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Metabolic syndrome

Clustering of risk factors or medical disorders that increases the risk of developing cardiovascular disease or type II diabetes

Definition (IDF):

Central obesity
(usually BMI > 30 kg/m²),
plus 2 of the following:

- TGs > 150 mg/dL
- HDL < 40-50 mg/dL
- ↑ blood pressure
- hyperglycemia

“ syndrome X...

... cardiometabolic syndrome

insulin resistance syndrome...

... Reaven's syndrome “

... Reaven's syndrome “

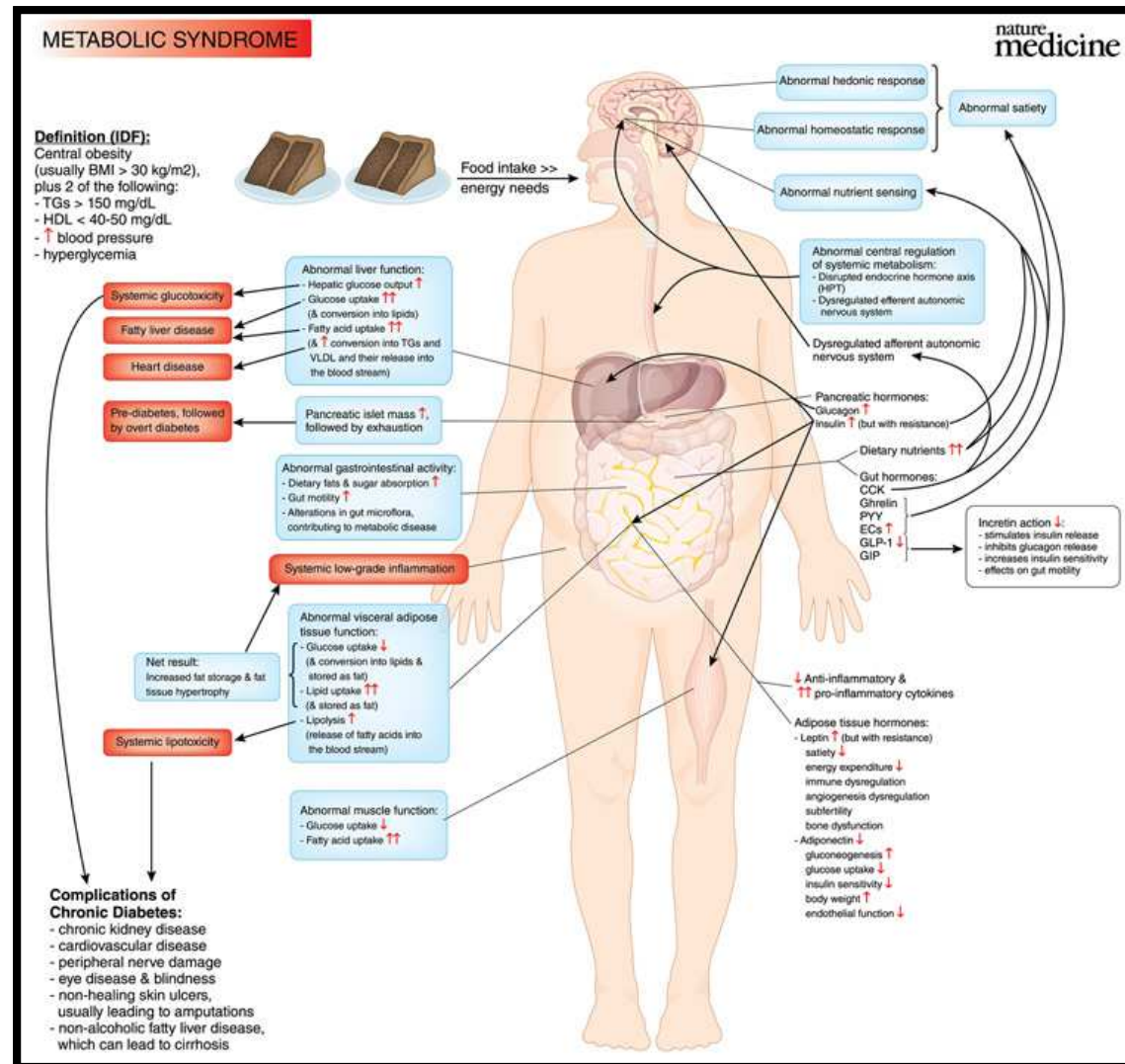
insulin resistance syndrome...



