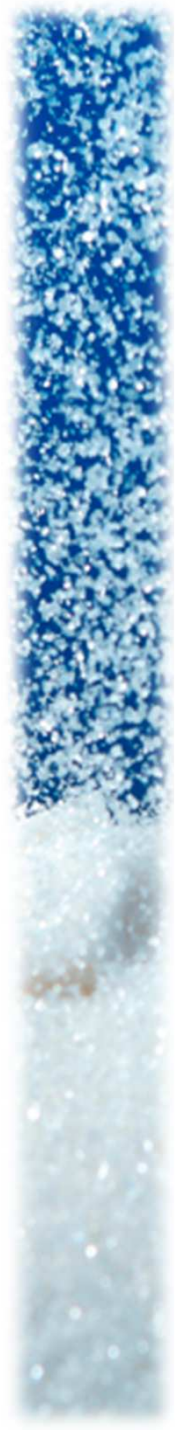
Dades de la "Encuesta Nacional de Salud de España 2011/12"



Canvis en l'estil de vida

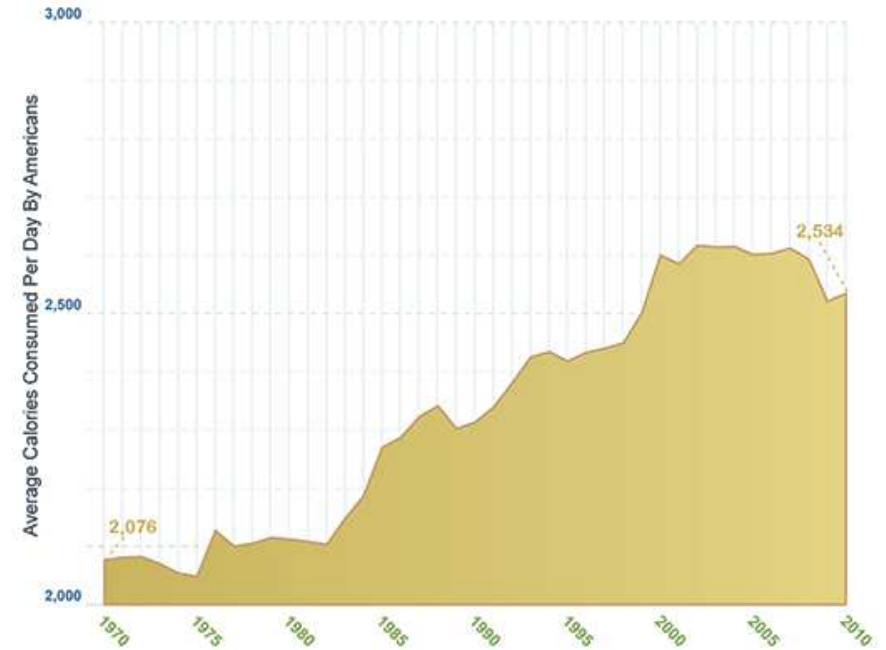


Sedentarisme
Dieta hipercalòrica
Excés de greixos i sucres simples



Augmenta el consum calòric...

Average Daily Per Capita Calories Consumed
U.S. food availability, adjusted for spoilage and other waste 1970-2010



Source: U.S. Department of Agriculture, Economic Research Service, 2012. Calories: average daily per capita calories from the U.S. food supply, adjusted for spoilage and other waste. Loss-Adjusted Food Availability Data.

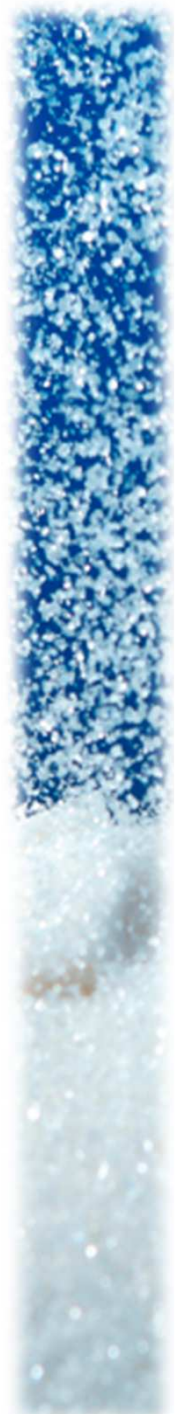
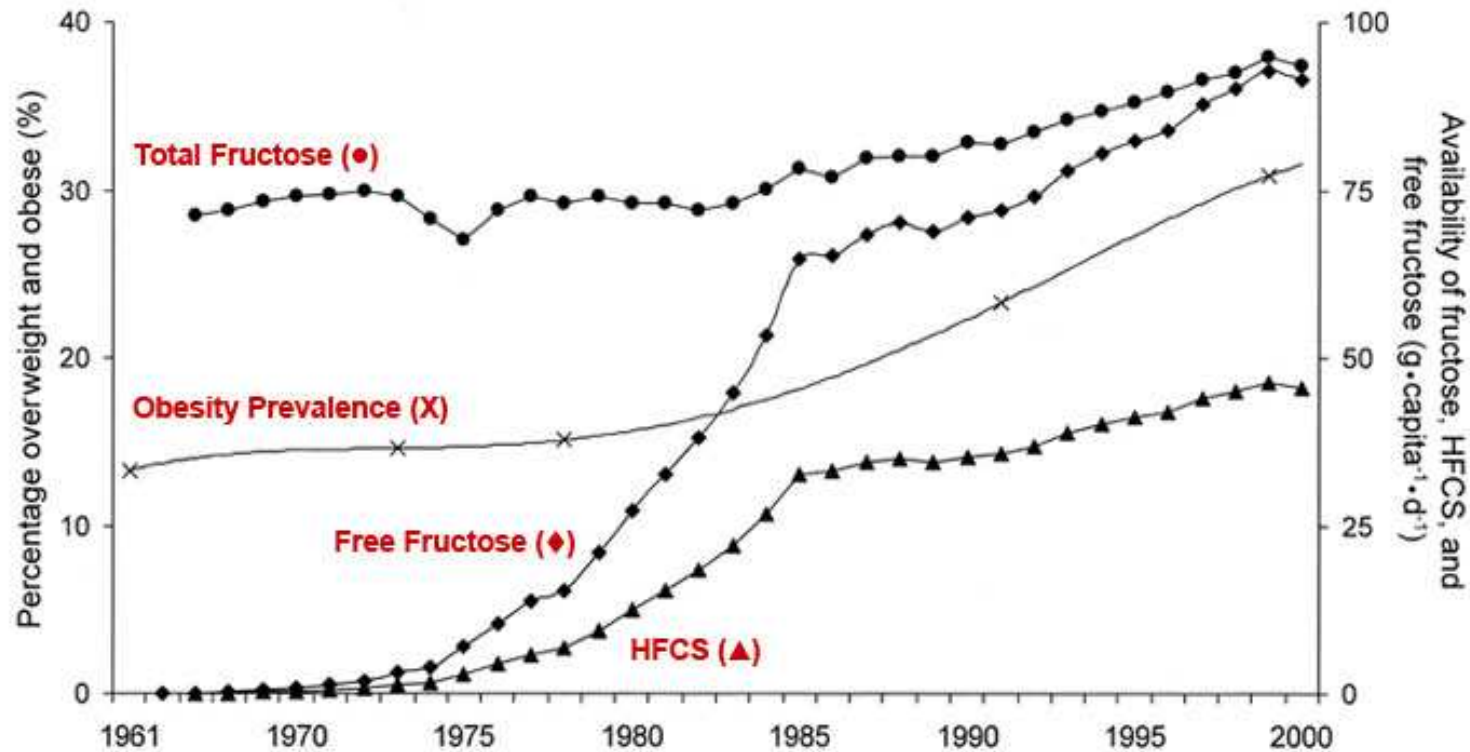
Per Capita Consumption of Caloric Sweeteners vs. Obesity & Diabetes
1970-2010



...i hi ha canvis qualitatis



L'augment en el consum de fructosa és paral·lel a l'increment de prevalència de sobrepès/obesitat



Opinions contrastades

2 FEBRUARY 2012 | VOL 482 | NATURE | 27



The toxic truth about sugar

Added sweeteners pose dangers to health that justify controlling them like alcohol, argue Robert H. Lustig, Laura A. Schmidt and Claire D. Brindis.

SUMMARY

- Sugar consumption is linked to a rise in non-communicable disease
- Sugar's effects on the body can be similar to those of alcohol
- Regulation could include tax, limiting sales during school hours and placing age limits on purchase

Curr Opin Clin Nutr Metab Care 2012, 15:357–361

EDITORIAL



Fructose toxicity: is the science ready for public health actions?

Luc Tappy^{a,b} and Bettina Mittendorfer^c

KEY POINTS

- There is some evidence that suggests excessive fructose consumption especially when combined with excess energy intake may have adverse effects on metabolic health.
- The results from clinical trials do not support a significant detrimental effect of fructose on metabolic health when consumed as part of a weight-maintaining diet in amounts consistent with the average estimated fructose consumption in Western countries.
- Public health policies to eliminate or limit fructose in the diet should be considered premature.
- Crucial studies that will provide definitive answers to the concerns of fructose toxicity and others, which should guide decisions of public policy makers are still missing.

New York Plans to Ban Sale of Big Sizes of Sugary Drinks



Char

Mayor Michael R. Bloomberg on Wednesday with Linda I. Gibbs, deputy mayor for health, as he dis large sugary beverages. Next to each soda is the amount of sugar in it.

By MICHAEL M. GRYNBAUM

Published: May 30, 2012 | 1426 Comments

New York City plans to enact a far-reaching ban on the sale of large sodas and other sugary drinks at restaurants, movie theaters and street carts, in the most ambitious effort yet by the [Bloomberg administration](#) to combat rising obesity.

Judge Blocks New York City's Limits on Big Sugary Drinks



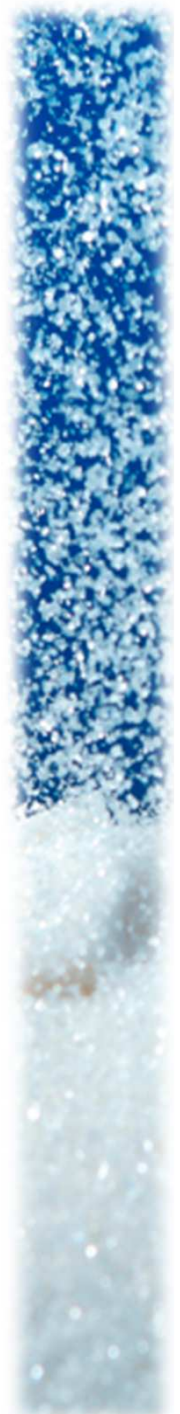
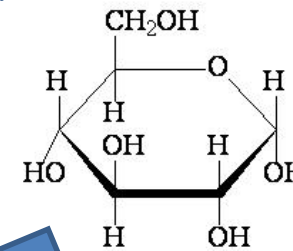
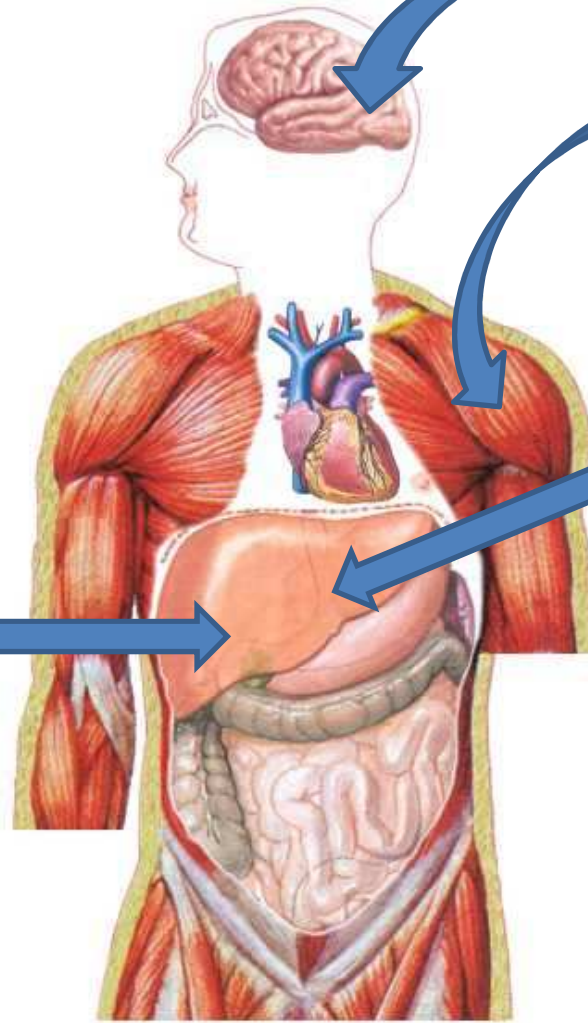
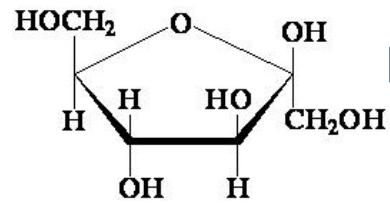
Michelle V. Agins/The New York Times

