The Role of Dietary Proteins in Maternal Diet in Risk of Development of Glucose Intolerance and Diabetes Mellitus in Offspring

A. Jahan-mihan. PhD. RDN.

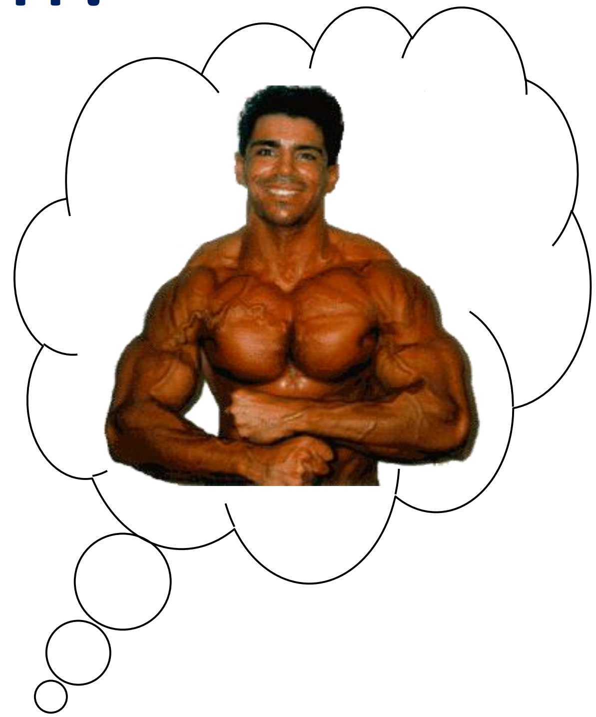
University of North Florida
Department of Nutrition and Dietetics

Diabetologists 2016
Dallas, Texas, USA

Outlines

- Proteins: Nutritional and Physiological Characteristics
- Proteins: Food intake, glucose and fat metabolism
- Proteins during development
- Summary

Why Protein?



Role of Proteins in the Diet

Source of essential amino acids

- Protein synthesis
- Hormones and enzymes
- Synthesis of small molecules
  (serotonin, cathecholamines, glutathione, taurine, nucleic acids)

Source of calorie

Sources of Proteins

Animal vs. plant proteins:

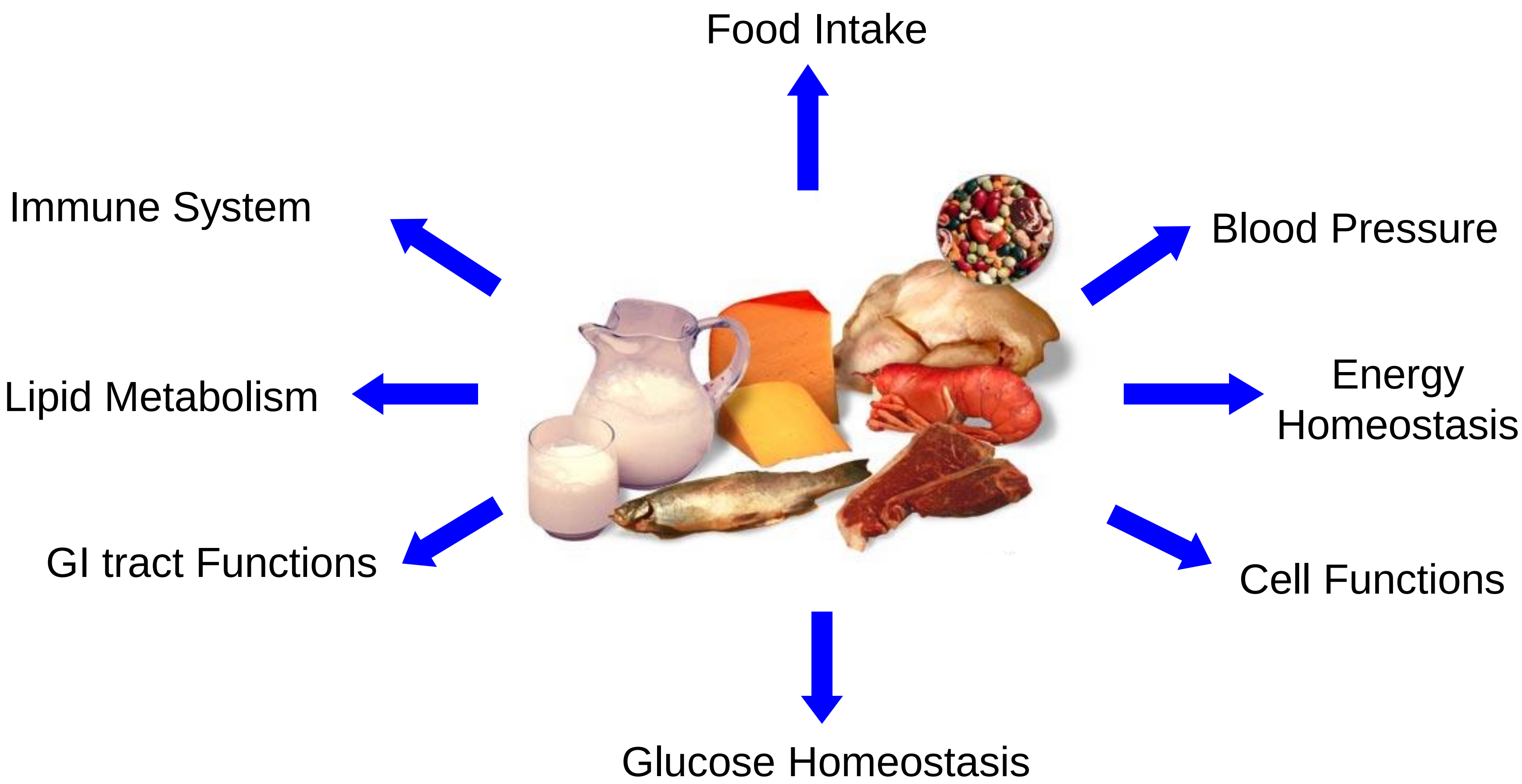
- Amino acid (AA) composition: Limiting AA
- Non-protein components
- Quality of protein

Quality of protein: NPU, BV, PDCAAS:*

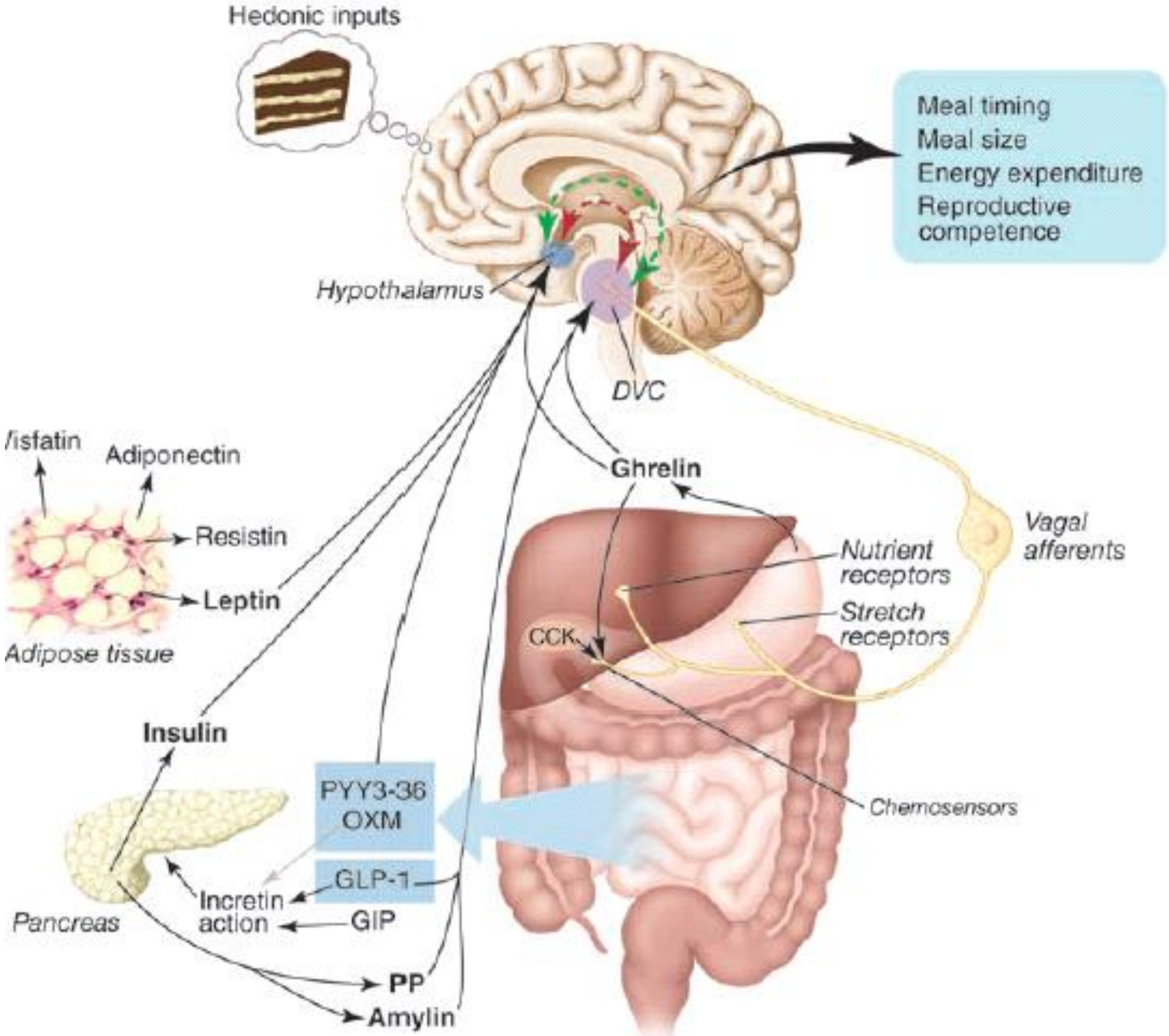
- AA balance
- Bioavailability of proteins:
  - Digestion and absorption
  - Utilization by intestine
  - Digestion kinetics