Metabolic syndrome

Insulin
resistance

Ectopic fat /
lipotoxicity

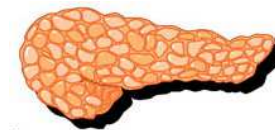
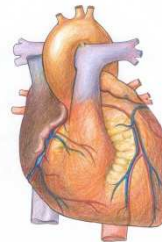
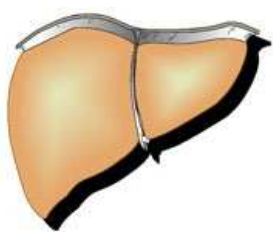


Ectopic Fat / Lipotoxicity

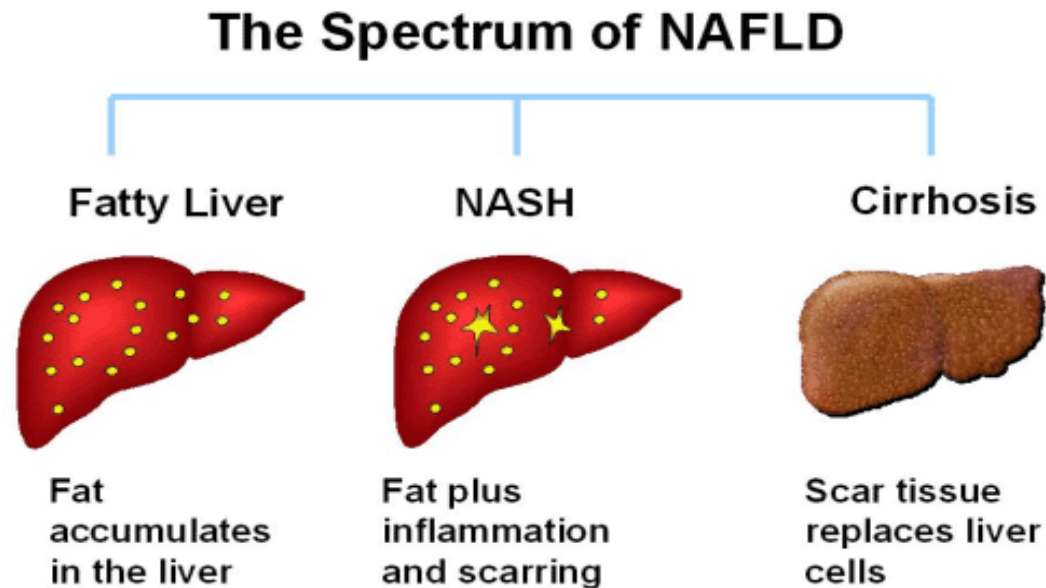
'when tissues overeat'

the deposition of triglycerides within cells of non-adipose tissue that normally contain only small amounts of fat

leading to cell dysfunction or cell death.



Intra Hepatic lipids (IHL)



■ Consequences:

- *Hepatic insulin resistance*
- *Decreased insulin clearance*
- *Disturbed lipid metabolism*

■ High Prevalence

(e.g. 33.6% in the Dallas Heart study;
Szczepaniak, L.S. et al, 2005)