"We believe that the judge's decision was clearly in error, and we believe we will win on appeal," Michael Bloomberg said Monday.

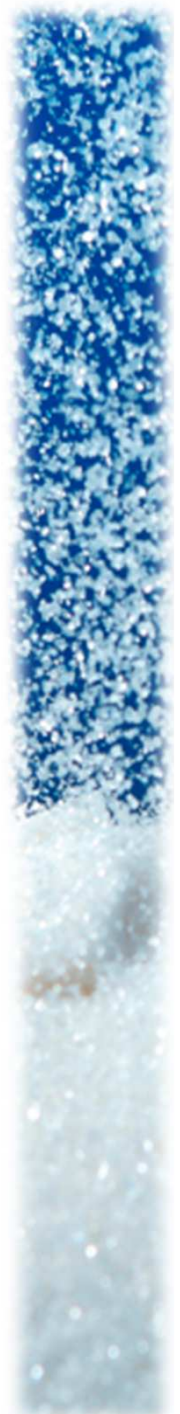
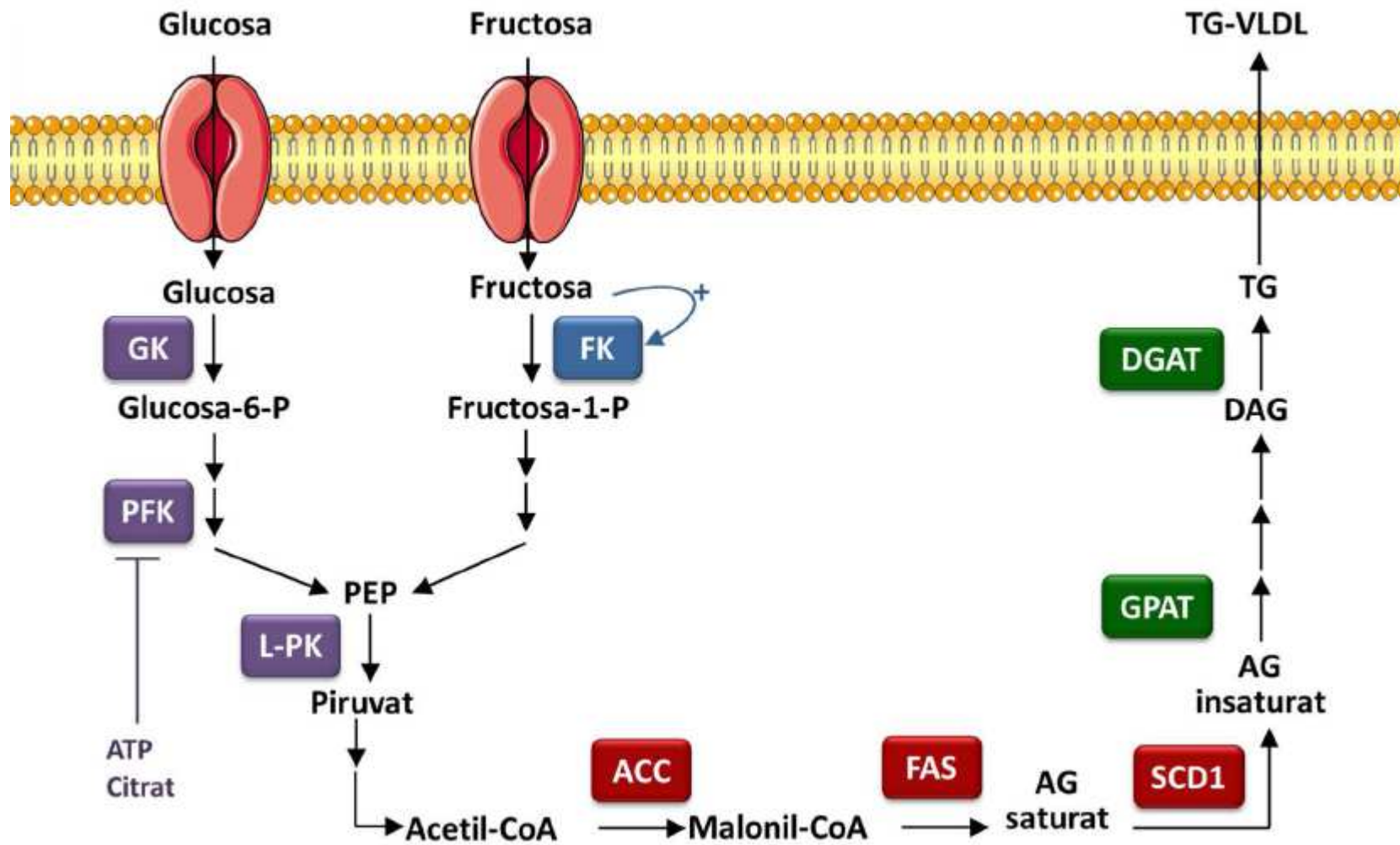
By MICHAEL M. GRYNBAUM

Published: March 11, 2013 | 338 Comments

Per què la fructosa?



Per què la fructosa?



La rata com a model

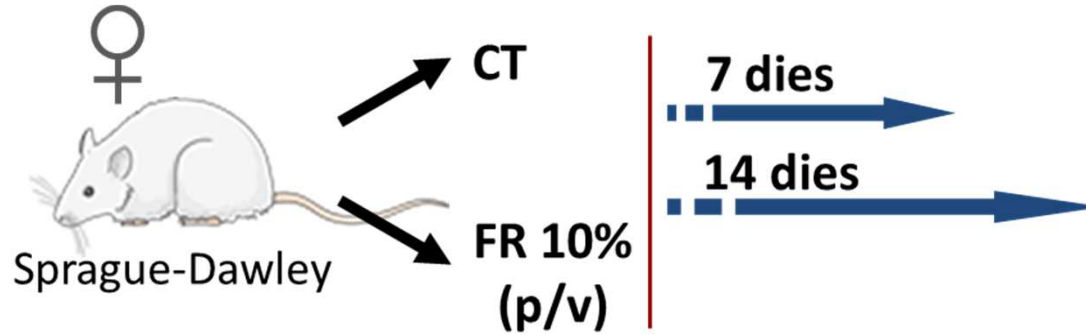


- Metabolisme de fructosa similar a espècie humana
- Fructosa promou alteracions metabòliques similars als humans amb Smet
- Models
 - Fructosa sòlida 60%
 - Fructosa líquida 10%

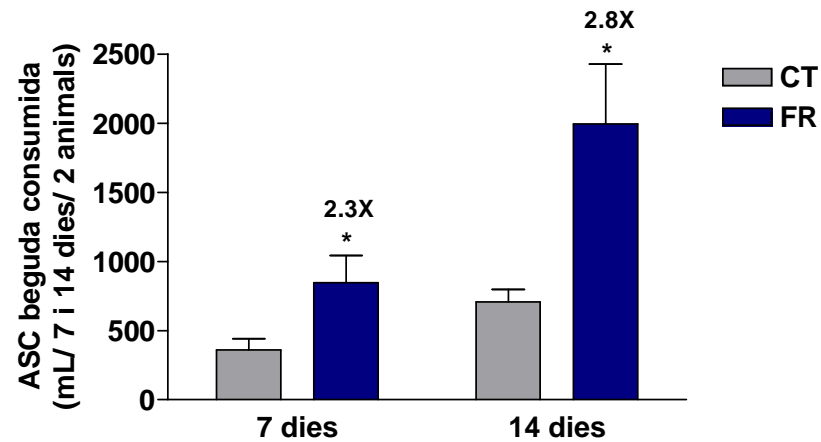
10% FRUCTOSA P/V 14d	RATES	
	♂	♀
Esteatosi hepática	X	X
Hiperleptinèmia	X	X
(-)Metabolisme àc. grassos	X	X
Hipertrigliceridèmia	X	X
Hiper glucèmia		X
Hiperinsulinèmia		X
Intolerància oral a la glucosa		X

- Roglans N et al. *J Pharmacol Exp Ther.* 2002;**302**:232.
- Roglans N et al. *Hepatology* 2007;**45**:778.
- Vilà L et al. *Hepatology* 2008;**48**:1506.
- Vilà L et al. *Toxicol Appl Pharmacol.* 2011;**251**:32.
- Vilà L et al., *J Nutr Biochem.* 2011;**22**:741.