*Protein Digestibility-Corrected Amino Acid Score

Biological Functions of Proteins



Food Intake Regulatory System



The Gut and Energy Balance: Science March 25 2005

Protein, Food Intake and Body Weight Regulation

- Proteins suppress food intake more than fats and carbohydrate
- High protein diets more satiating than low protein diets and preserve lean body mass
- Protein source as well as quantity is a factor in intake regulation
- Mechanisms accounting for the role of peptides and amino acids in intake regulation are unknown

Protein: Quantity and Source

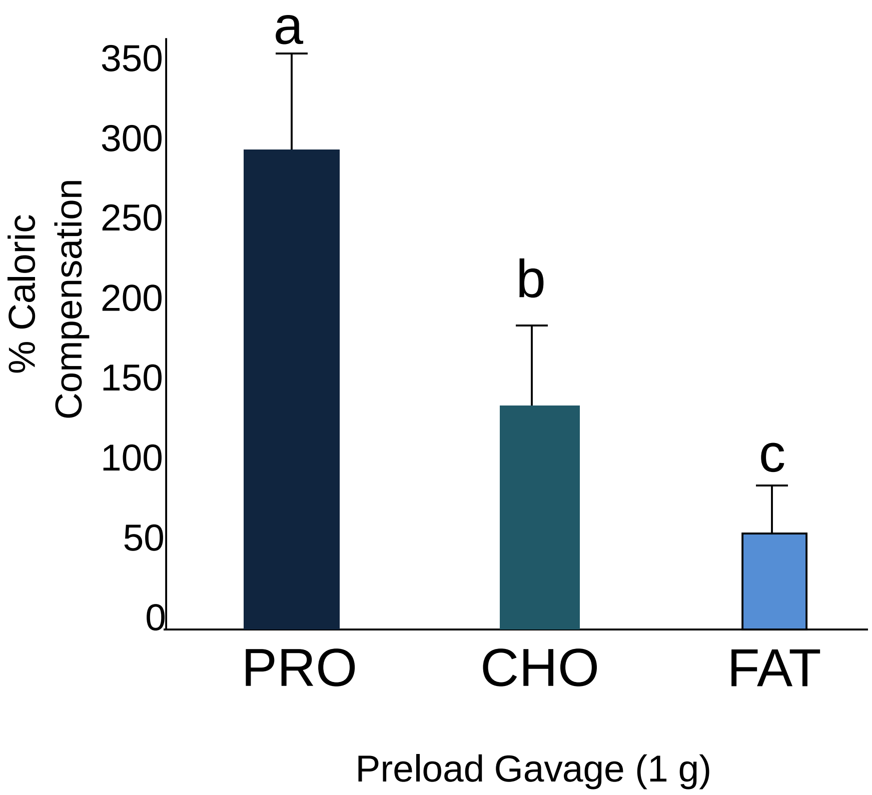
Quantity:

- High Protein Diet
- Low Protein Diet

Source:

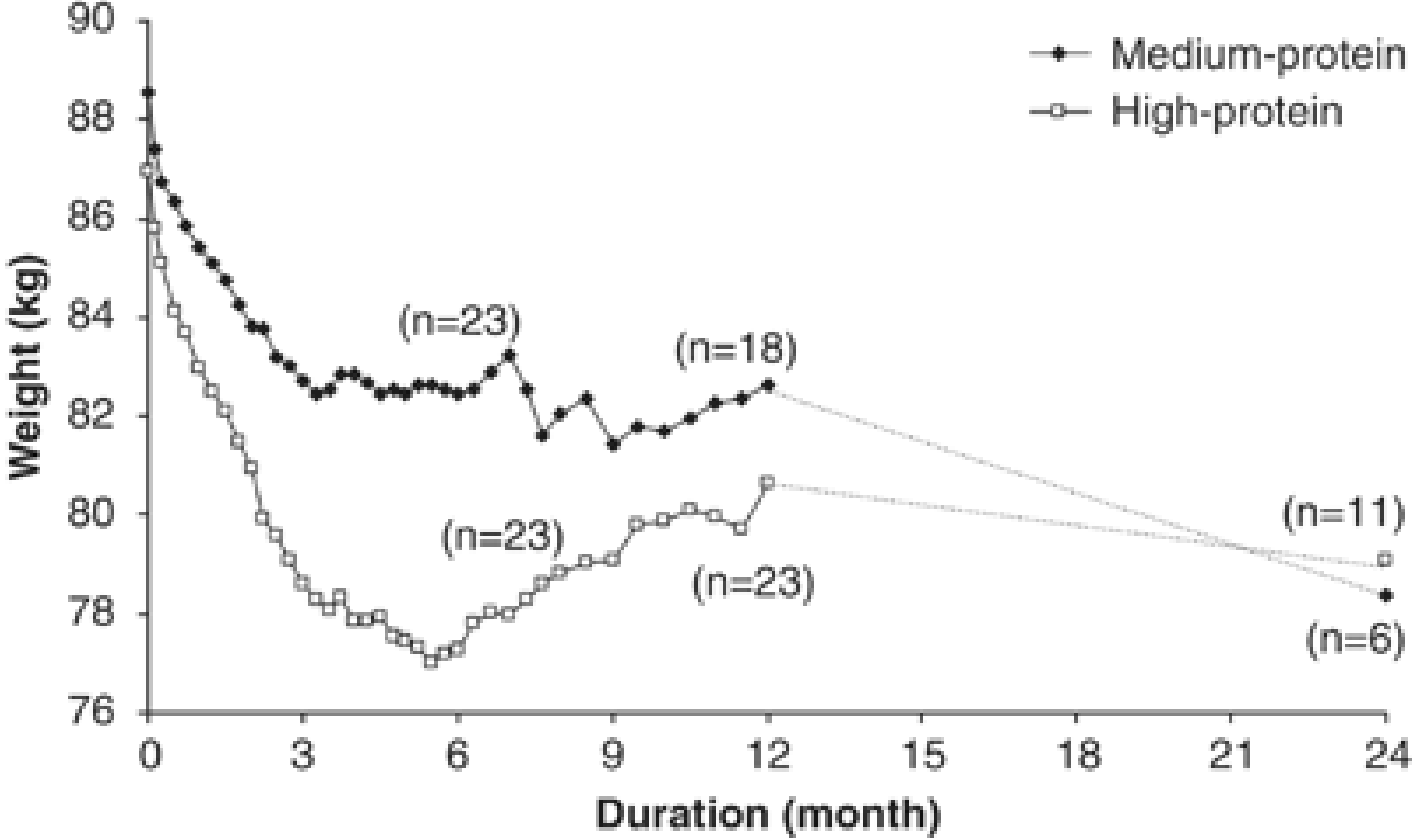
- Amino acid composition
- Amino acid sequence: Bioactive peptides
- Digestion kinetics
- Non-protein components

