Dietary Protein and the Metabolic syndrome

Opportunities for marine ingredients?

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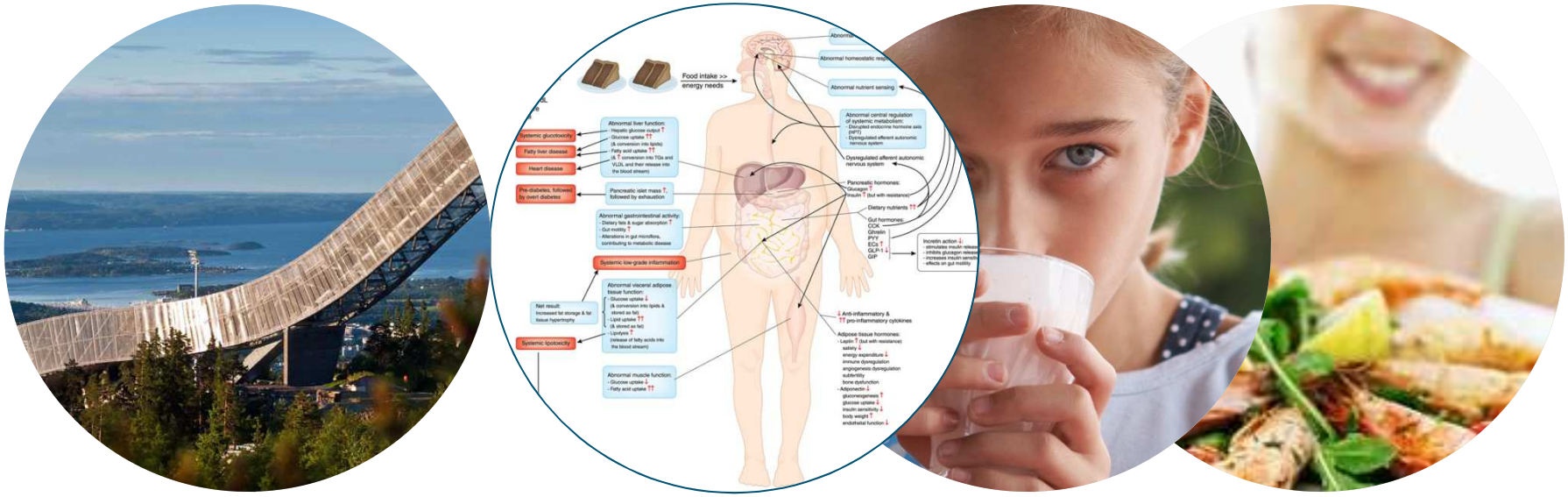
Division of Human Nutrition, chair Nutrition and Health

MIC 2013, Oslo, Norway



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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