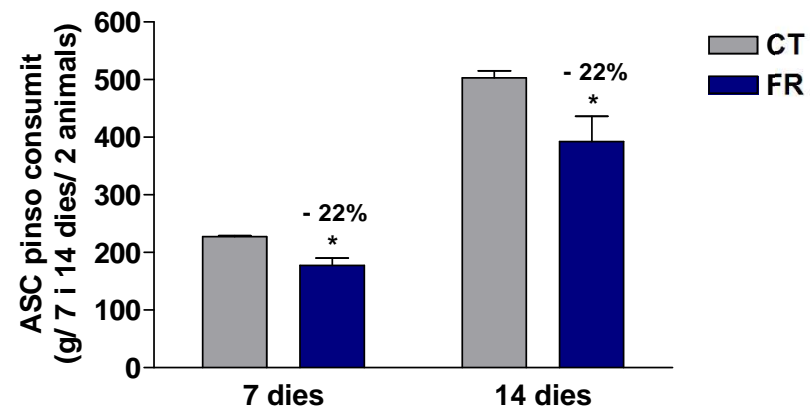
Manca de compensació energètica



Consum beguda

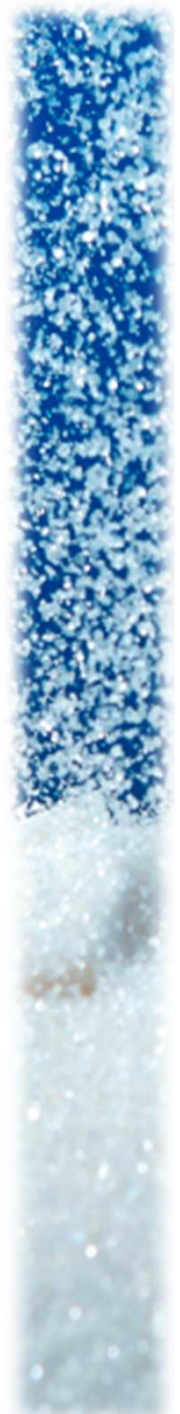


Consum pinso

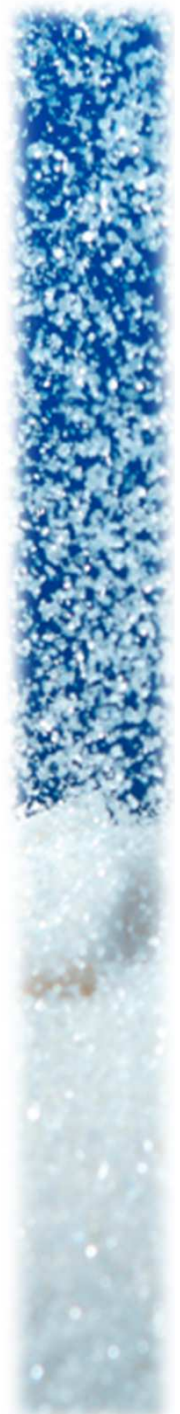
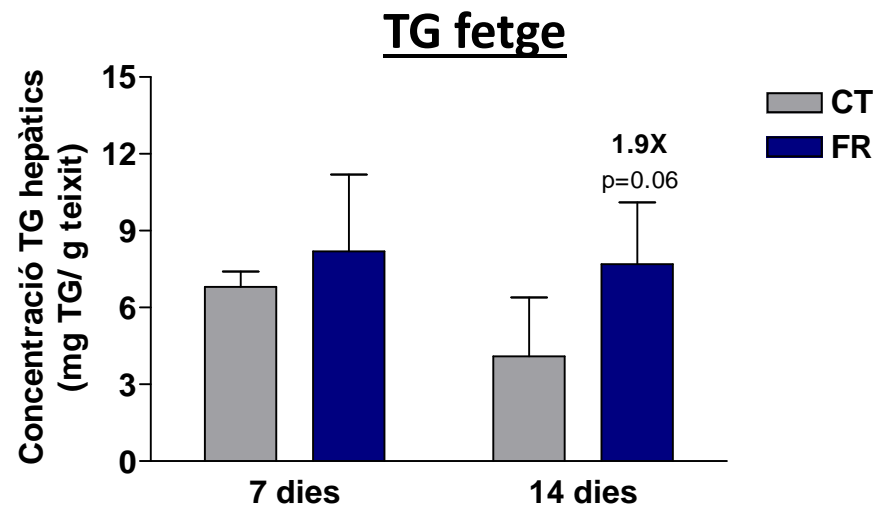
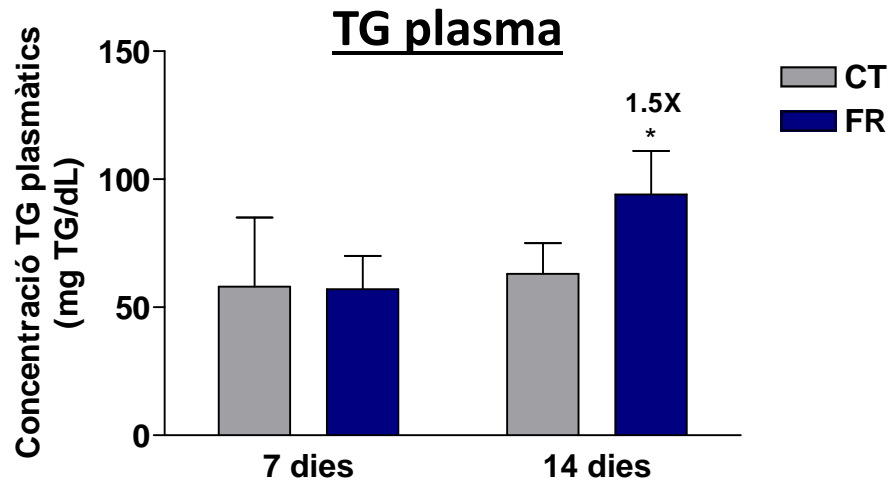