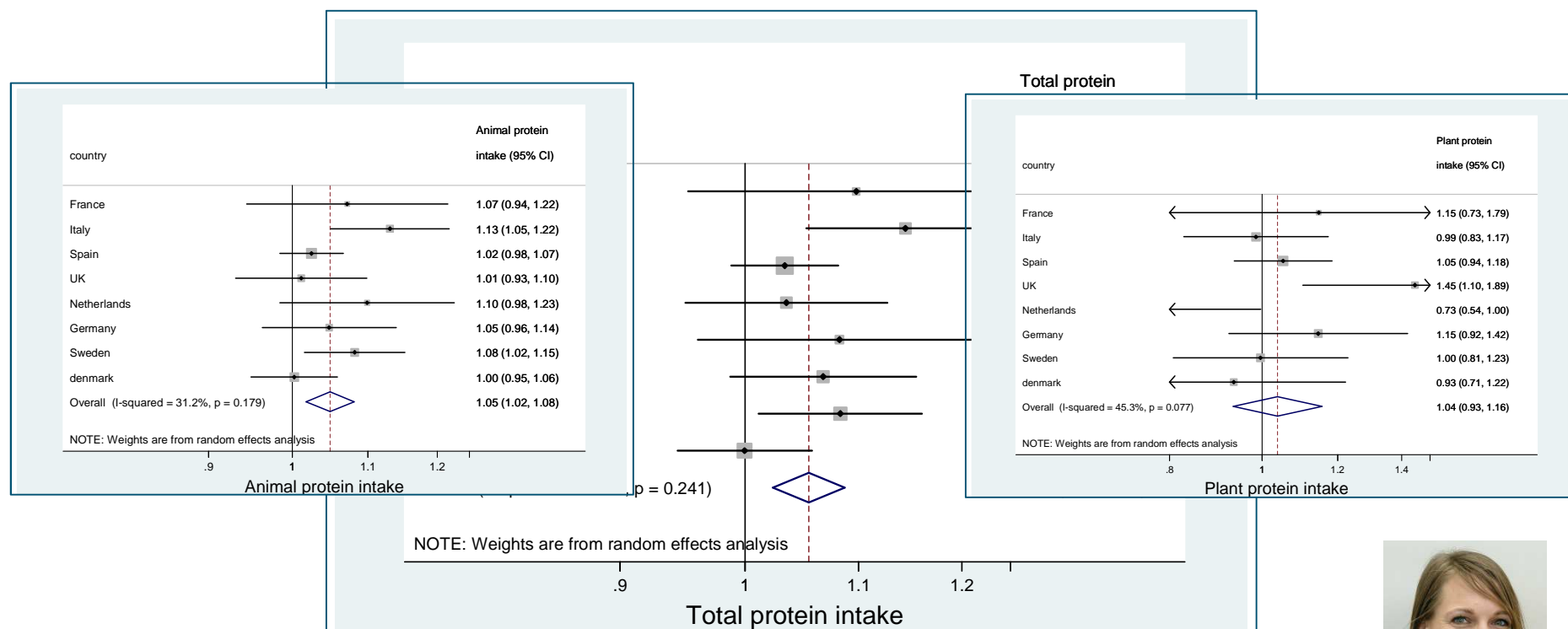
DIETARY PROTEINS



Dietary Protein & Metabolic Syndrome

- Epidemiological data
 - Increased risk type 2 diabetes mellitus

Dietary protein intake and incidence of Type 2 Diabetes in Europe: *The EPIC-InterAct Case-Cohort Study.*



Dietary Protein & Metabolic Syndrome

- Epidemiological data
 - Increased risk type 2 diabetes mellitus

- BCAA: biomarker associated with DM risk
 - Cross-sectional and prospective

- Infusion amino acids
 - Decrease insulin sensitivity



Dietary Protein & Metabolic Syndrome

- Weight-loss, improved weight maintenance
 - Preservation lean mass
 - Increased satiety
 - Increased thermogenesis
- Metabolic improvements
 - Insulin secretion
 - Glucose homeostasis, insulin resistance
- Liver metabolism
 - Decrease IHL, lower circulating markers of liver dysfunction
 - reduced lipogenesis, increased gluconeogenesis and glycogen synthesis (*rodent data*)