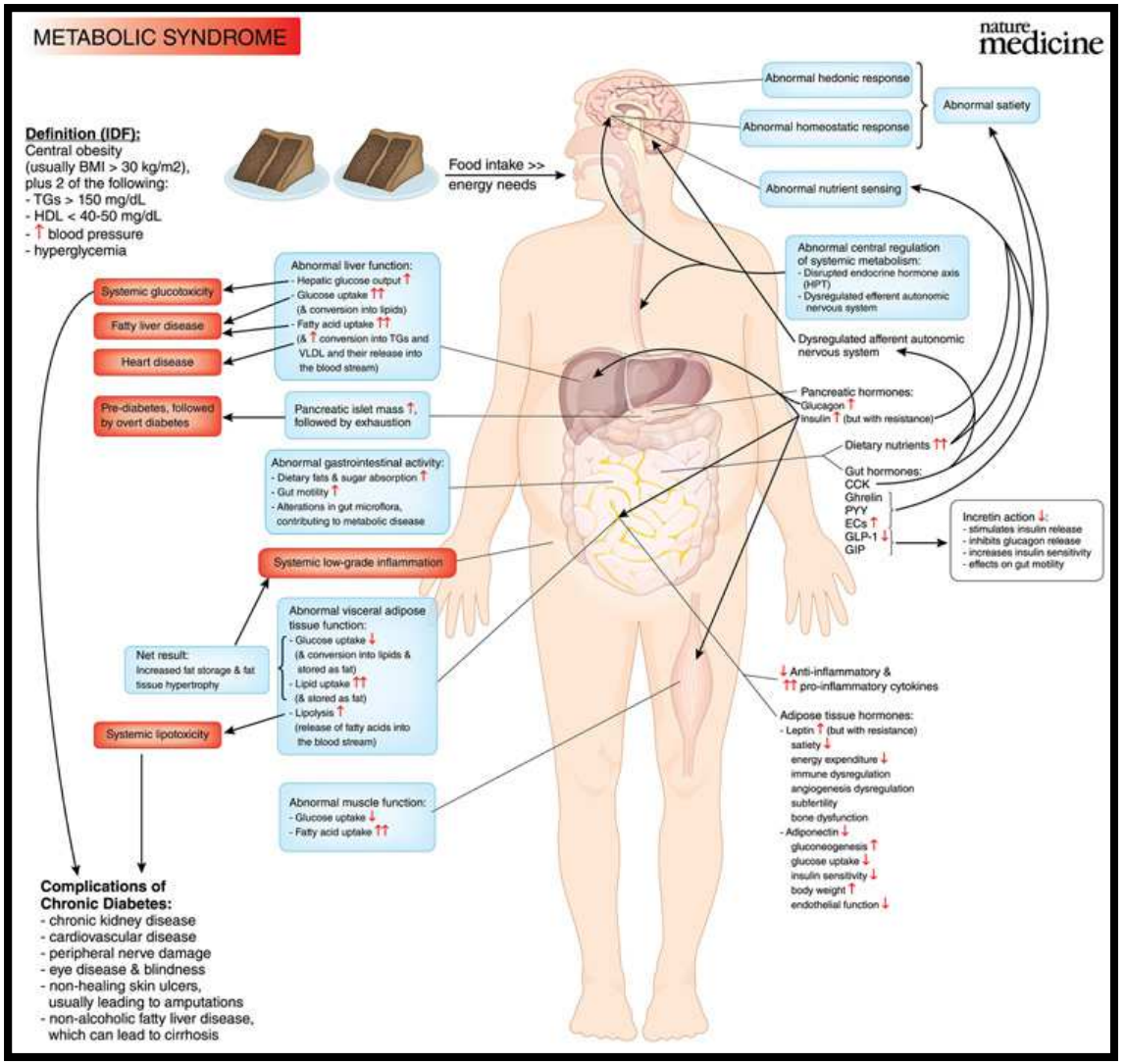
Definition (IDF):
Central obesity
(usually BMI > 30 kg/m2),
plus 2 of the following:
- TGs > 150 mg/dL
- HDL < 40-50 mg/dL
- ↑ blood pressure
- hyperglycemia

" syndrome X...
... cardiometabolic syndrome
insulin resistance syndrome...
... Reaven's syndrome "

Metabolic syndrome

Insulin resistance

Ectopic fat / lipotoxicity

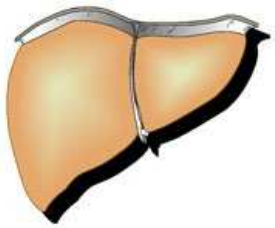


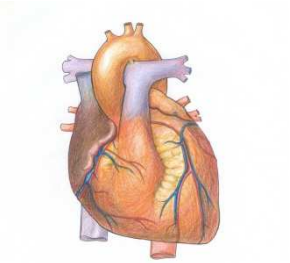
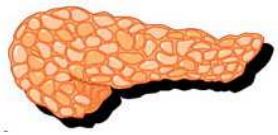
Ectopic Fat / Lipotoxicity

'*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.