↑ 1.24X

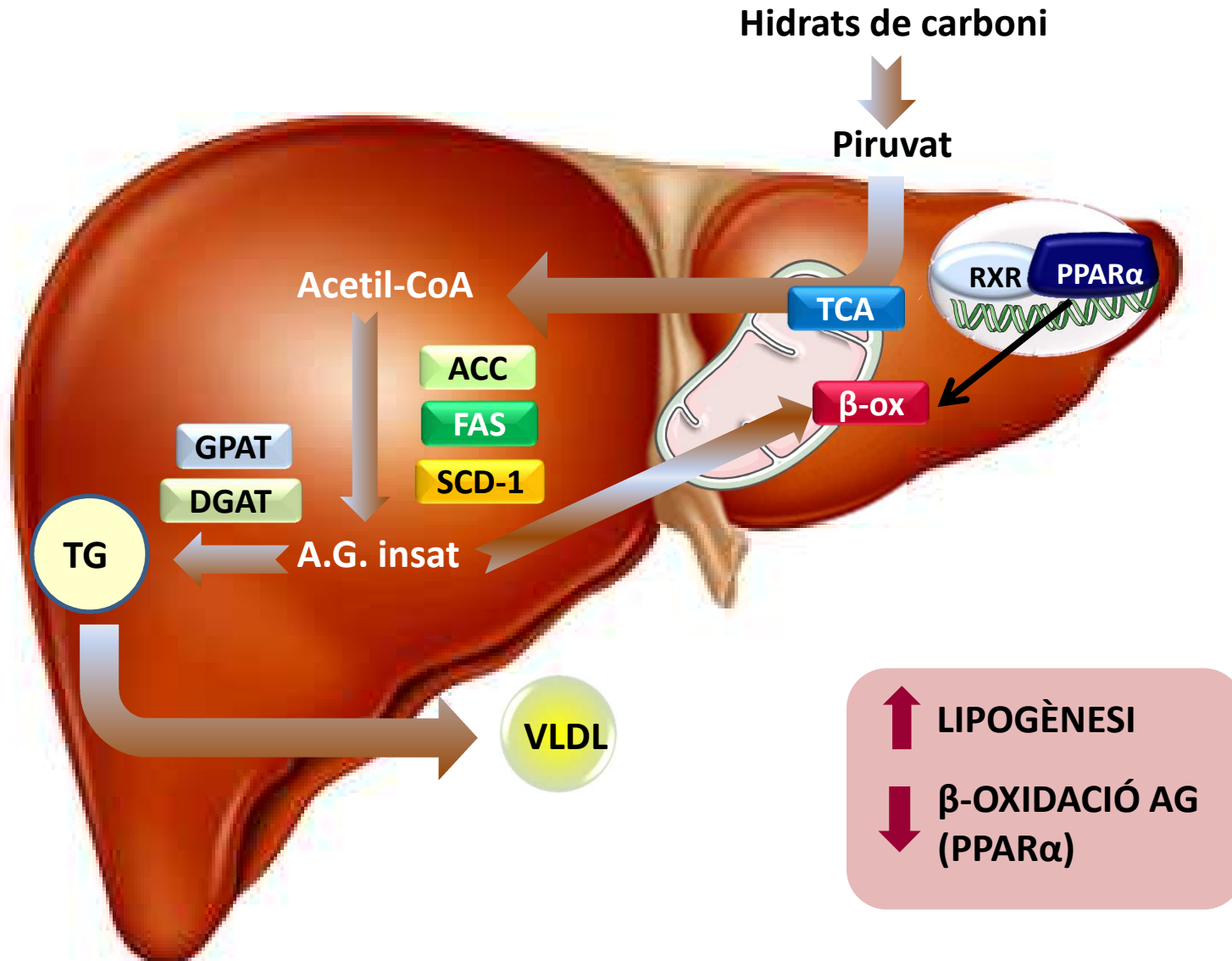
↑ 1.27X cal



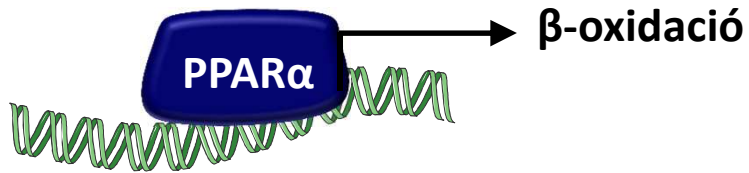
Increment dels triglicèrids



Lipogènesi/catabolisme AG

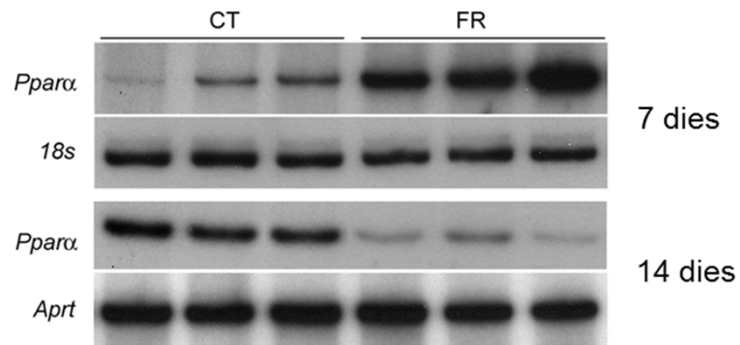


Efectes sobre PPAR α

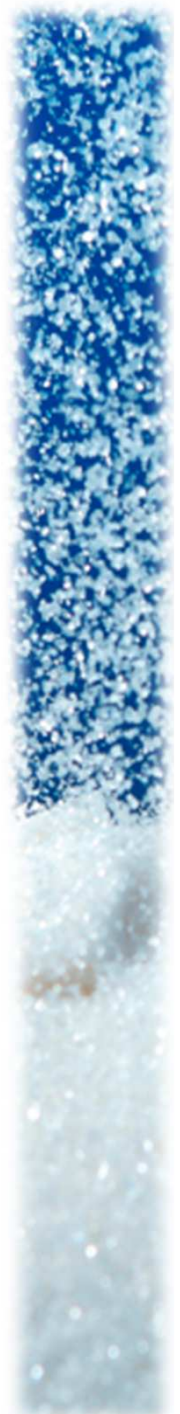
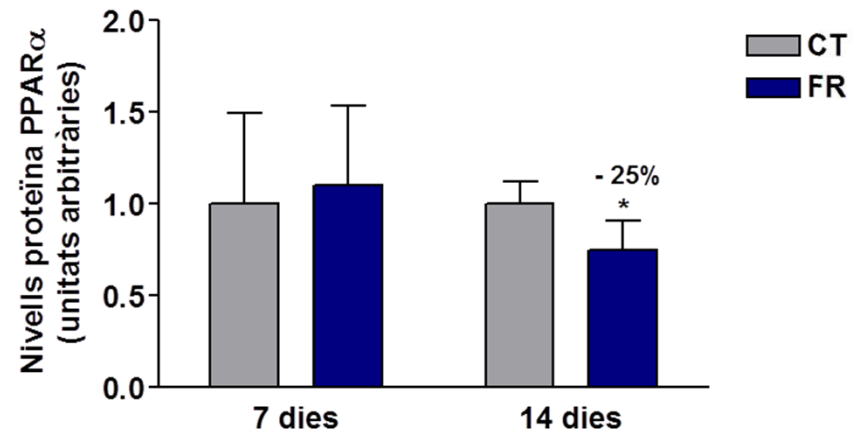
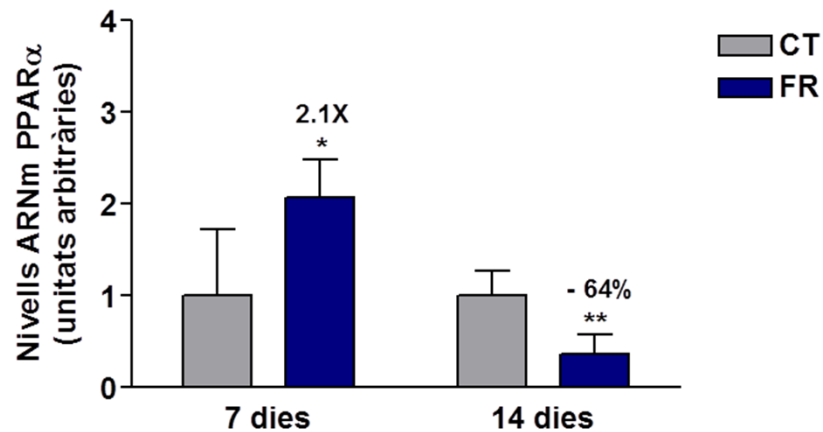
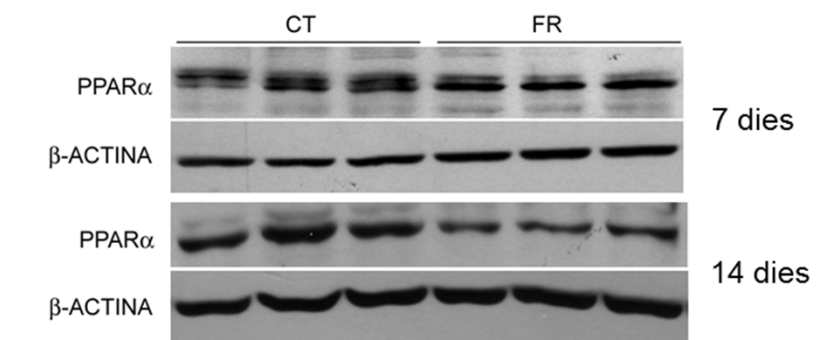


PPAR α

ARNm

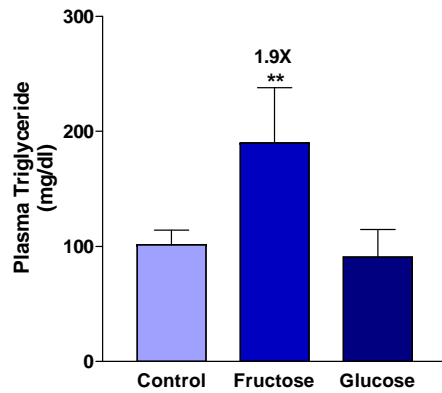


PROTEÏNA

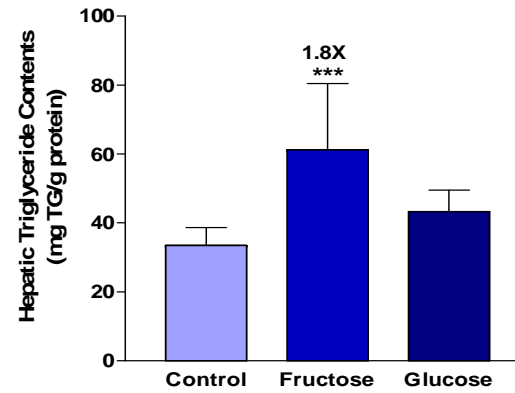


Són les calories?

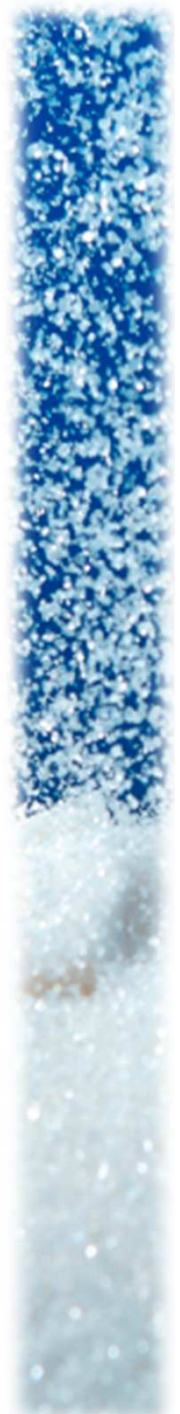
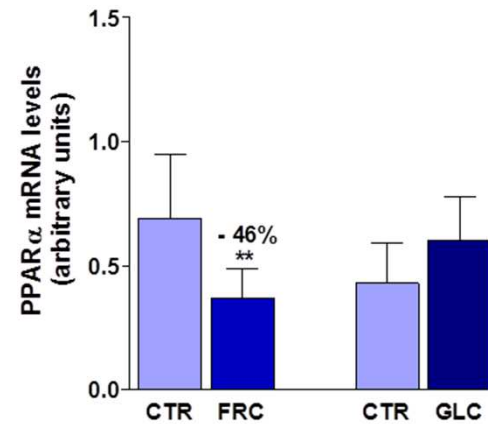
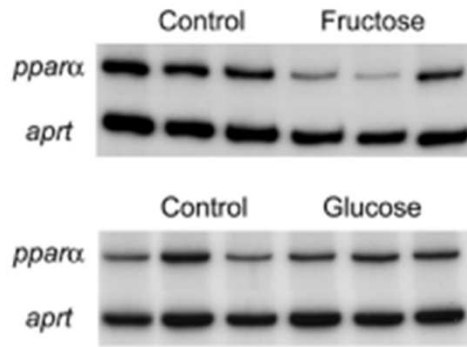
TG plasmàtics



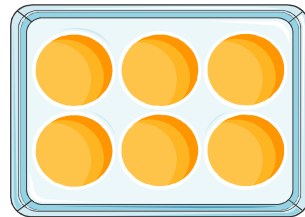
TG hepàtics



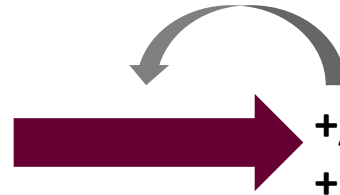
PPAR α



I en humans, què passaria?

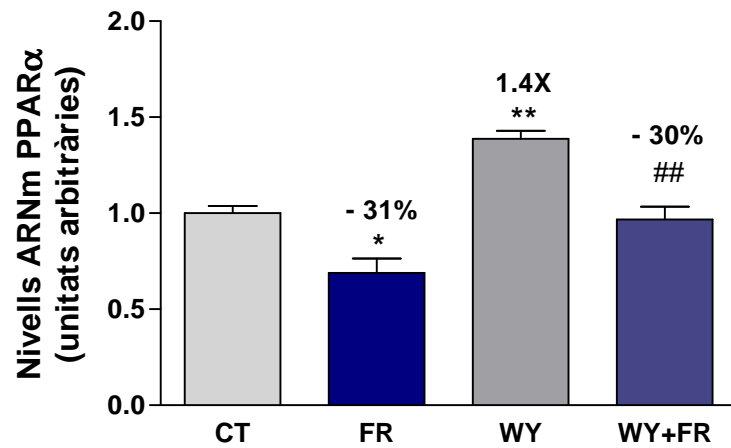
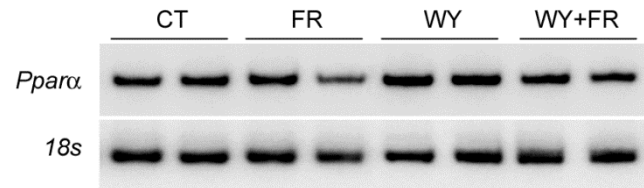


Hepatòcits humans

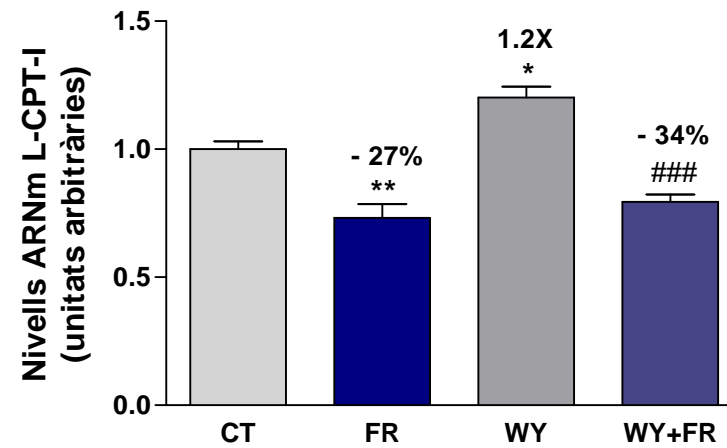
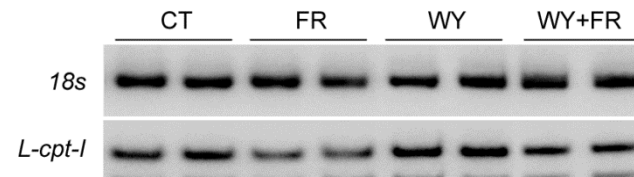


+/- FRUCTOSA 25 mM
+/- WY 14.643 100 μ M
24h

PPAR α



L-CPT-I

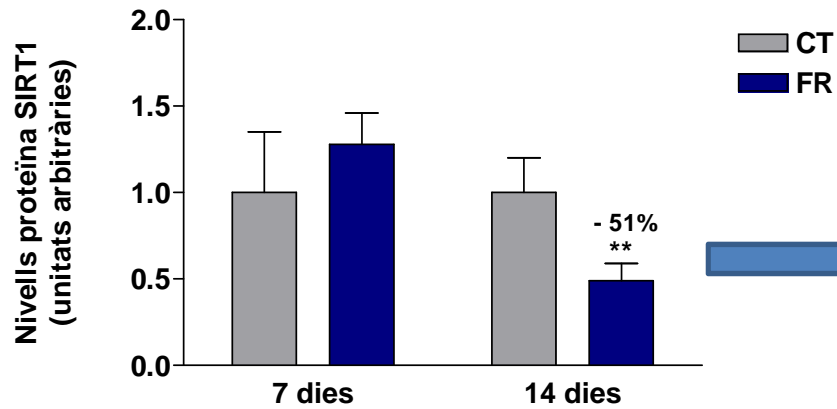
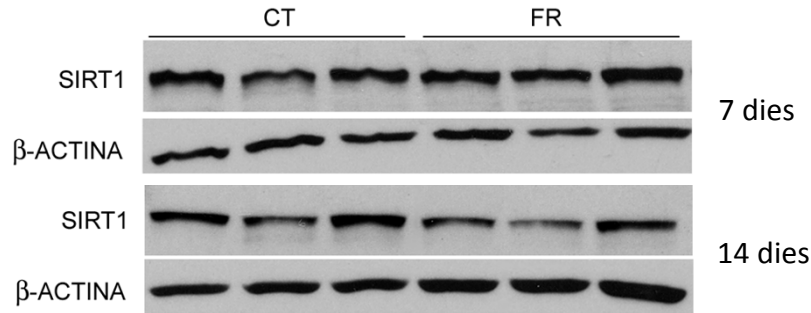


Mecanisme?