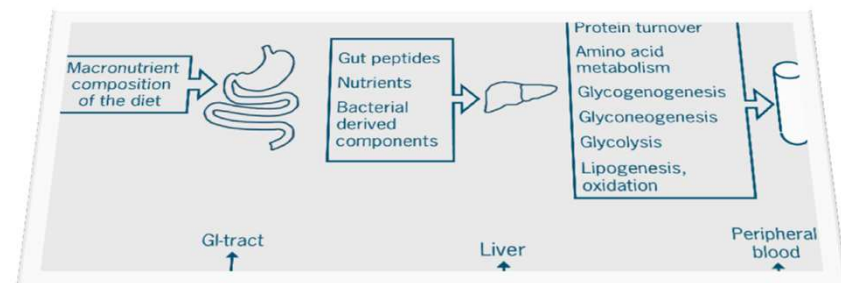


Influence of dietary protein on metabolic phenotype and gene expression in the gut-liver axis



To understand the effects of **increasing protein intake at the expense of carbohydrates**, in a high-fat-hypercaloric-diet

- on **phenotype adaptation** of body composition, intra hepatic lipids and the gut.
- on *nutrients homeostasis*, risk of metabolic disorders and associated diseases.
- on *gene expression in liver, adipose tissue and intestine*

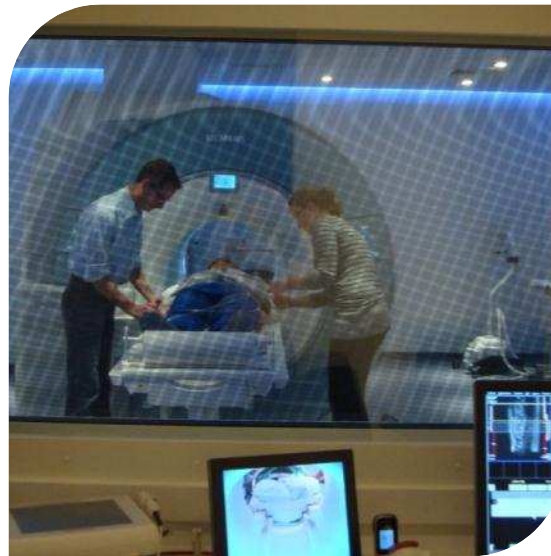


Human Research Facilities

Division of Human Nutrition



Controlled intervention
Dietary Facilities



Hepatic steatosis
Nutritional Imaging

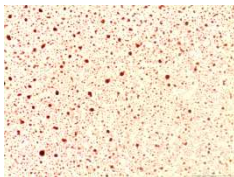
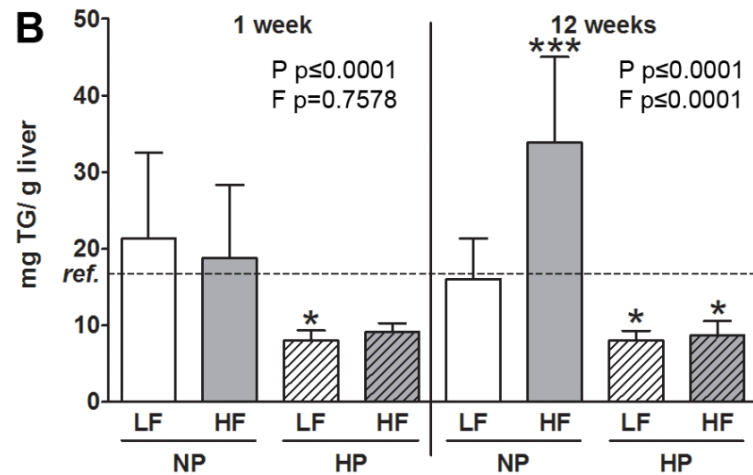


Metabolism
Metabolic Ward



Protein manipulation modifying phenotype: *prevention of fat induced increase in liver fat*

Mouse study:

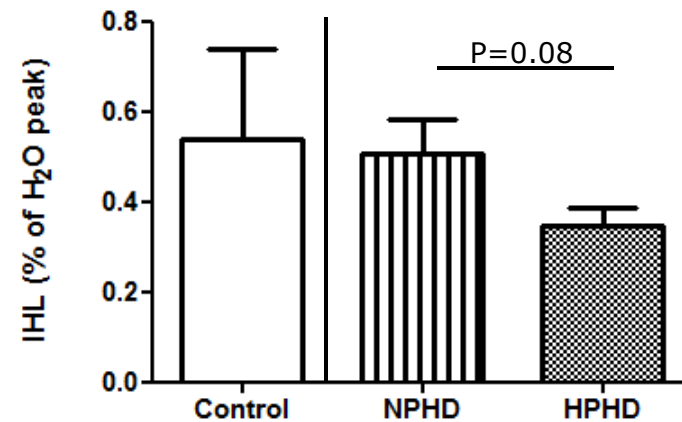


15 en% protein (NP)