Food Intake Compensation 0-2 Hours Following Macronutrient Preloads In Rats

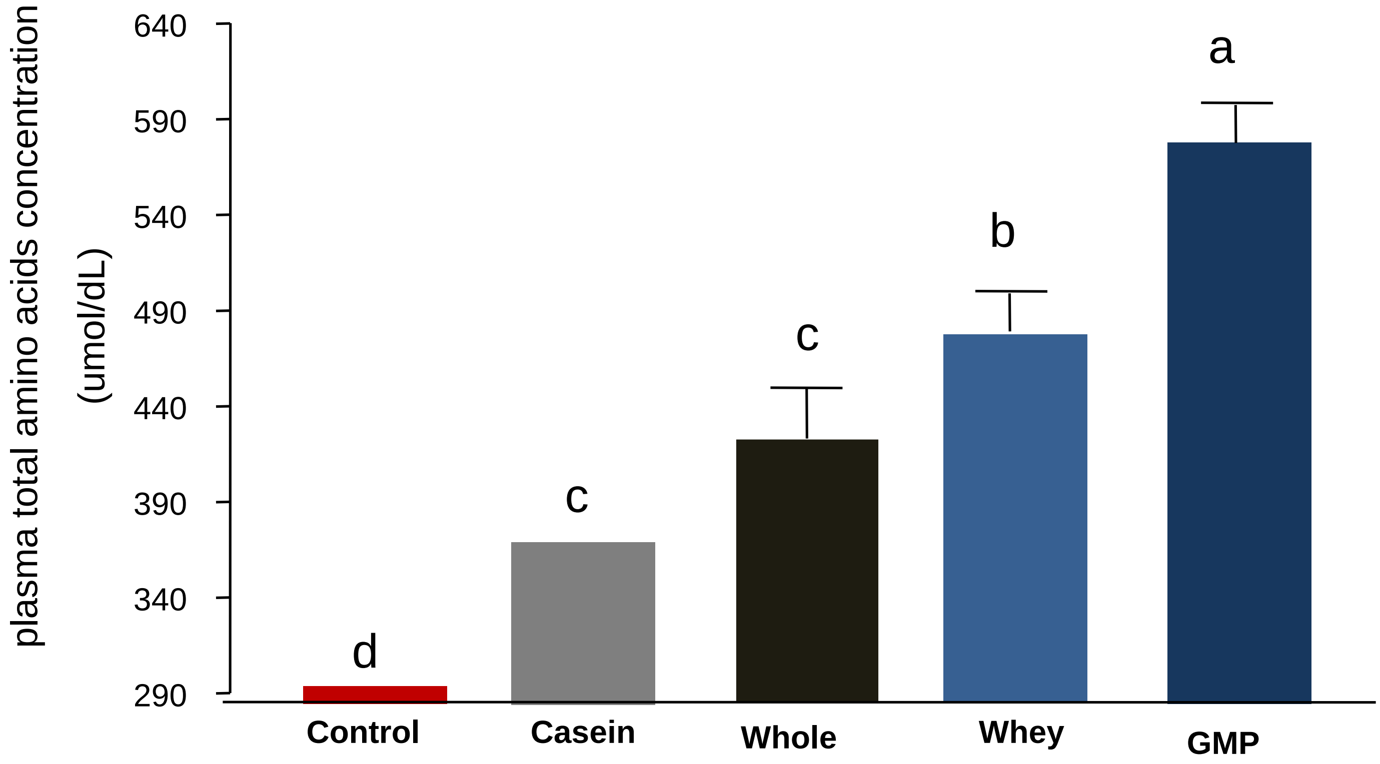


[a]Different letters indicate significant difference, $p<0.05$, Tukey's post-hoc , N=14, Modified from Peters C, Anderson, G.H. et al, J. Nutr. 131:264, 2001

Long-term Effect of High Protein Diet

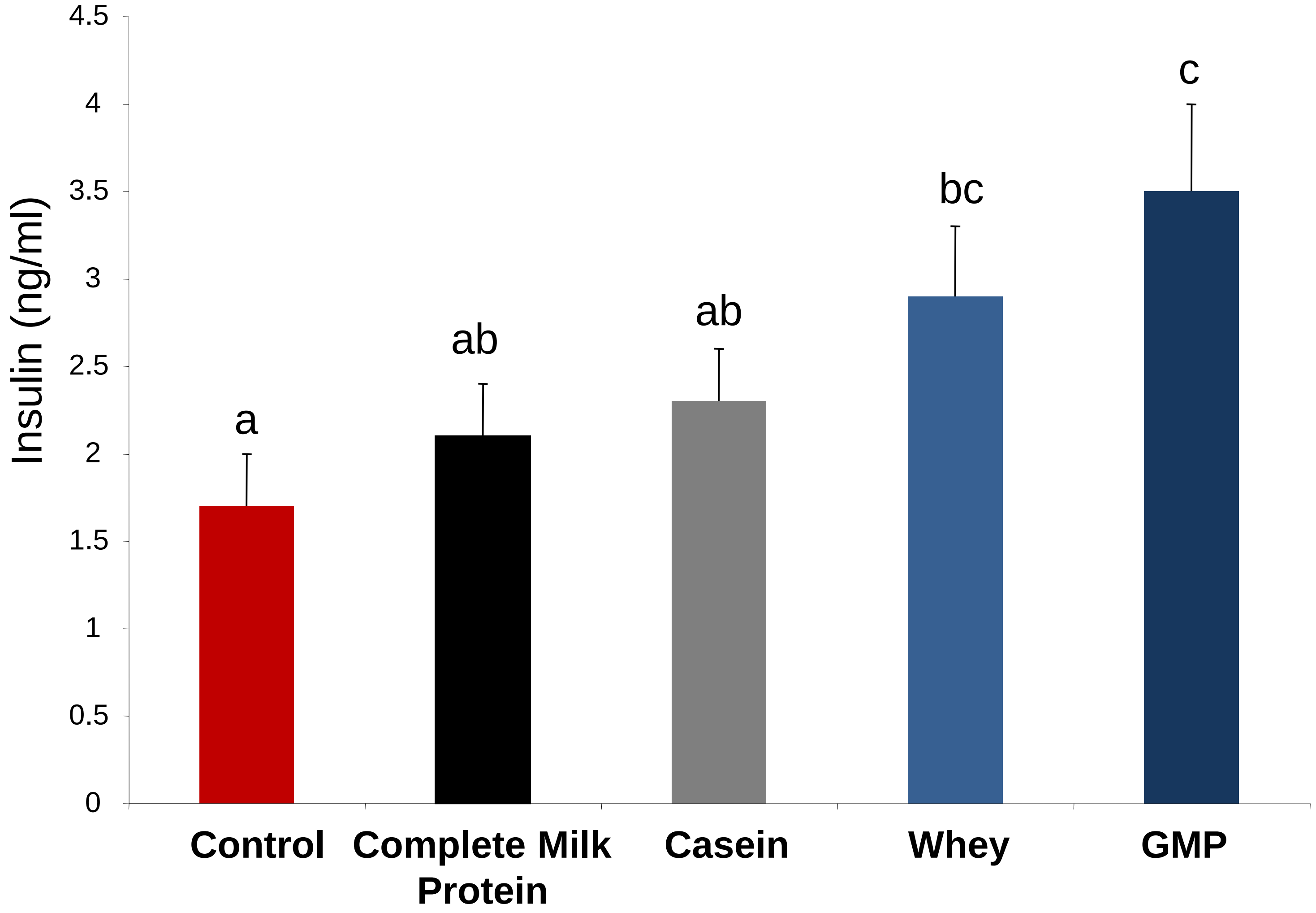


Effects of GMP, Casein, Whey and Complete Milk Protein on Plasma Total Amino Acids Concentrations (0.5h) in Rats