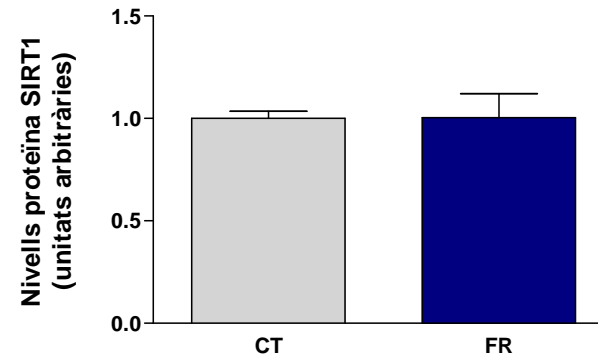
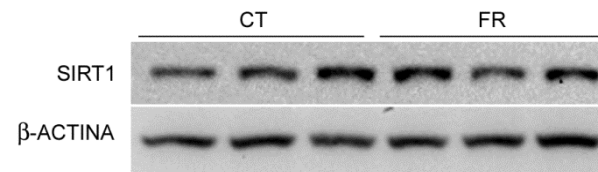


Feige *et al.*, Cell Metab 2008; 8:347-358.

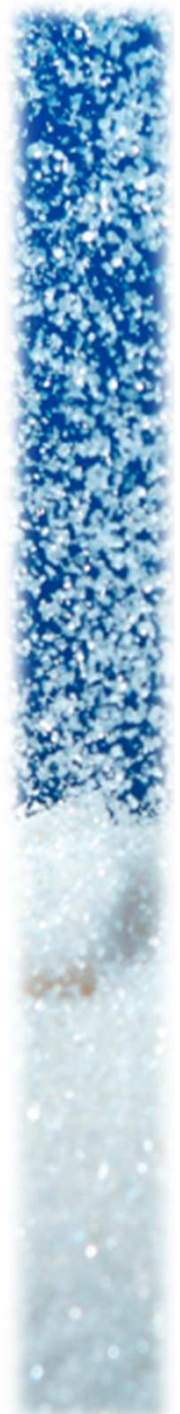
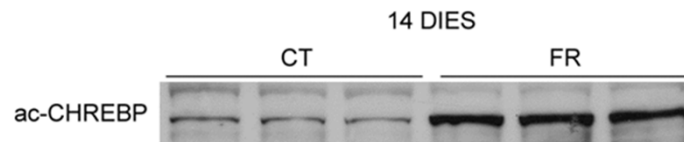
SIRT1 (rata)



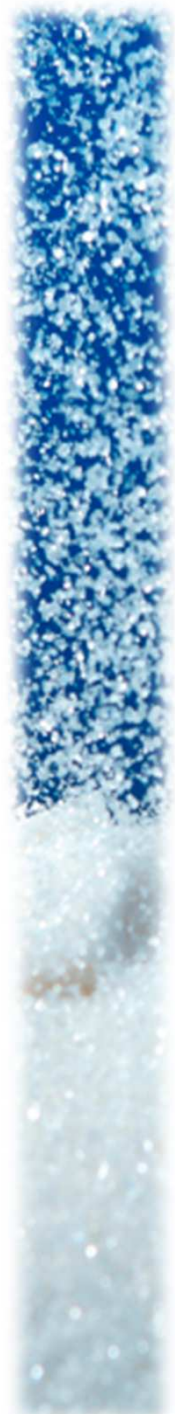
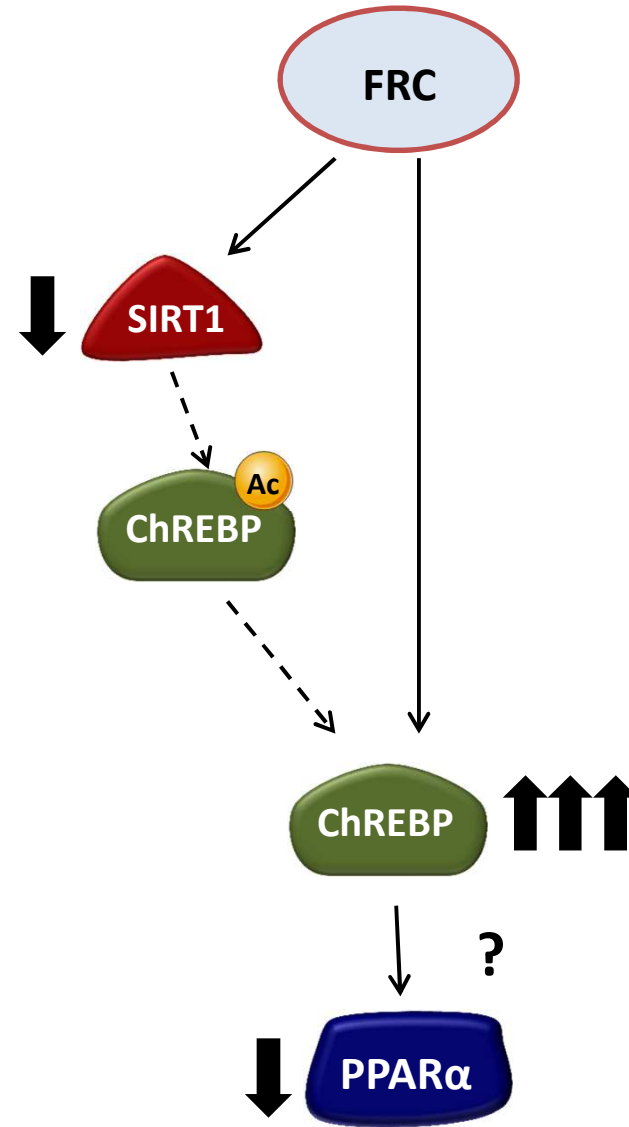
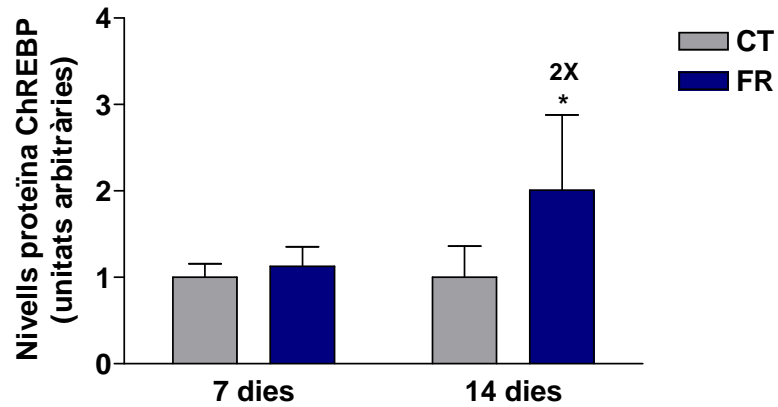
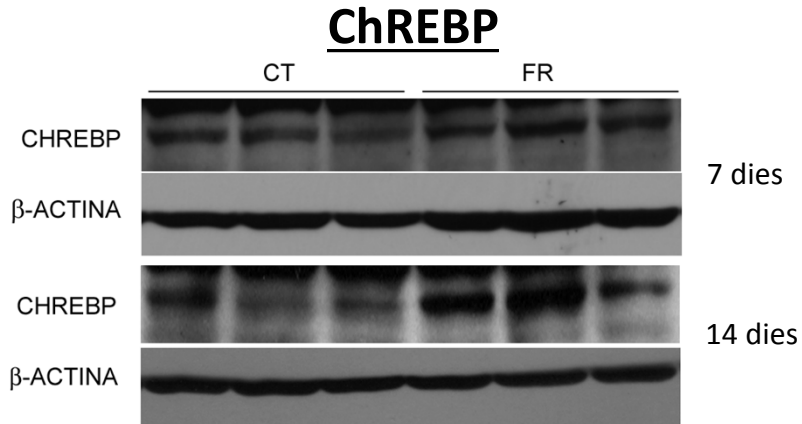
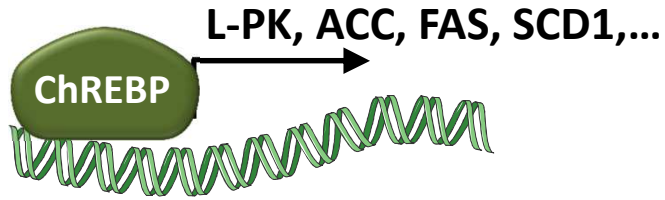
SIRT1 (FaO)



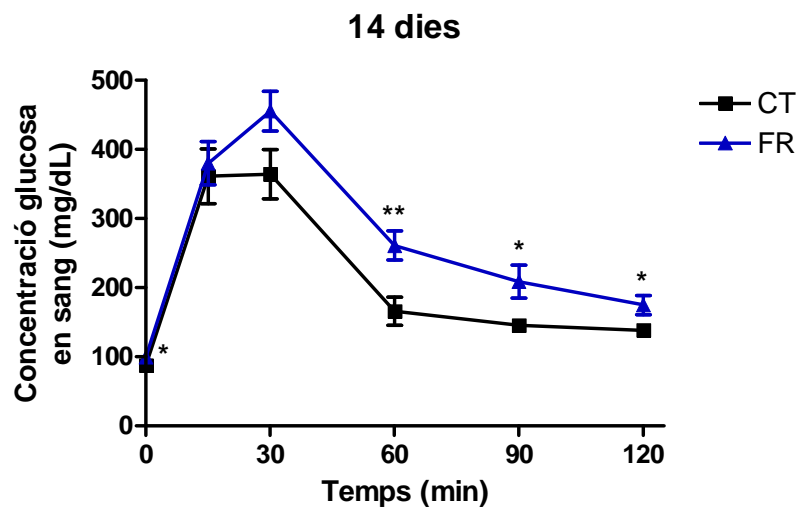
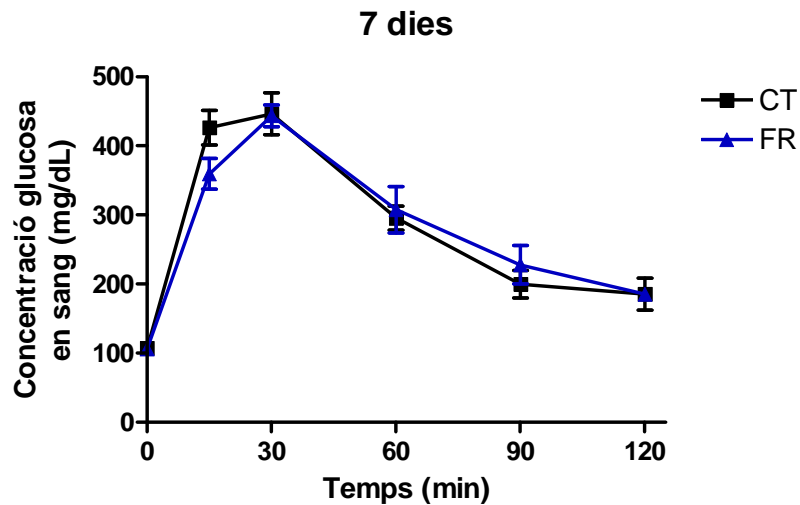
ac-CHREBP (rata)



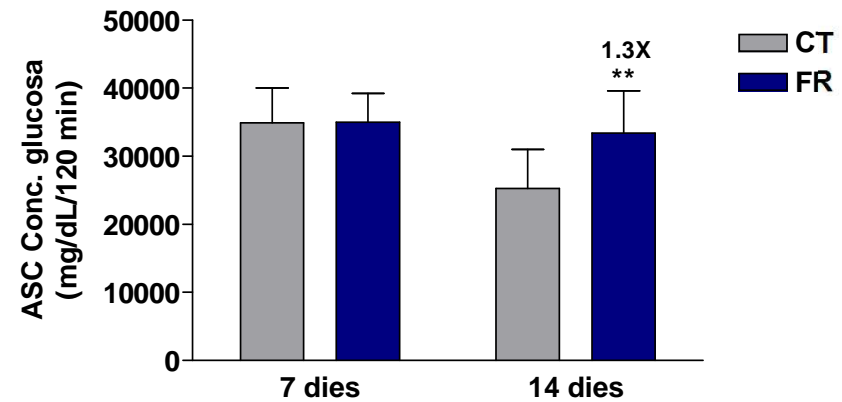
Mecanisme?