50 en% protein HP

Human study:



Rietman, A. *unpublished data*

Chaumontet, C. *unpublished data*

Schwarz, J. et al., PLoS ONE 2012.



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Dietary Protein and IHL

High protein intake reduces intrahepatocellular lipid deposition in humans¹⁻³

Murielle Bortolotti, Roland Kreis, Cyrille Debard, Bertrand Cariou, David Faeh, Maud Chetiveaux, Michael Ith, Peter Vermathen, Nathalie Stefanoni, Kim-Anne Lê, Philippe Schneider, Michel Krempf, Hubert Vidal, Chris Boesch, and Luc Tappy

HEPATOLOGY

Open-labeled pilot study of cysteine-rich whey protein isolate supplementation for nonalcoholic steatohepatitis patients

Taned Chitapanarux,* Prasong Tienboon,[†] Suwalee Pojchamarnwiputh[‡] and Donrawee Leelarungrayub[§]

Effects of a whey protein supplementation on intrahepatocellular lipids in obese female patients

Murielle Bortolotti^{a,d}, Elena Maiolo^{a,d}, Mattia Corazza^{a,d}, Eveline Van Dijke^{a,d}, Philippe Schneider^{a,e}, Andreas Boss^{b,f}, Guillaume Carrel^{a,e}, Vittorio Giusti^{c,g}, Kim-Anne Lê^{a,h}, Daniel Guae Quo Chong^{b,f}, Tania Buehler^{b,f}, Roland Kreis^{b,f}, Chris Boesch^{b,f}, Luc Tappy^{a,c,*}

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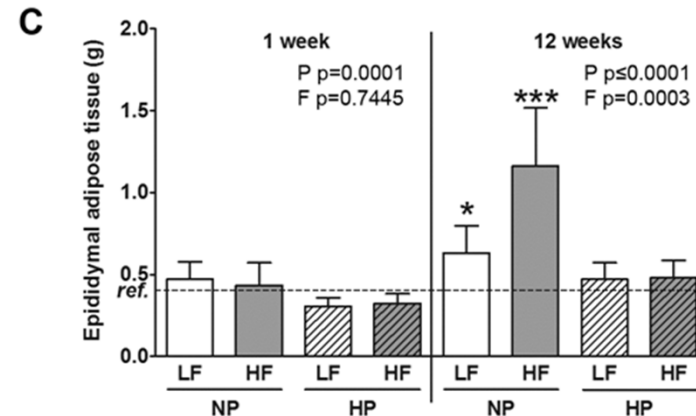
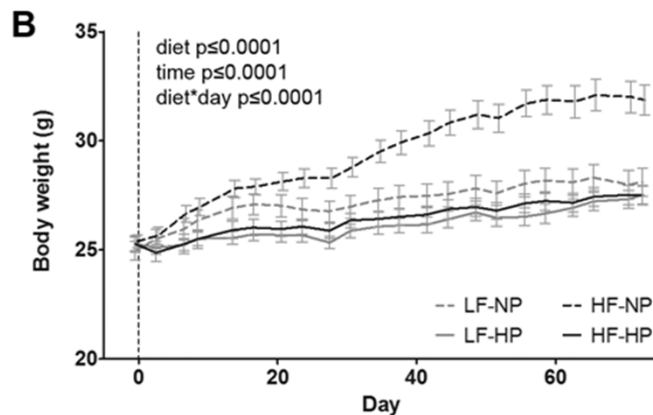