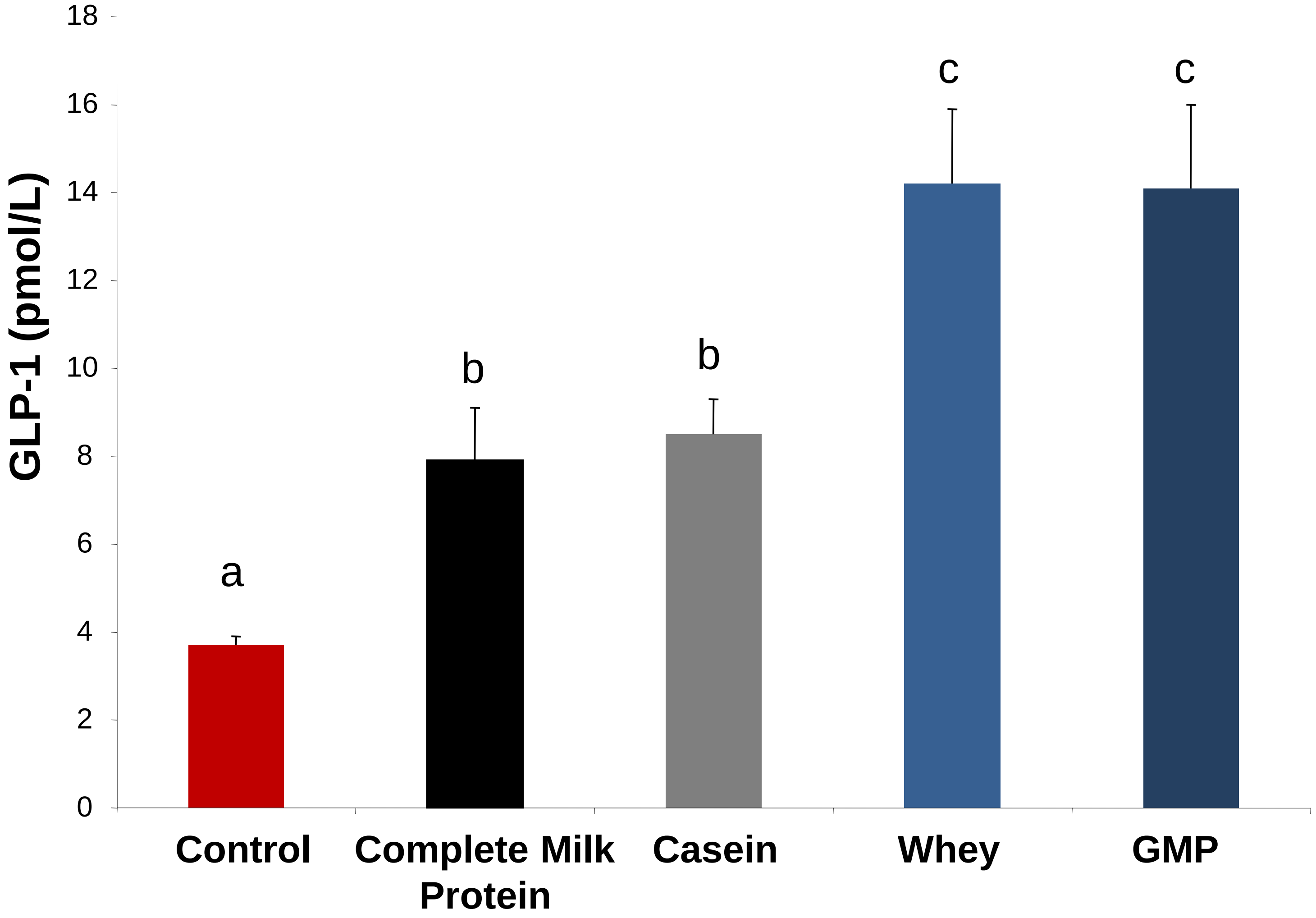
Data are presented as mean (treatment – control) (g) ± SEM, n=6. 0.5g preload gavaged in 4ml water. Means with different letters differ, $p<0.05$.

Effect of milk proteins on plasma insulin 30 min after preload in rats[1]



[1] 0.5 g of protein
Means ± SEM, n=5-6, Means in a row with different letters differ, $P<0.05$

Effect of milk proteins on plasma GLP-1, 30 min after preload in rats[1]



[1] 0.5 g of protein
Means ± SEM, n=5-6, Means in a row with different letters differ, P<0.05

The effect of proteins depends on:

- Source
- Time
- Dose

Dietary Proteins and Type 2 Diabetes Mellitus

High Protein Diet:

Insulin↑, weight loss↑

- Controversial results in epidemiological studies
- Beneficial effect in RCT

(Improve glycemic control, Wt loss)

Protein Source:

AA composition: BCAA, digestion kinetics (e.g. Whey)

BAPs

Characteristics of Proteins

- AA composition
- AA sequence
- Digestion kinetics
- BAPs
- Non-protein components conjugated with proteins
- What else?

BAPs: Surviving in the GI Tract

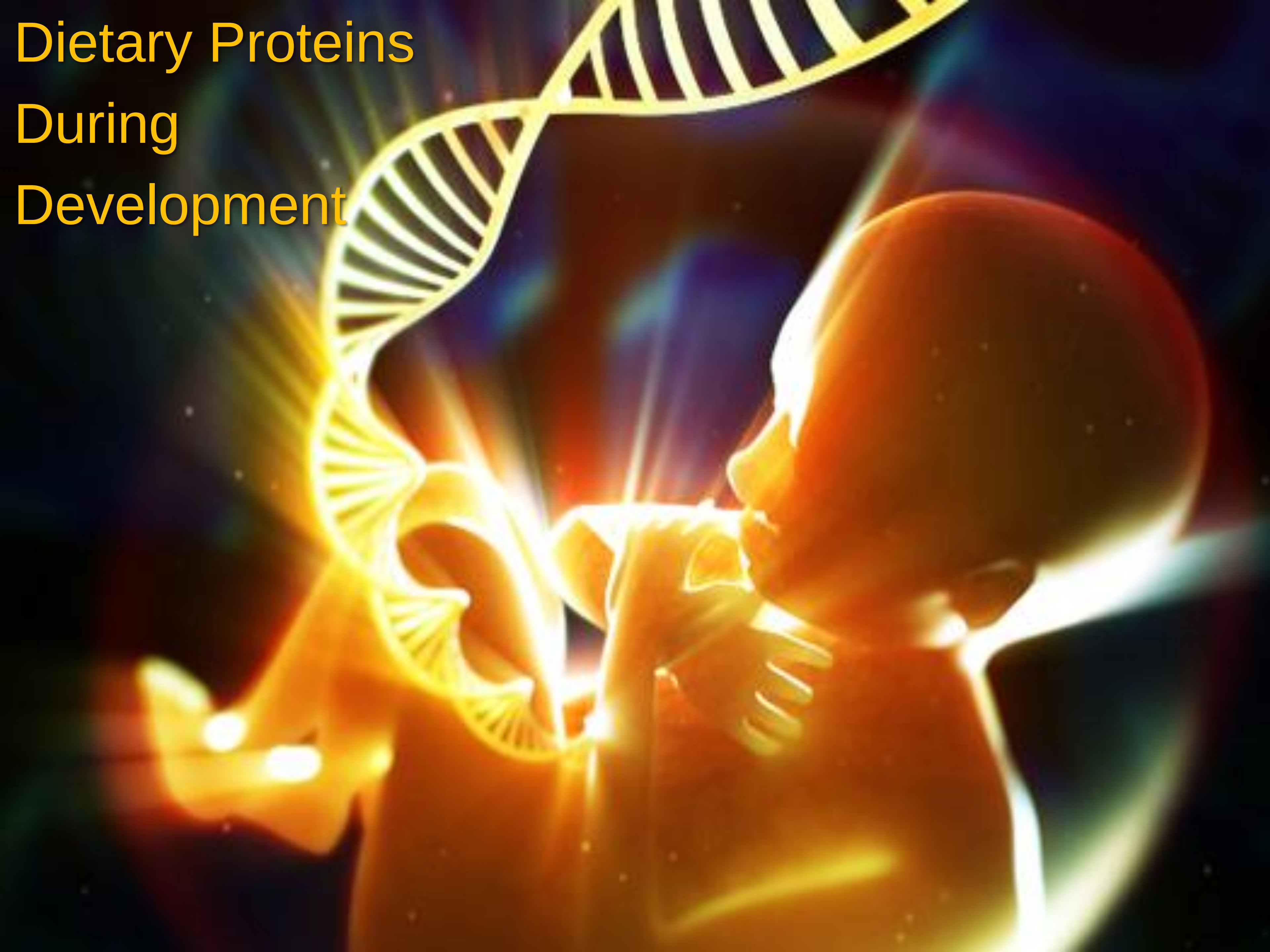
To be biologically active, it is essential for BAPs to survive proteolysis in the luminal contents of the GI tract.

The stability of several BAPs have been reported, including casomorphins, somatostatin, lactoferrin and Epidermal Growth Factor (EGF).

However, It is still not clear which exact characteristics do prevent the breakdown of these BAPs.

Dietary proteins and peptides may also influence the stability of endogenous peptides and consequently influence their physiological functions.