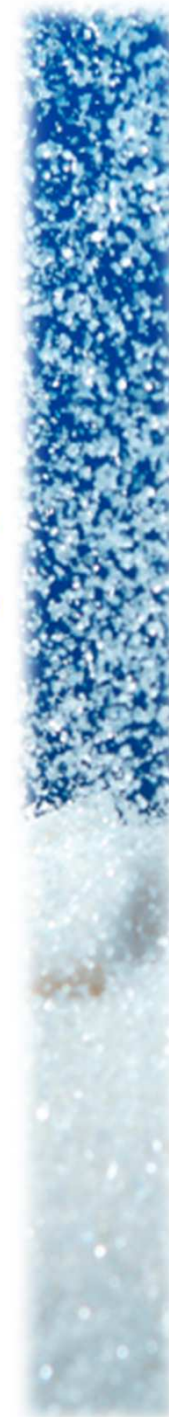
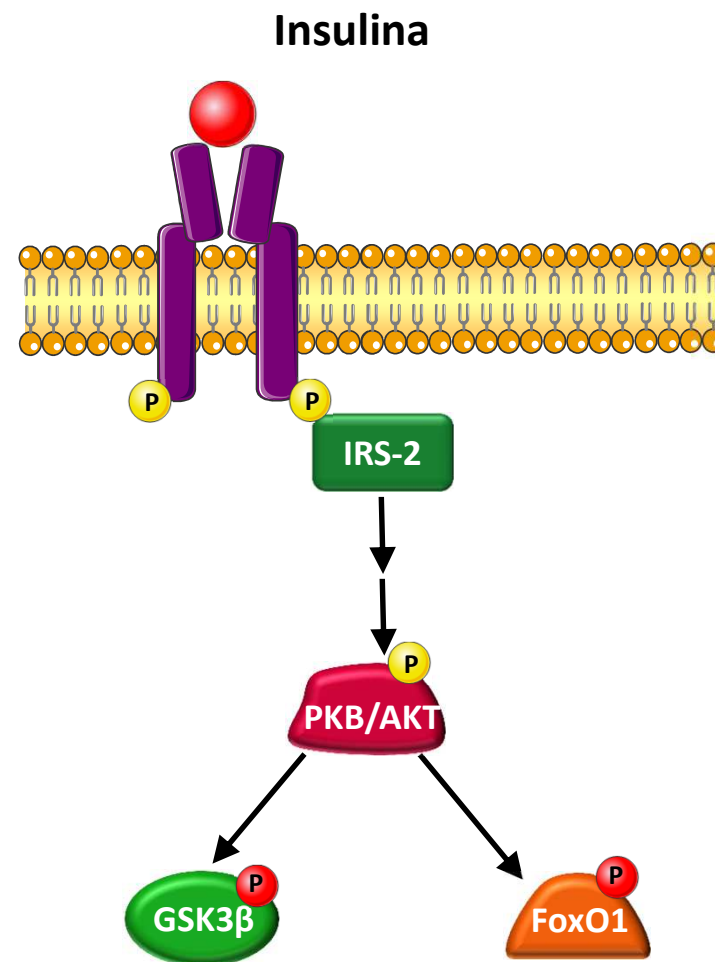
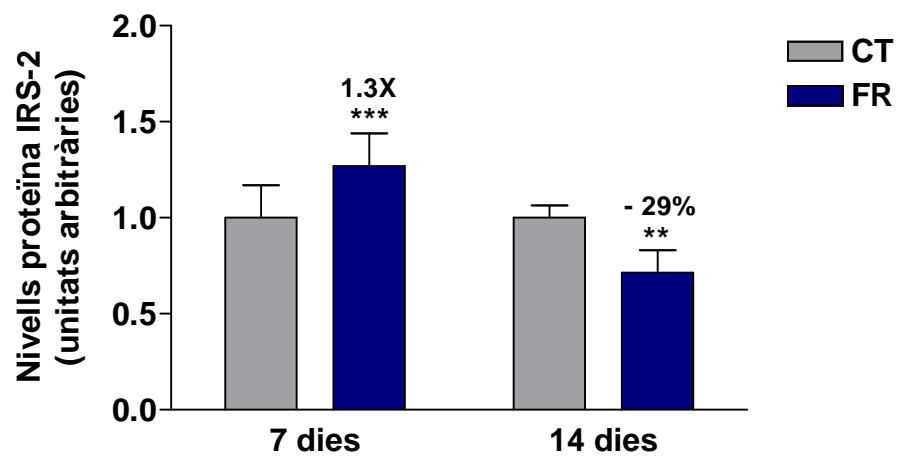
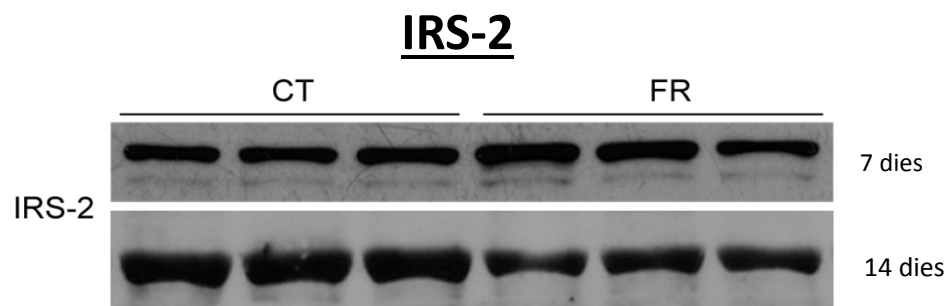
Intolerància a la glucosa



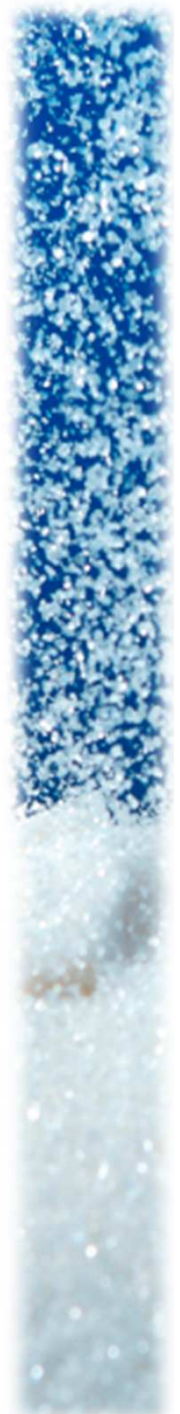
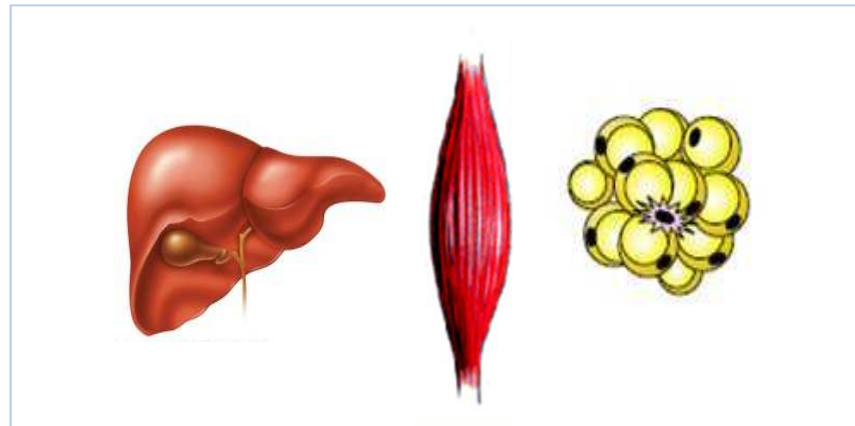
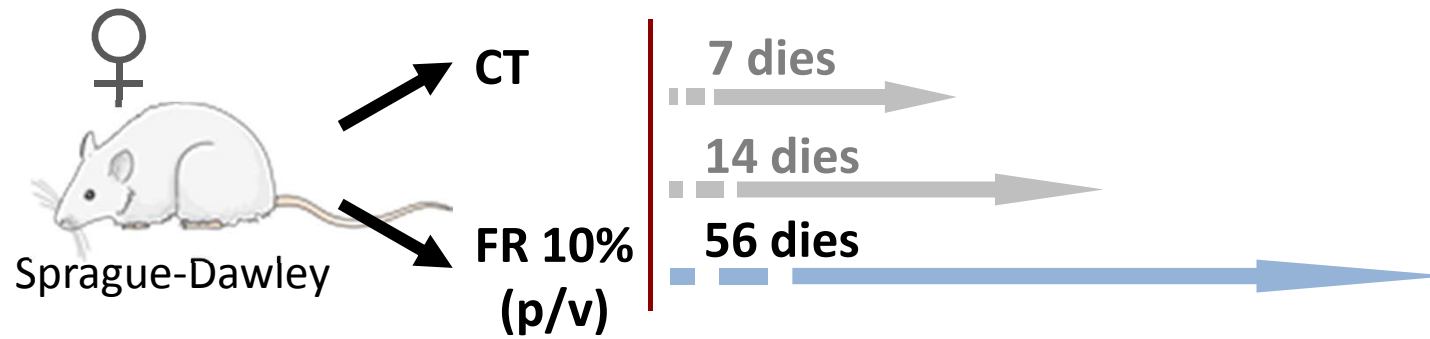
TEST DE TOLERÀNCIA A LA GLUCOSA



Mecanisme?