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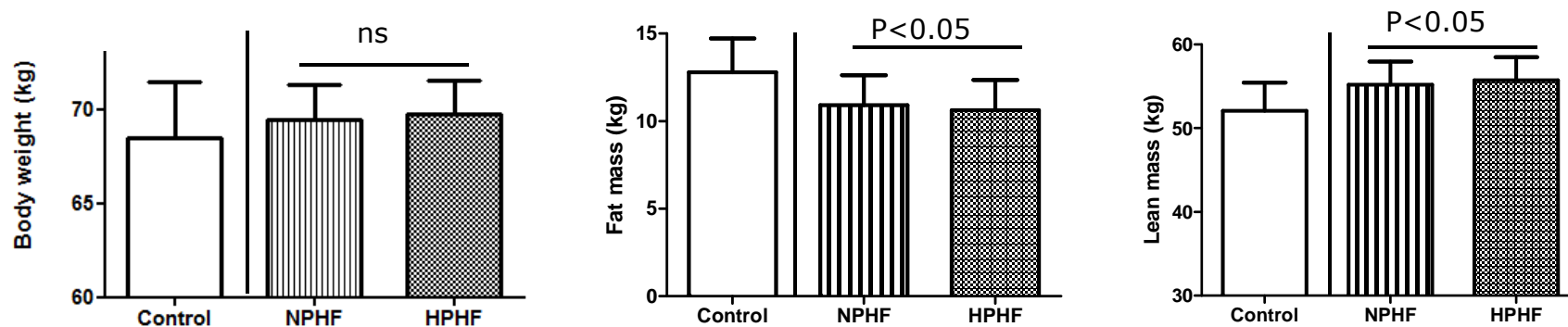
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Protein manipulation modifying phenotype: *prevention of increase BW and adipose tissue*

Mouse study:



Human study:



Protein manipulation modifying phenotype: *insulin resistance*

Human study:

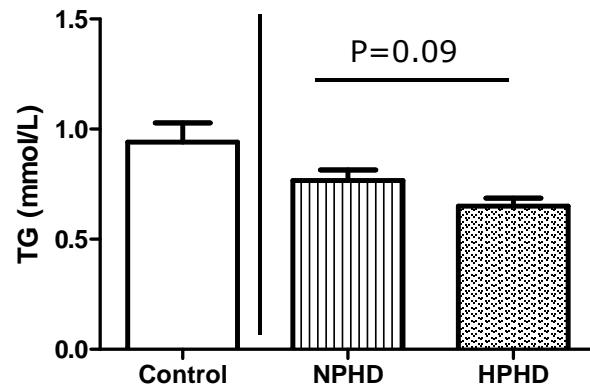
	control	HD	
	2 weeks	NPHF	HPHF
HOMA-IR ² (mmol/L × μU/ml)	0.91 ± 0.14	0.95 ± 0.14	0.90 ± 0.15
Glucose (mmol/L)	5.07 ± 0.04	5.03 ± 0.08	5.05 ± 0.09
Insulin (μU/L)	4.01 ± 0.62	4.21 ± 0.62	3.95 ± 0.63

Rat study:

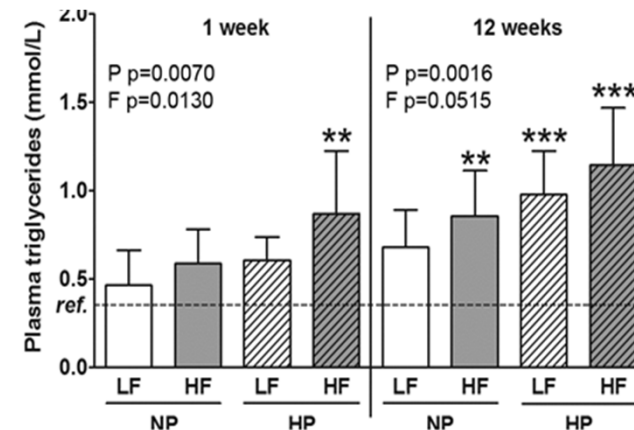
- No effect of increasing protein intake on several markers of insulin action and glycemic control

Protein manipulation modifying phenotype: *blood lipids*

Human study:



Mouse study:



Rat study:

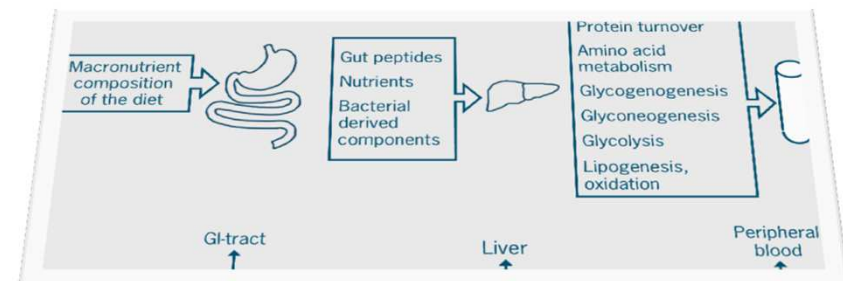
Study:	NP			HP			
	C	HS	HS-HF	C	HS	HS-HF	
Fasted							
Triglyceride (mM/l)	0.9±0.9	1.0±0.4	1.1±0.3	0.6±0.1	0.6±0.1	0.6±0.1	P (<0.001)
Cholesterol (mM/l)	1.8±0.2	1.9±0.3	1.8±0.2	2.0±0.5	1.7±0.5	2.1±0.5	NS
HDL (mM/l)	1.2±0.1	1.2±0.2	1.2±0.1	1.4±0.3	1.2±0.3	1.4±0.3	P (<0.05)



Conclusions

Impact of high dietary protein on biomarkers of metabolic syndrome when fed a high-fat diet:

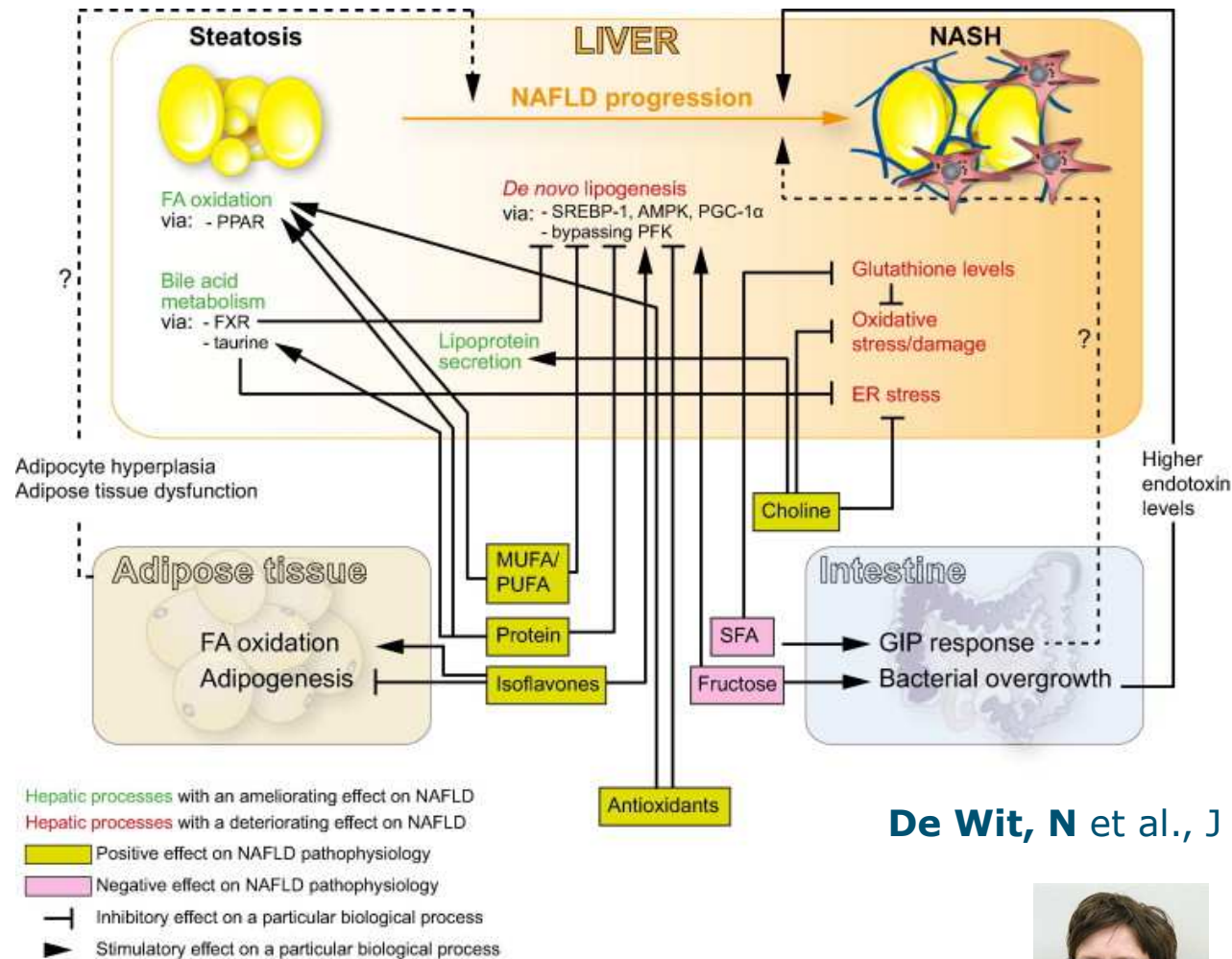
- Liver lipids (IHL): reduced
- *Central* adiposity: reduced
- Lipids
 - Triglycerides: decreased / increased
 - HDL-cholesterol: increased
- Insulin sensitivity:
 - no effect in a young, metabolic flexible population