Dietary Proteins During Development

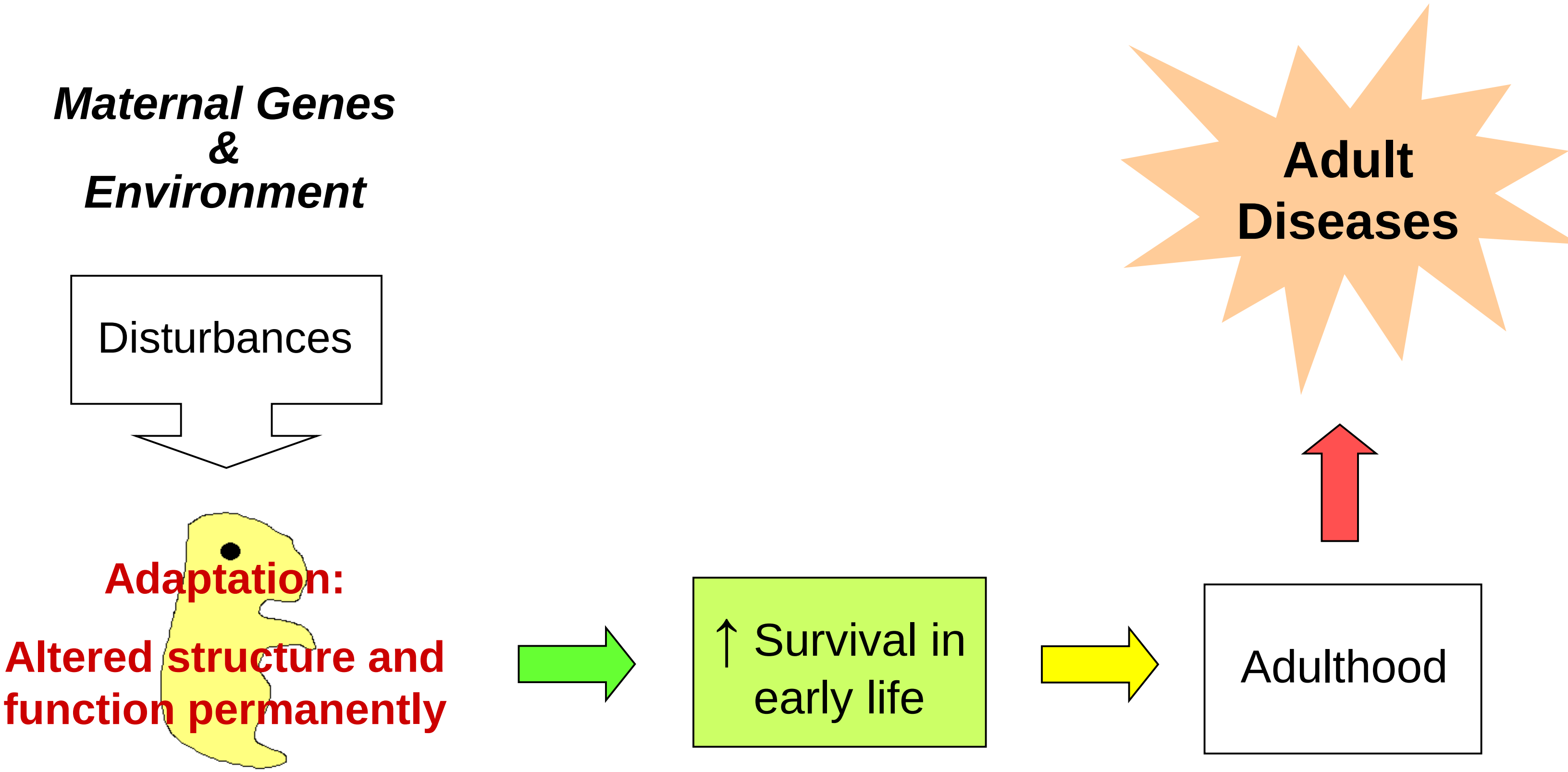


Your blood pressure is really high. Do you have any idea about your mother's diet when she was pregnant?!!

Maternal Nutrition
&
Developmental Origin of Health and Diseases

Developmental Origin of Health and Diseases

"Barker Hypothesis"



Barker DJP et al. *Lancet* 1993; 341: 938-41.
Hales, CN & Barker, DJP. *Diabetologia* 1992; 35(7): 595-601.

Fetal Programming

A stimulus or insult at a critical period of development that has a lasting effect on the structure or function of the body which explicitly manifests itself in adulthood

Barker 2004, J. Epid. Com. Health, 58:114-15

Developmental Origins of Health and Disease
4th World Congress, Univ. Utrecht, Sept 2006

Predictive Adaptive Response (PAR)

- Adaptive responses that may be made by the developing organism in response to the environment, which have no obvious immediate value but are made in expectation of the future environment.

- A mismatch between the early developmental environment and that experienced in mature life

Greater risk of disease

(Gluckman, 2005)

Maternal Under-nutrition
Stages of Pregnancy

- Energy Deficits:
  - Early gestation: coronary heart disease (human)
  - Mid-Late gestation: Low birth weight, glucose intolerance (human, rats)
  - Whole gestation: Low birth weight, higher weight gain, hypertension, glucose intolerance (rats)

- Protein Deficiency:
  - Late gestation: hypertension (human)
  - Whole gestation: low birth weight (human, rats), insulin resistant, hypertension & CVD (rats)

Protein Content of Maternal Diet and Fetal Programming

Low Protein Diet ↘ *High Protein Diet* ↙

Blood pressure [1,5]

Body weight [2,4]

Adiposity [3,6]

↑

1- Woods L, 2007
2- Zamborano, 2006
3- Sasaki A, 1982
4- Zang J, 2005
5- Thone Reinke, 2006
6- Metges C, 2002

Factors Influencing Development

Pre-natal Environment
(mother)

Metabolic, Hormonal, Nutritional Signals

Fetal Development

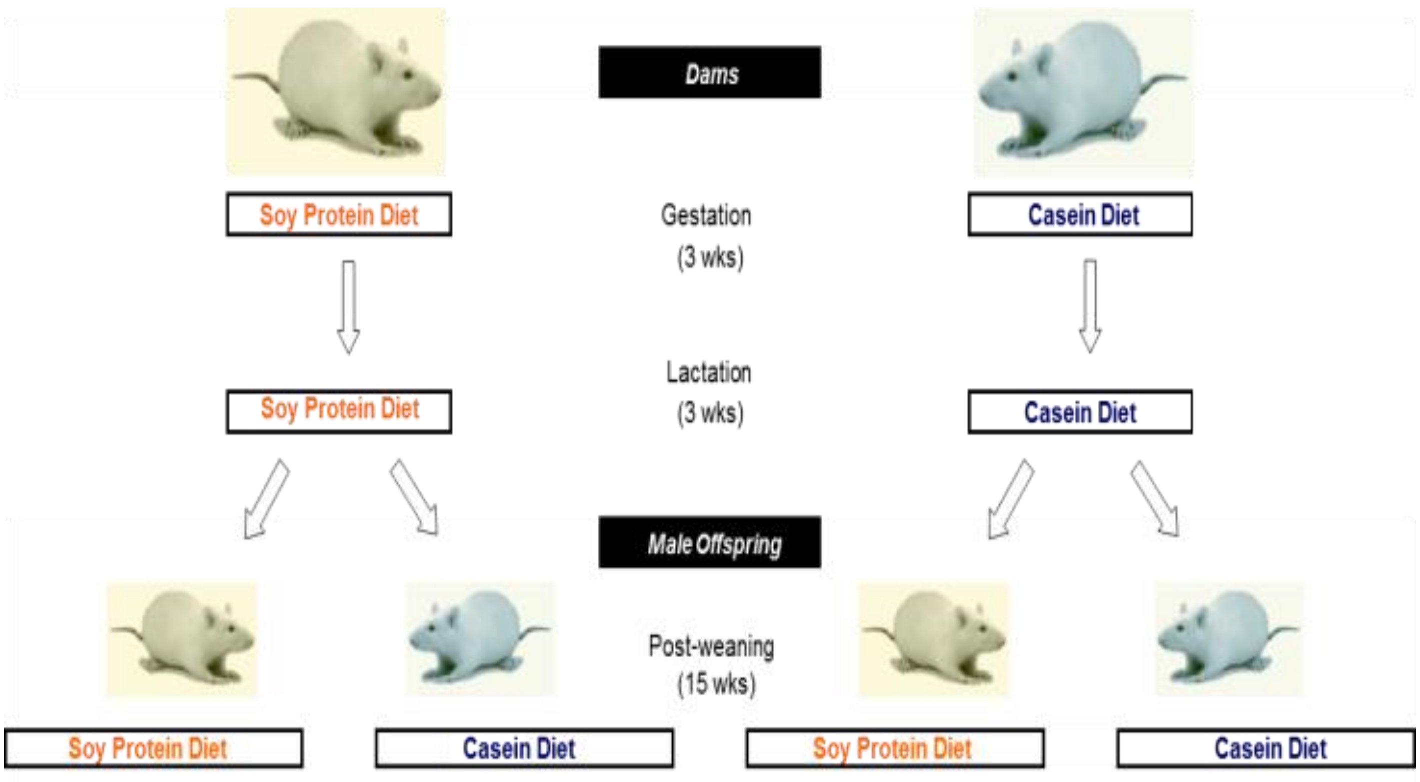
Post-natal Environment
(infant)