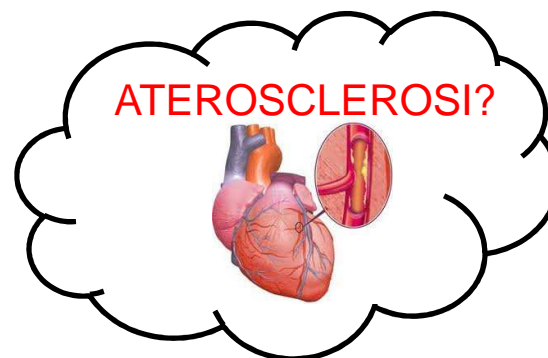
Projectes actuals



Projectes actuals



Factors de risc
CV



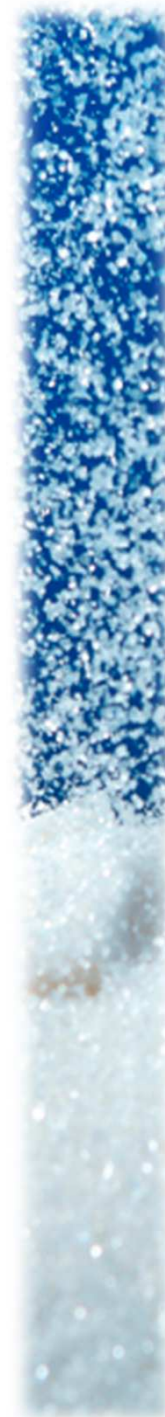
C57/BL6

Poc susceptible a la formació de lesions



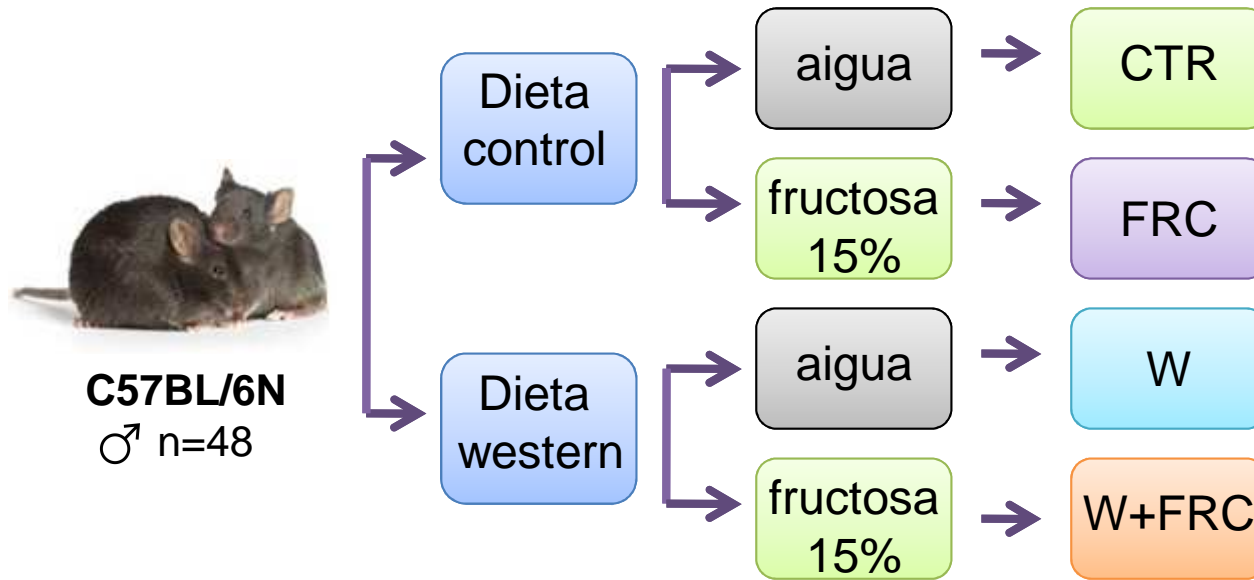
rLDL^{-/-}

- Modesta hipercolesterolèmia amb dieta normal
- Requereix dietes modificades per desenvolupar aterosclerosi
- Lesions en arrel aòrtica, morfologia simple
- Bon model per l'estudi de malaltia hepàtica grassa no alcohòlica (NAFLD)

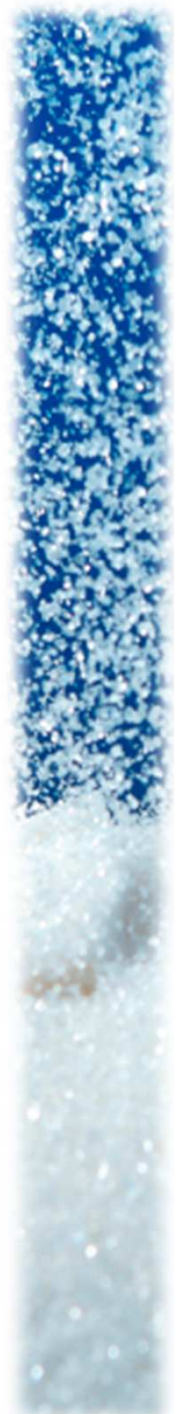


Projectes actuals

Ratolins C57BL/6N

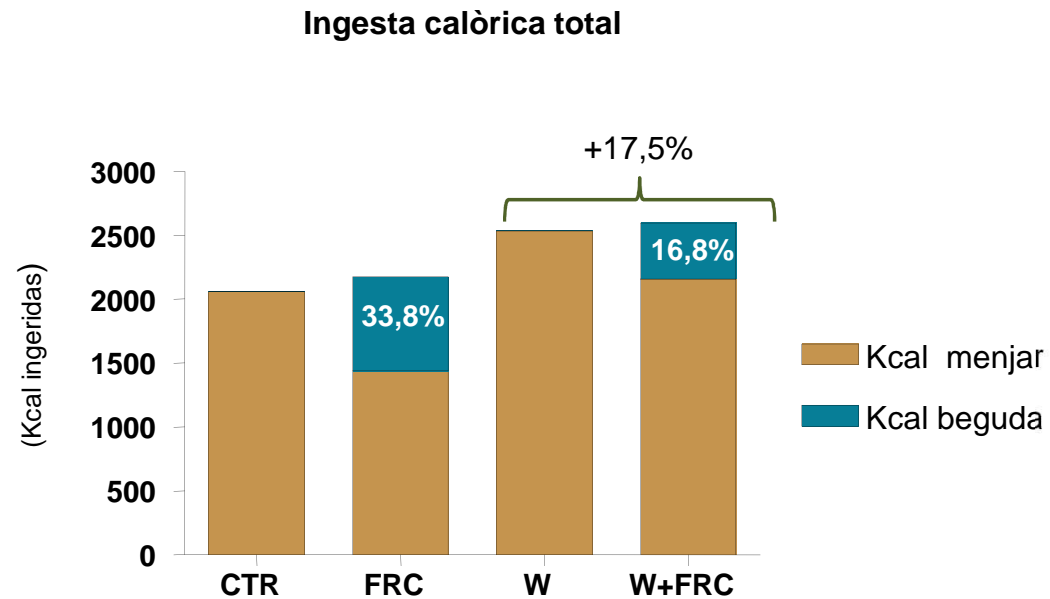
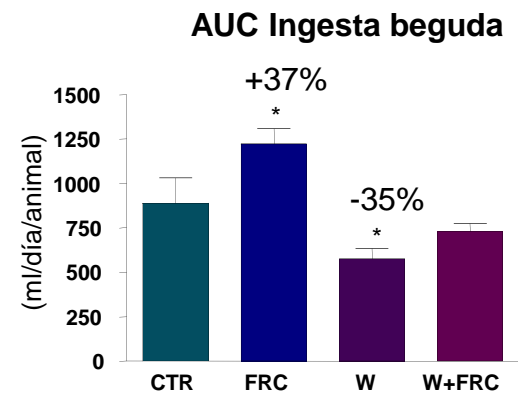
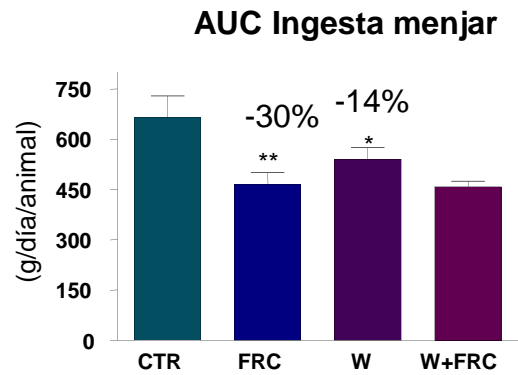


APORT	D. CONTROL	D. WESTERN
PROTEÏNES	24%Kcal	16%Kcal
H.de C	58%Kcal	43%Kcal
GREIX	18%Kcal	41%Kcal
CALORIES	3,1Kcal/g	4,7Kcal/g

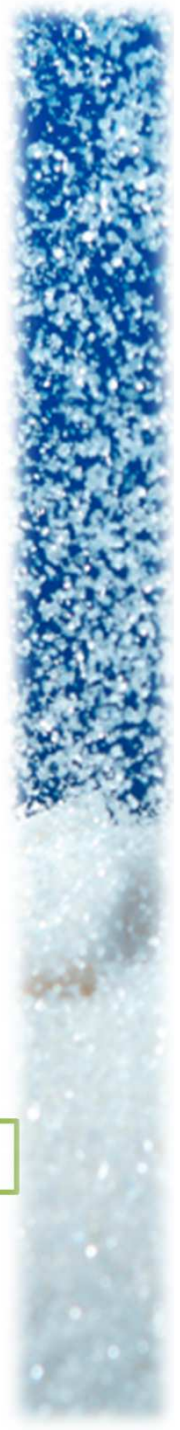


Projectes actuals

Ratolins C57BL/6N



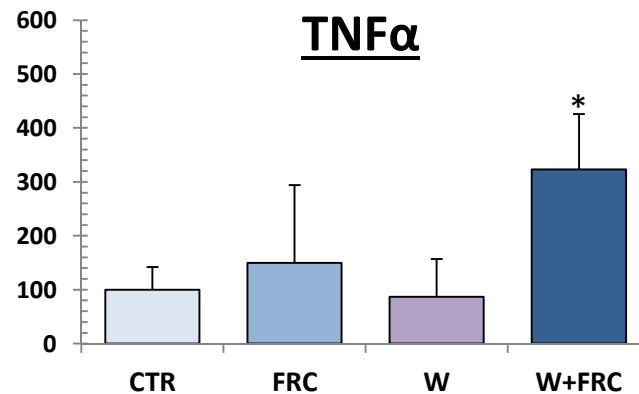
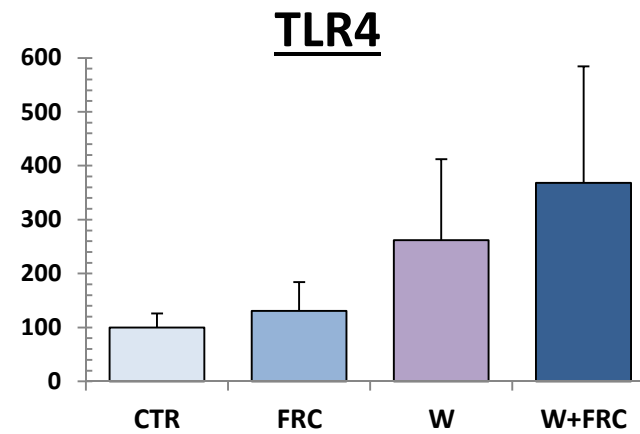
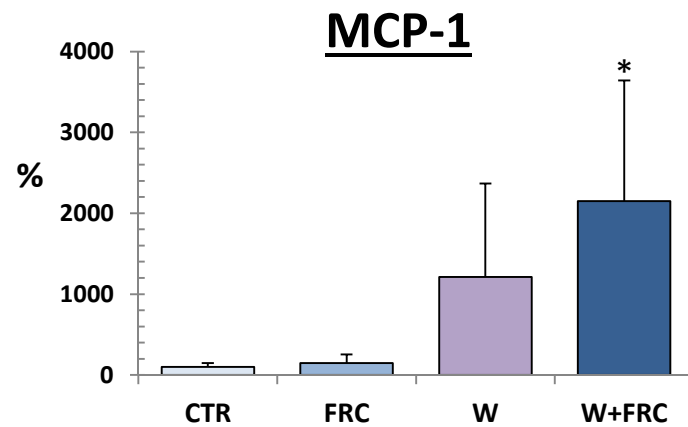
ÒPTIMA COMPENSACIÓ DE LA INGESTA CALÒRICA