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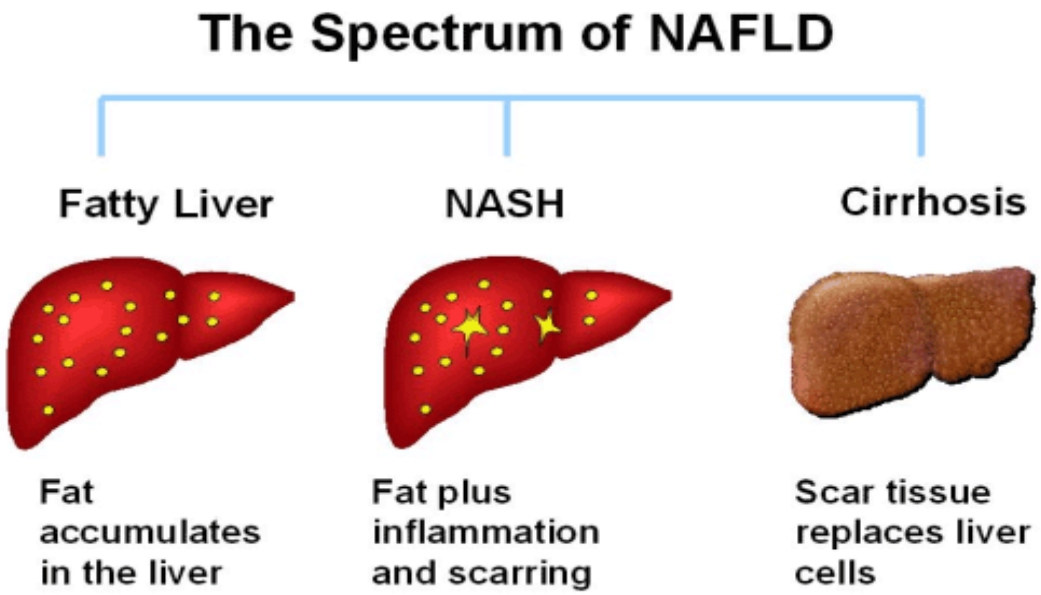
(Schaffer, Curr Opin Lipidol, 2003)

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*)

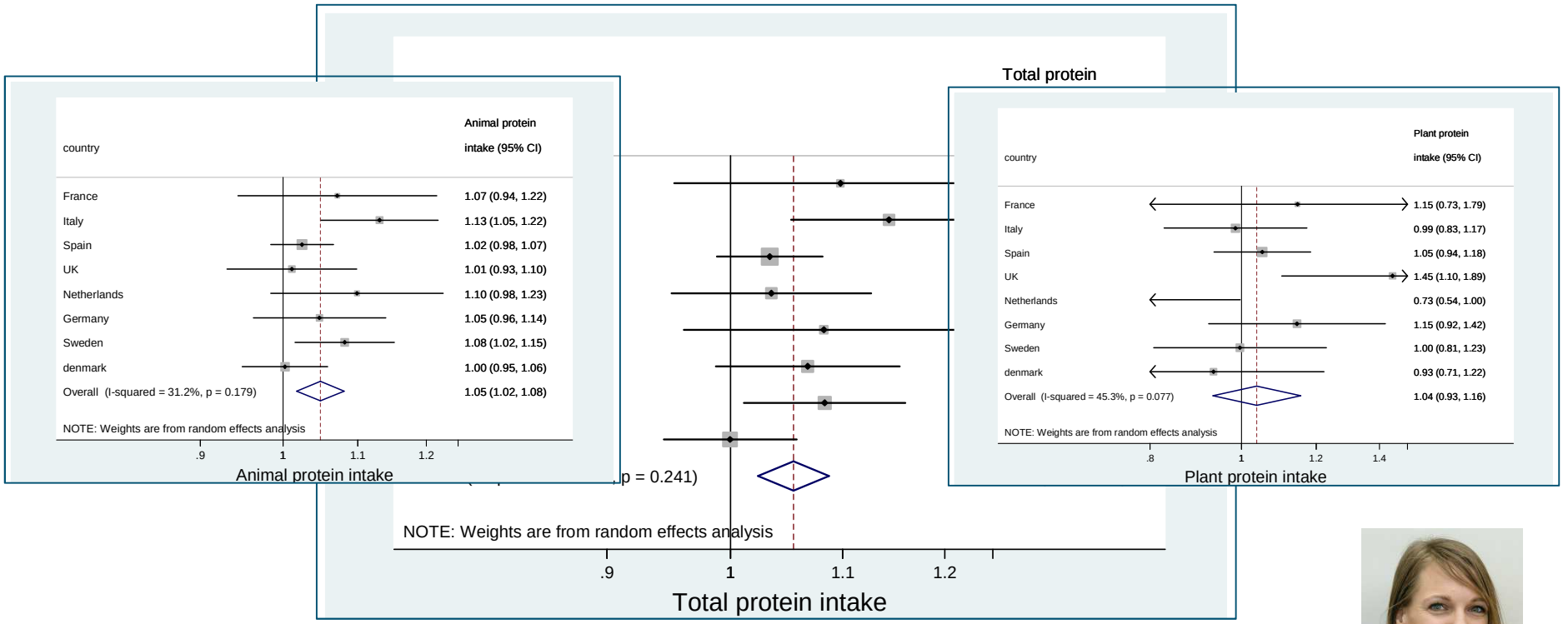
DIETARY PROTEINS

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.