Development of Regulatory Systems

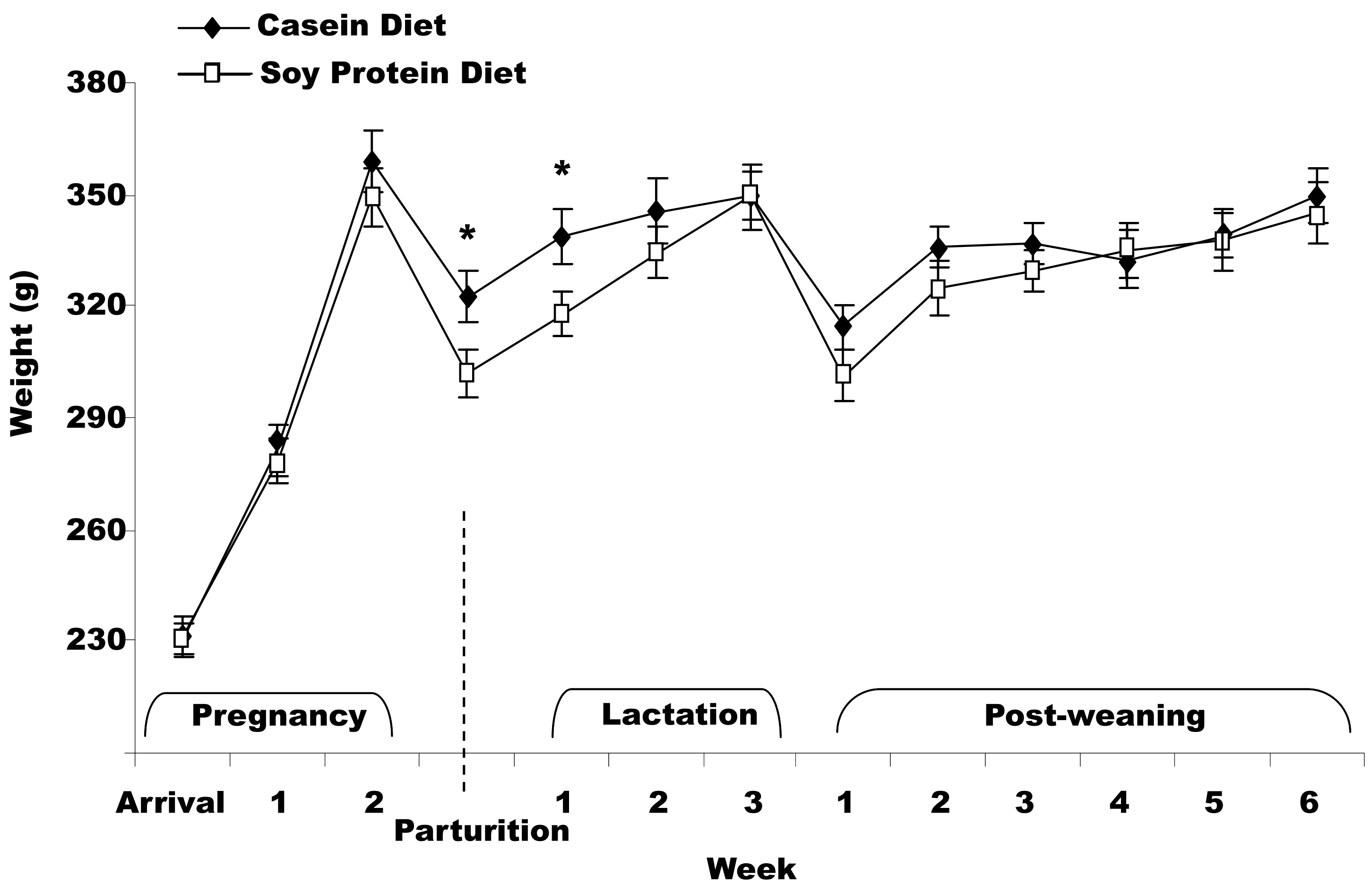
(Adaptation to Diet)