MARINE INGREDIENTS



'Phenotyping the effect of diet on NAFLD'



De Wit, N et al., J Hepatol 2012.



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Fish and NAFLD

■ Fish oil

- consumption of n-3 fatty acids reduce inflammation, steatosis, and liver damage in NAFLD
 - *MUFA may be useful*
 - *Fish oil improves circulating lipids and lipoproteins*

■ Fish Protein

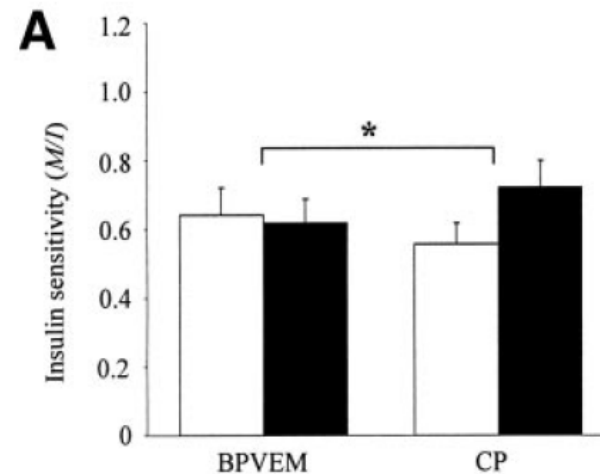
- Protein source important for steatosis (?)

■ Vitamin D

- Vitamin D concentrations have been shown to be associated with NAFLD

Fish protein and glucose metabolism

- **Cod** versus BPVEM
- 4 weeks isocaloric diets
- 19 en% protein
- ~60% of protein cod
- Equivalent amounts SFA/MUFA/PUFA



(Ouellet et al, Diabetes Care 2007)

- Fish protein supplements improve glycemic control in overweight adults (Vikøren, British J Nutrition 2013)



Conclusion - *Opportunities*

■ **High-protein diets** can be considered in people with the metabolic syndrome

- *supports weight loss and improves body composition*
- *Improve insulin action/glucose homeostasis*
- *Reduces intrahepatic lipids*

➤ *Need to know the consequences of (excess) protein*

■ **Fish protein** could be a good quality protein

- More well-controlled human intervention studies needed



Acknowledgements

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Prof Edith Feskens

Jessica Schwarz

Annemarie Rietman

Monique van Nielen

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Prof Michael Muller

Dietetics:

Els Siebelink



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ALPRO FOUNDATION