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InterAct

Van Nielen, M. *unpublished data*

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

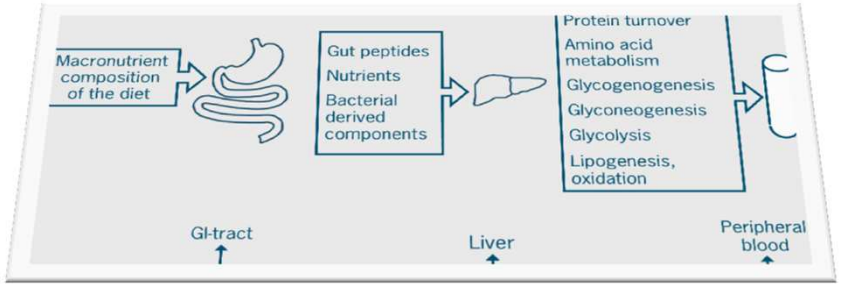
Dietary Protein & Metabolic Syndrome

- 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*



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Human Research Facilities

Division of Human Nutrition

Controlled intervention

Dietary Facilities

Hepatic steatosis

Nutritional Imaging

Metabolism

Metabolic Ward

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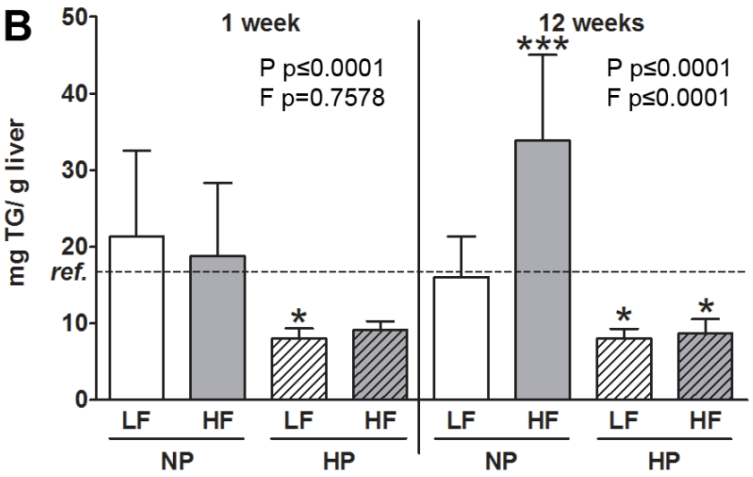
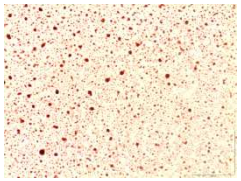
Protein manipulation modifying phenotype: *prevention of fat induced increase in liver fat*

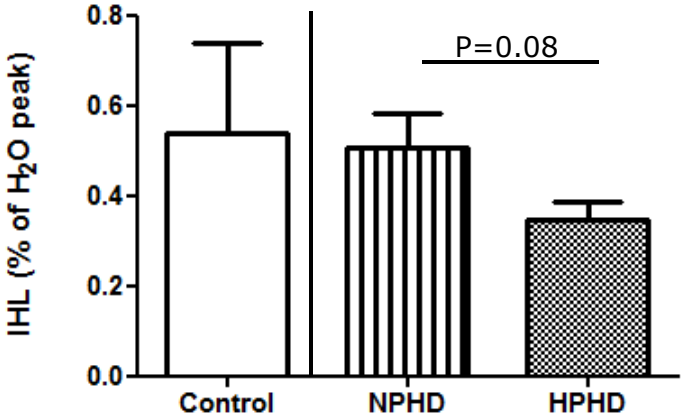
Mouse study:





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 humans[1–3]

Murielle Bortolotti, Roland Kreis, Cyrille Debard, Bertrand Cariou, David Faeh, Maud Chetiveaux, Michael Ith, Peter Vermathen, Nathalie Stefanoni, Kim-Anne Lê, Philippe Schneiter, 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 Schneiter[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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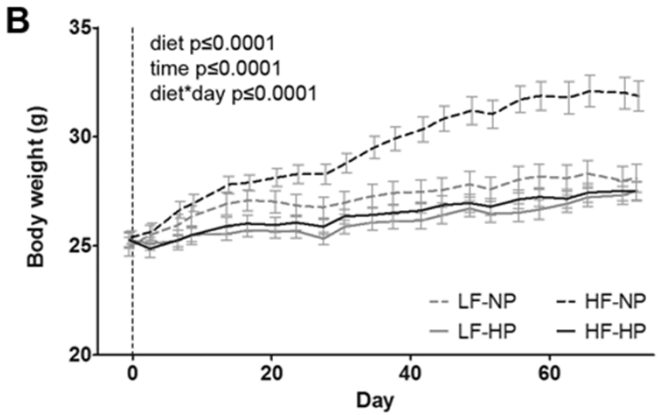
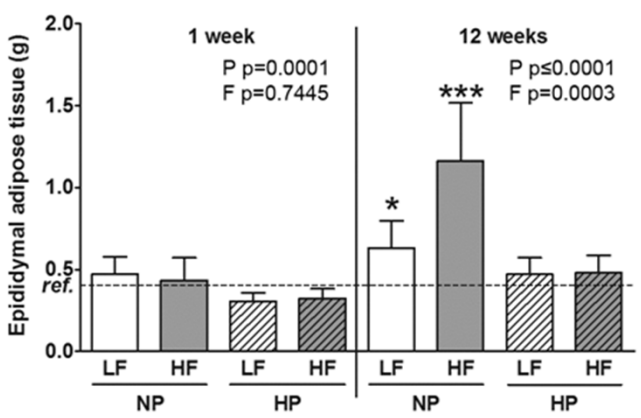
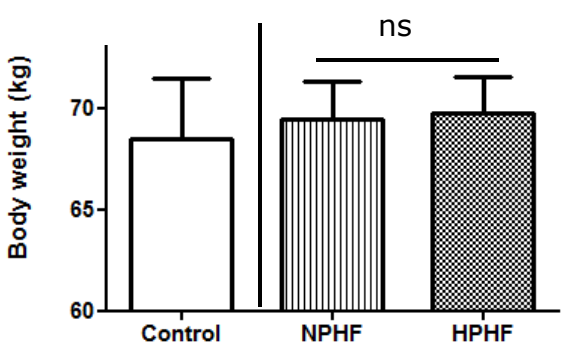
Protein manipulation modifying phenotype: *prevention of increase BW and adipose tissue*

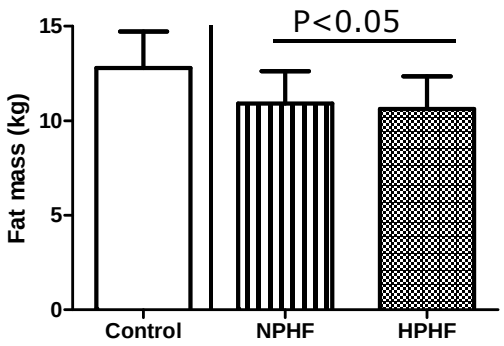
Mouse study:

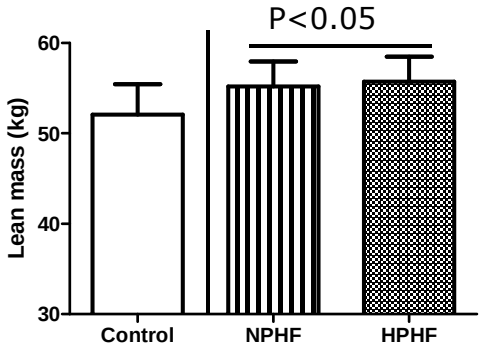




Human study:







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Protein manipulation modifying phenotype: *insulin resistance*

Human study:

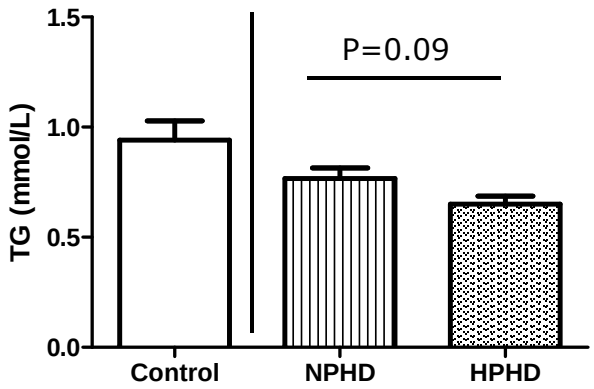
	control	HD	
	2 weeks	NPHF	HPHF
HOMA-IR² (mmol/L × µU/ml)	0.91 ± 0.14	0.95 ± 0.14	0.90 ± 0.15
Glucose (mmol/L)	5.07 ± 0.04	5.03 ± 0.08	5.05 ± 0.09
Insulin (µU/L)	4.01 ± 0.62	4.21 ± 0.62	3.95 ± 0.63

Rat study:

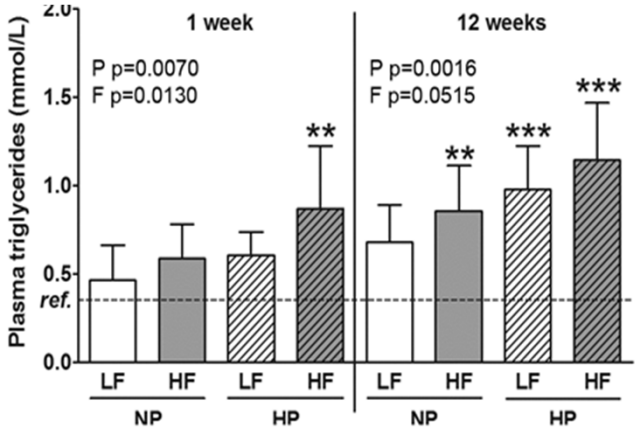
- No effect of increasing protein intake on several markers of insulin action and glycemic control

Protein manipulation modifying phenotype: *blood lipids*

Human study:



Mouse study:



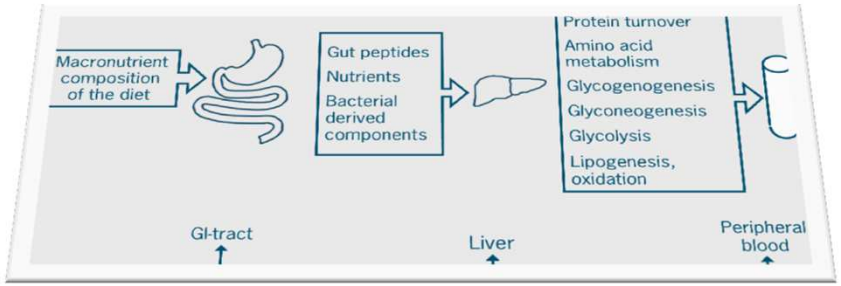
Rat study:

	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

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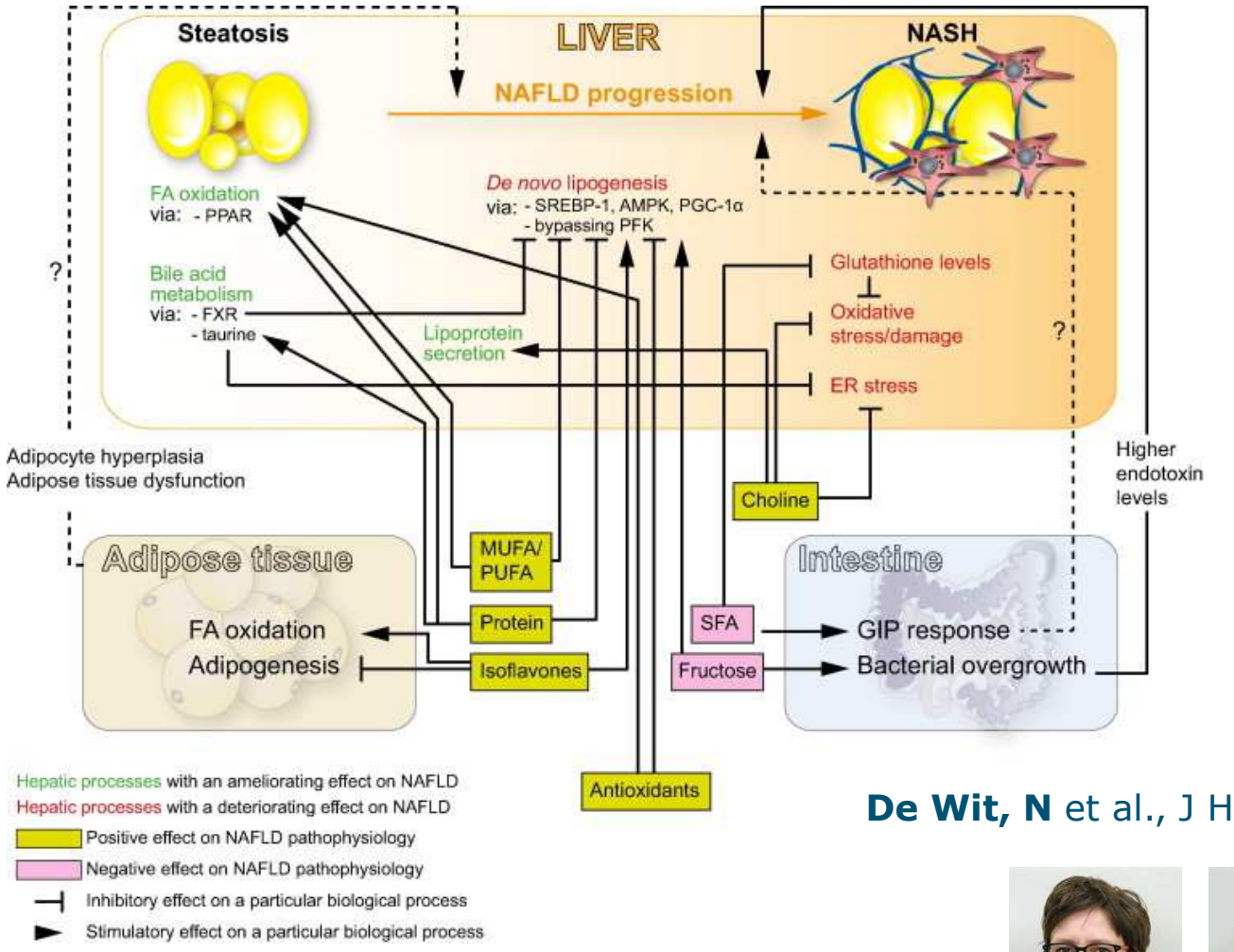
‘Phenotyping the effect of diet on NAFLD’



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

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Fish and NAFLD

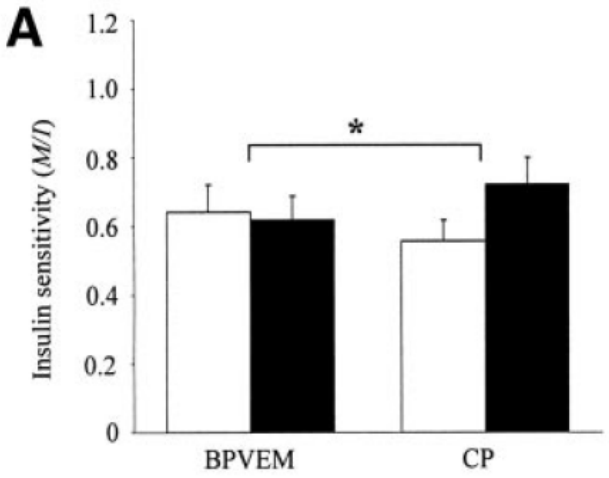
- Fish oil
  - consumption of n-3 fatty acids reduce inflammation, steatosis, and liver damage in NAFLD
  - ➢ *MUFA may be useful*
  - ➢ *Fish oil improves circulating lipids and lipoproteins*

- 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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nzo

nederlandse zuivel organisatie

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