Risk of Chronic Diseases

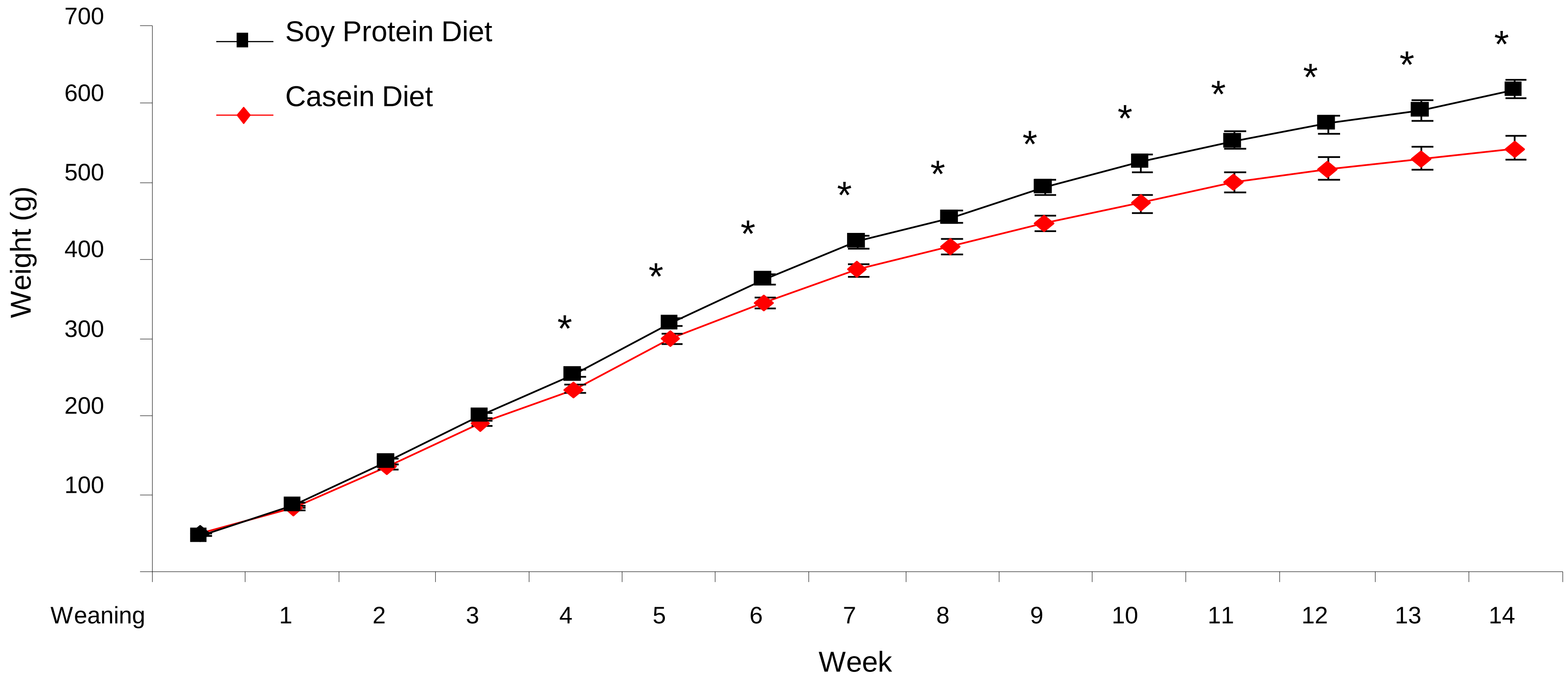
Study Protocol



The Effect of Maternal Diet on Body Weight in the Dams

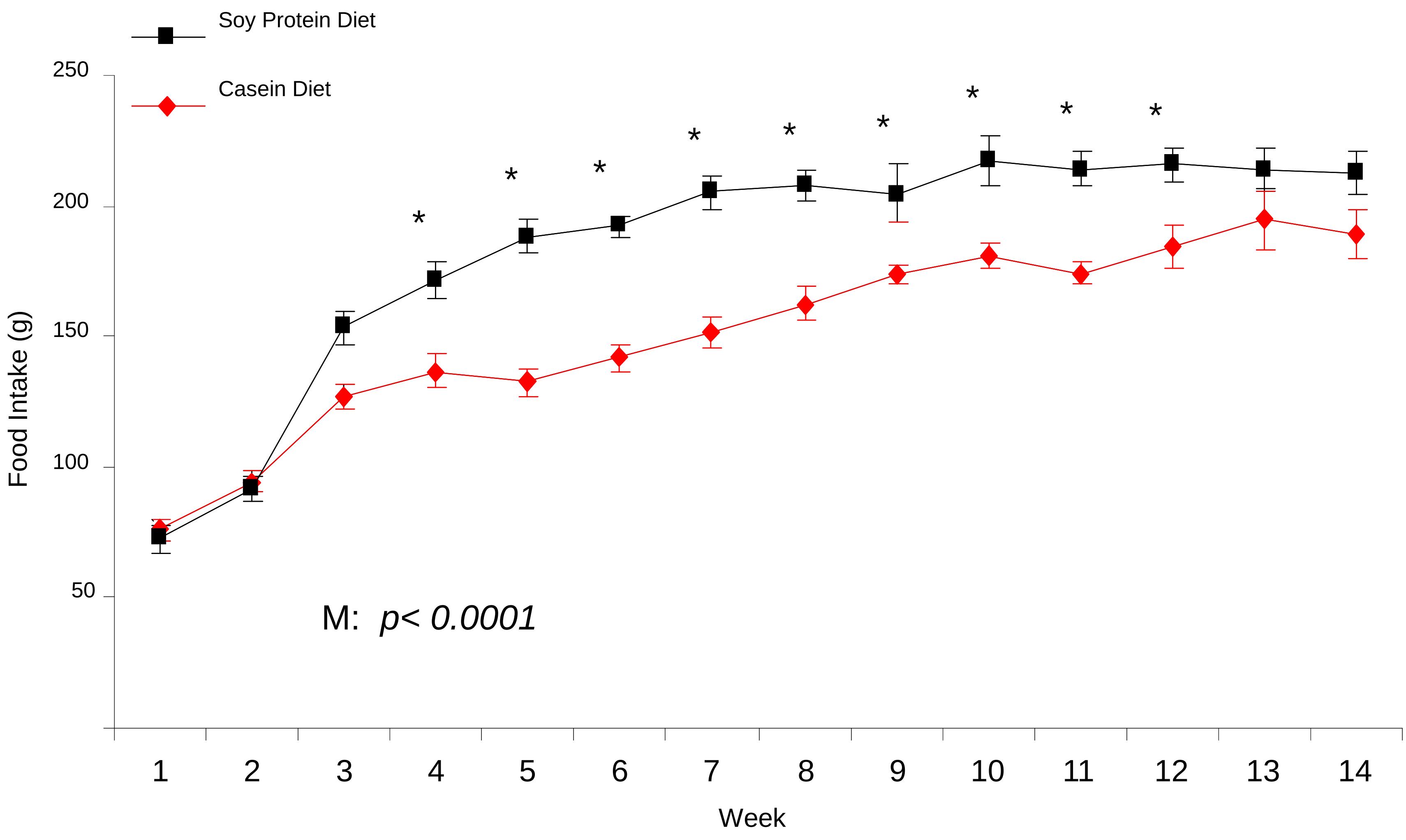


Maternal Diet Protein Source and Characteristics of Metabolic Syndrome in Male Offspring.



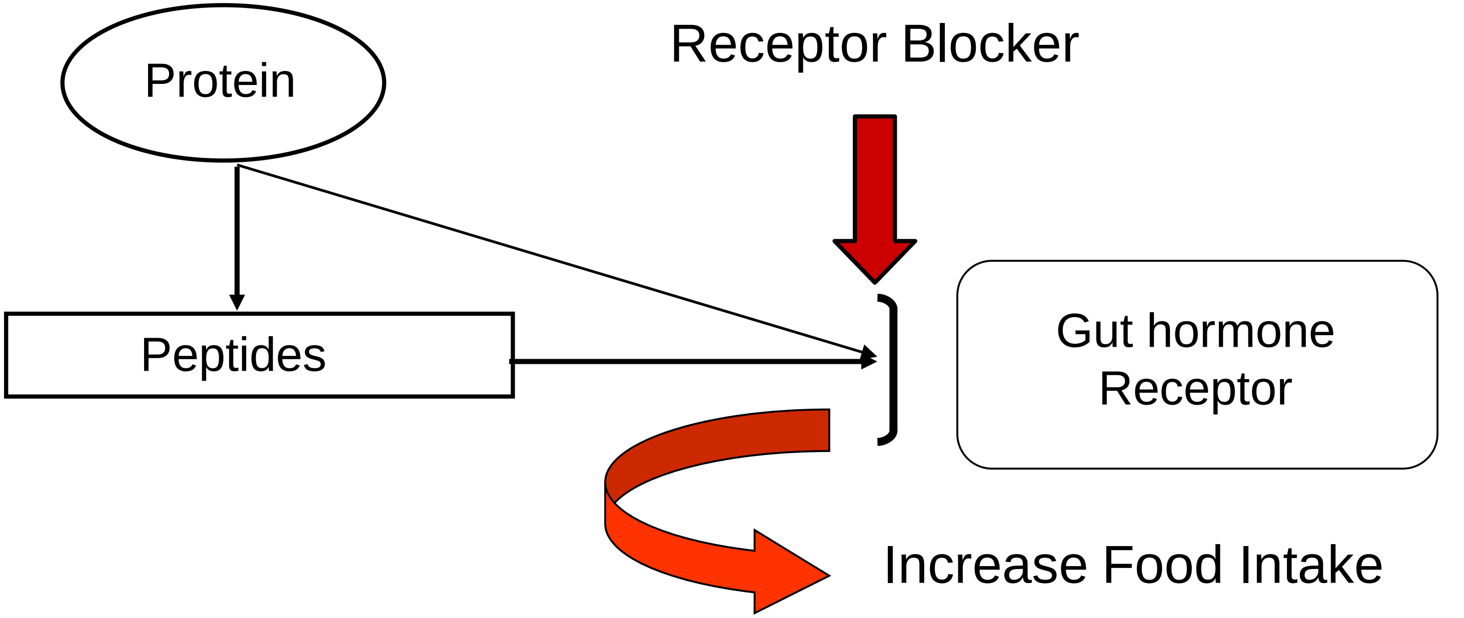
Data are means ± SD, MIXED MODEL, Tukey's post hoc test; (n=12/group); * p<0.05

Maternal Diet Protein source and Food Intake Regulation in Male Offspring

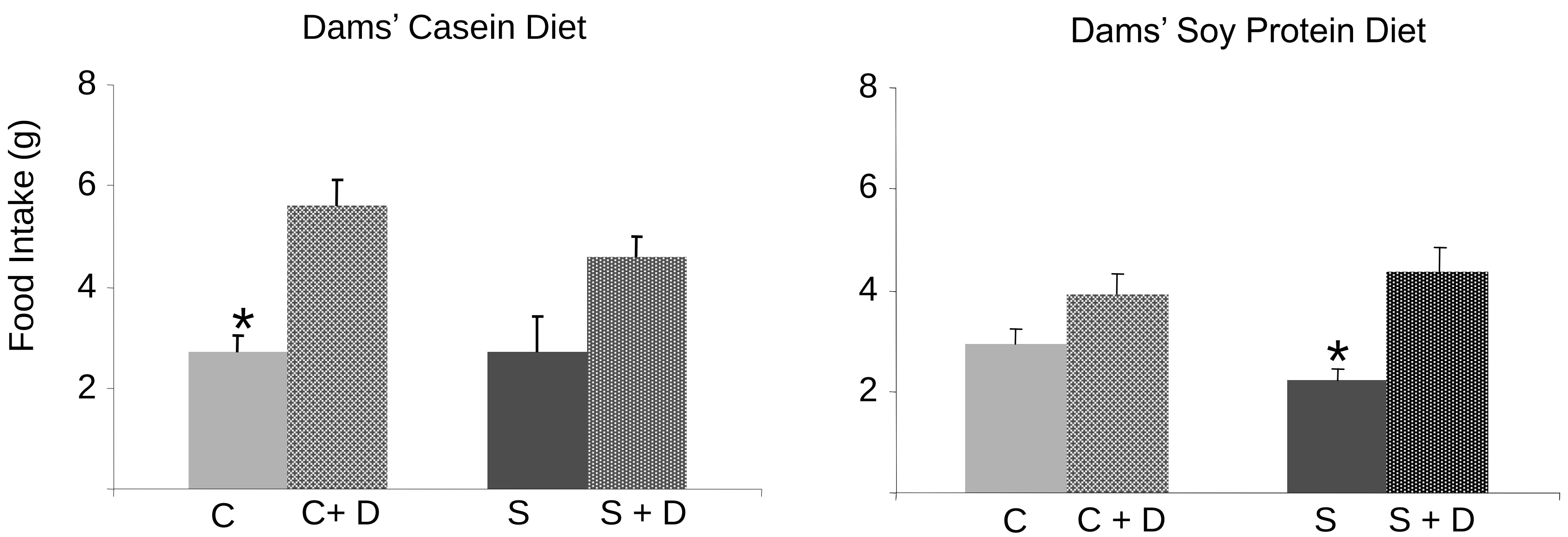


G: Gestational diet; *M:* Maternal diet; *W:* Weaning diet
Data are means ± SD, MIXED MODEL, Tukey's post hoc test; (n=12/group); * p<0.05

Effect of CCK-A Receptor Blockers on Food Intake in Response to Preloads



Effect of Devazapide (CCK-A Receptor Blocker) on Food Intake (1h) after Preloads
Depends on Maternal Diet