Projectes actuals

Ratolins C57BL/6N

- Teixit adipós. Inflamació

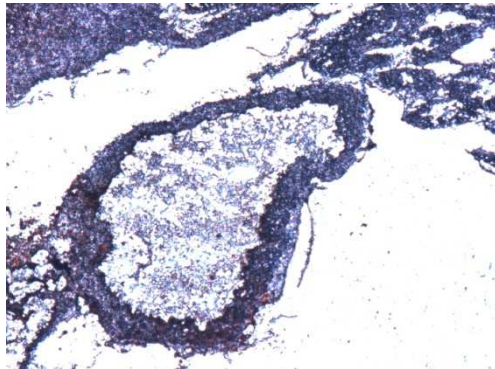


Projectes actuals

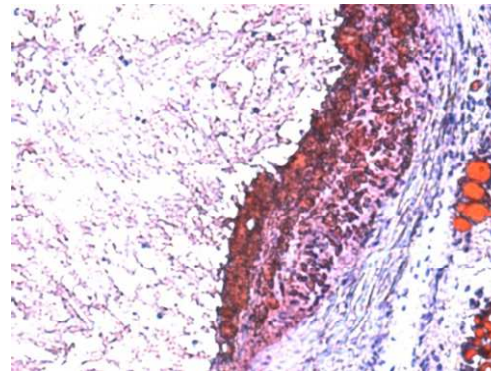
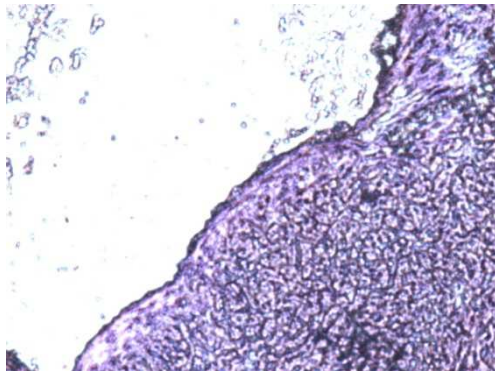
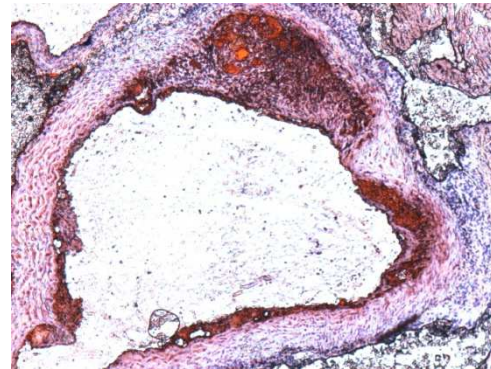
Ratolins rLDL^{-/-}

Talls aorta, tinció Oil Red O

Control

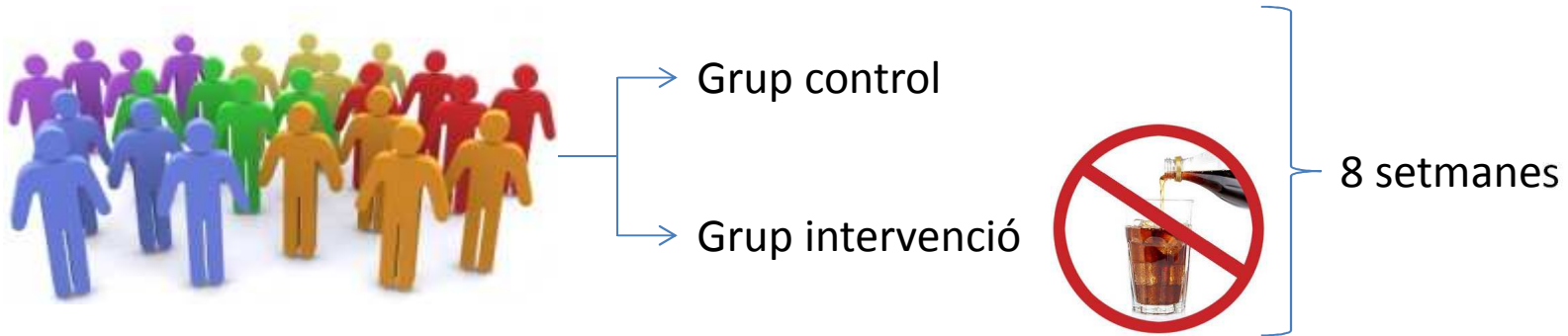


W+F

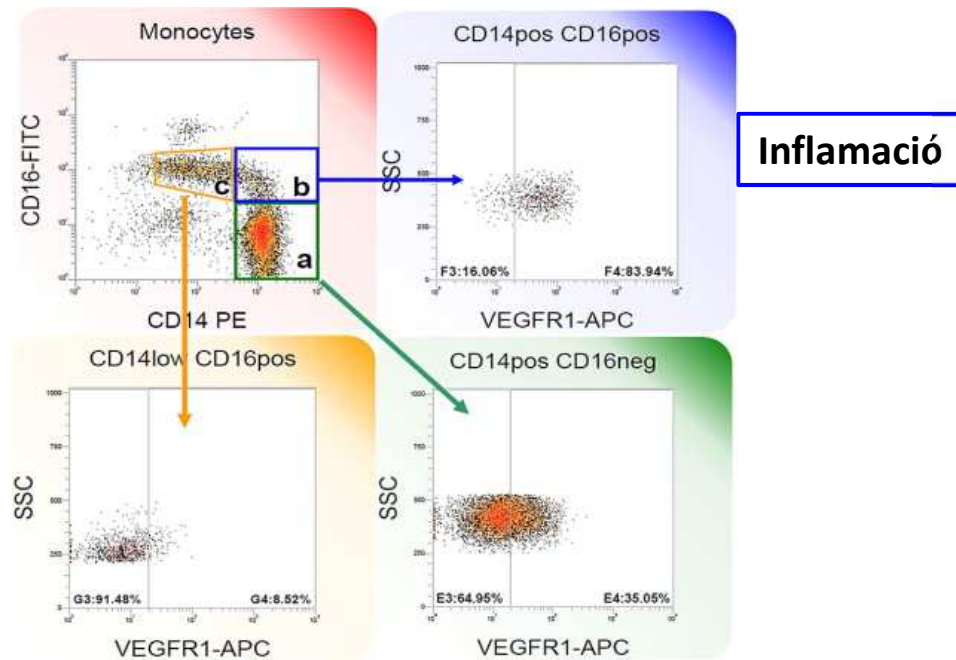


Projectes actuals

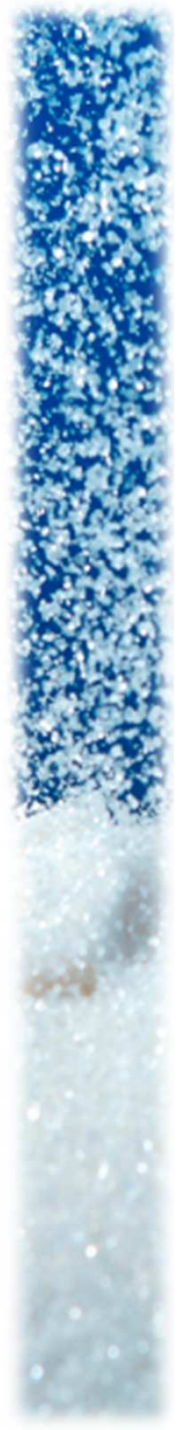
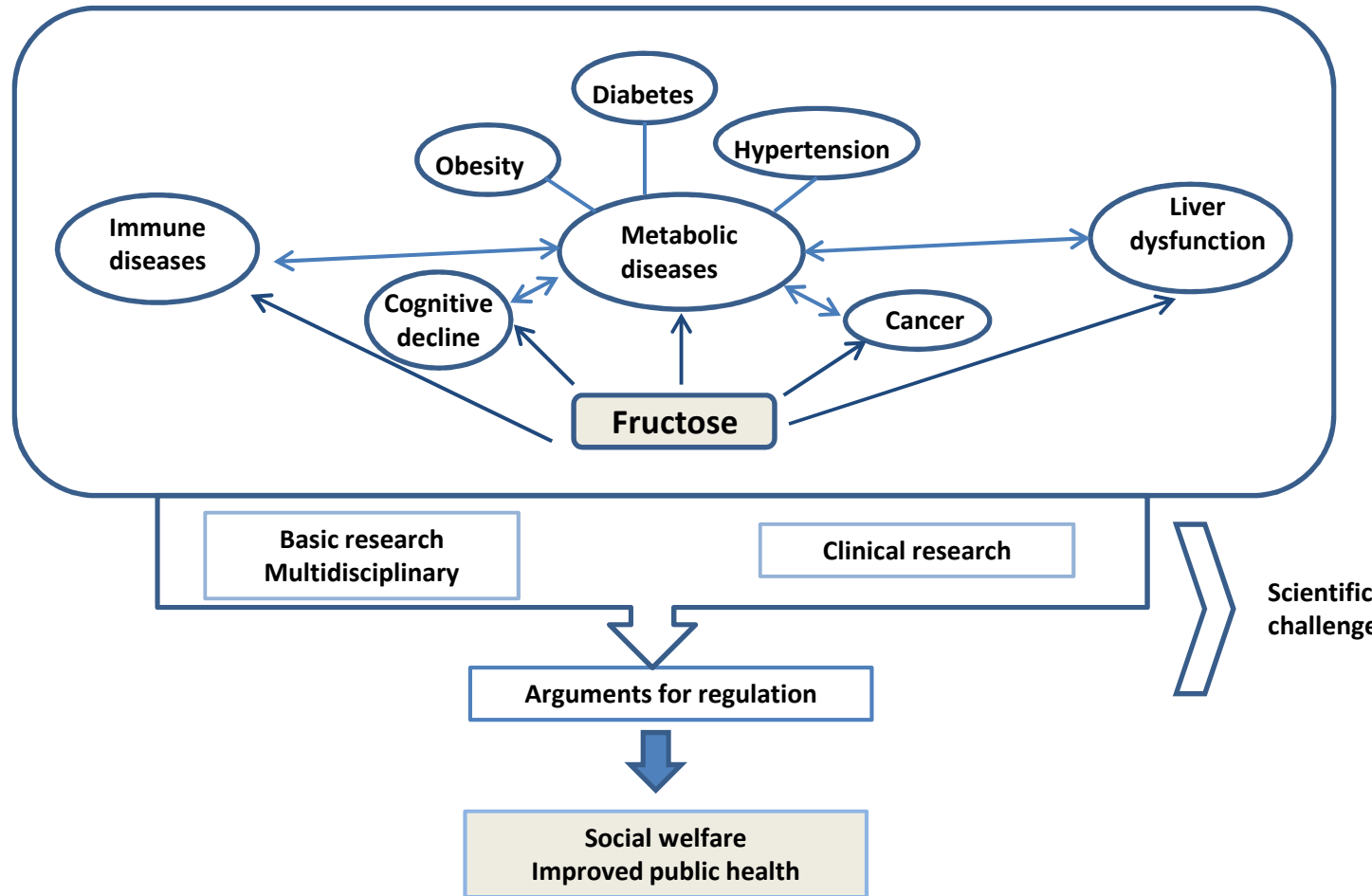
Estudi d'intervenció dietètica en humans (col·laboració amb
Clínica de Lípids, Hospital Clínic de Barcelona)



- 40 pacients amb síndrome metabòlica
- Ingesta $\geq 10\%$ de l'energia diària en forma de sucres simples, majoritàriament begudes edulcorades



Projectes futurs



Grup de recerca i col·laboracions



- Drs. Antoni Camins i Mercè Pallàs, Facultat de Farmàcia, Barcelona
- Dr. Emili Ros, Hospital Clínic, Barcelona
- Dr. Carlos Bocos, Universidad San Pablo-CEU, Madrid
- Dra. Roshanak Rahiminian, School of Pharmacy and Health Sciences, Univ. of the Pacific, Stockton, CA

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Centro de Investigación Biomédica en Red
Fisiopatología de la Obesidad y la Nutrición

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