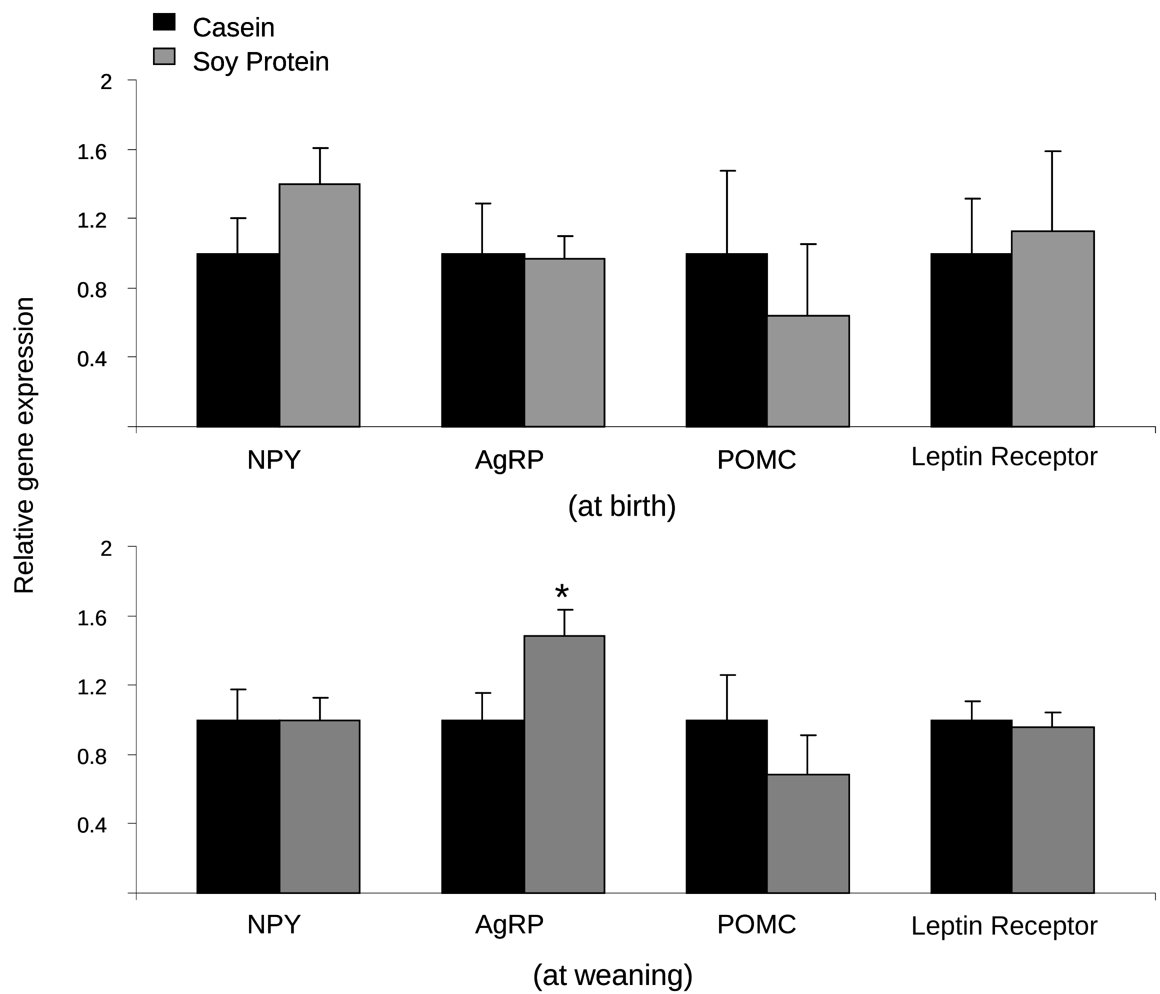


Dams' Diet: $p < 0.05$

C: Casein Preload; **S:** Soy Protein Preload; **D:** Devazepide

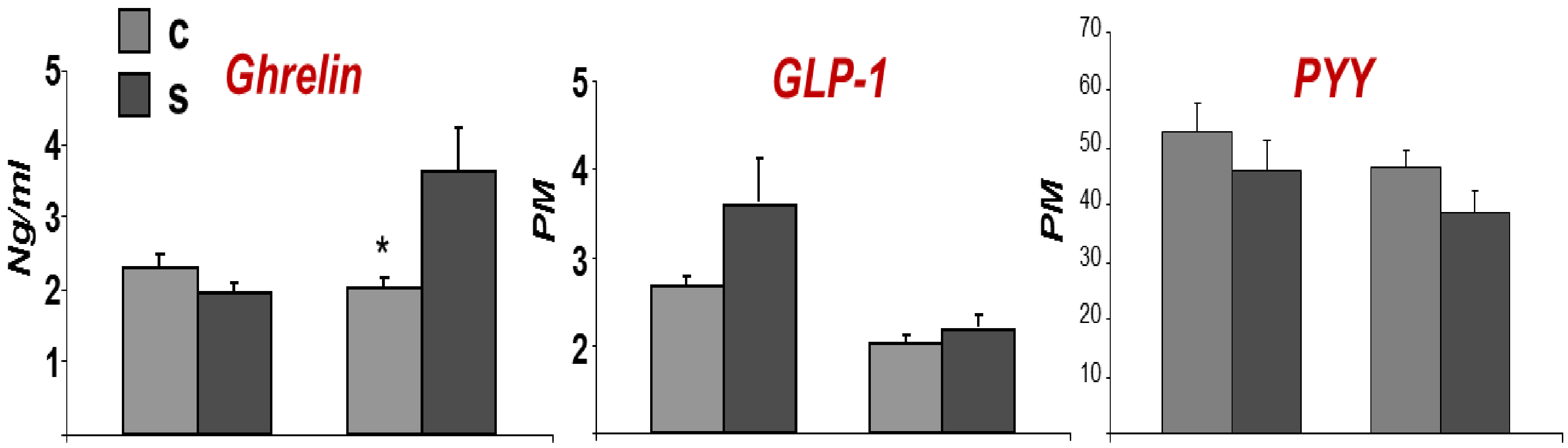
Data are means ± SD, MIXED MODEL, Tukey's post hoc test; (n=12/group); * p<0.05

Hypothalamic mRNA expression of genes regulating food intake



Data are means ± SD, Unpaired *t*-test; (n=8-9/group); * $p<0.05$

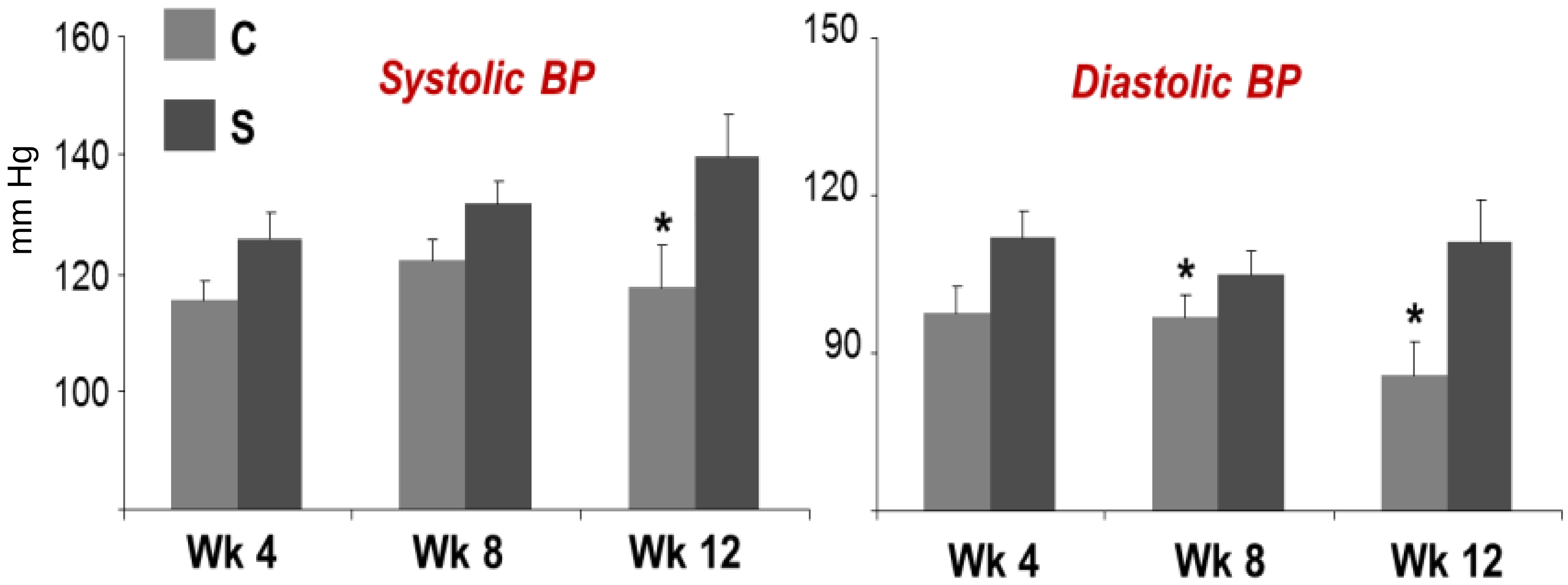
Food Intake Regulatory Hormones



C: Gestational Casein Diet **S:** Soy Protein Casein Diet

Data are means ± SD, MIXED MODEL, Tukey's post hoc test; (n=6/group); * p<0.05

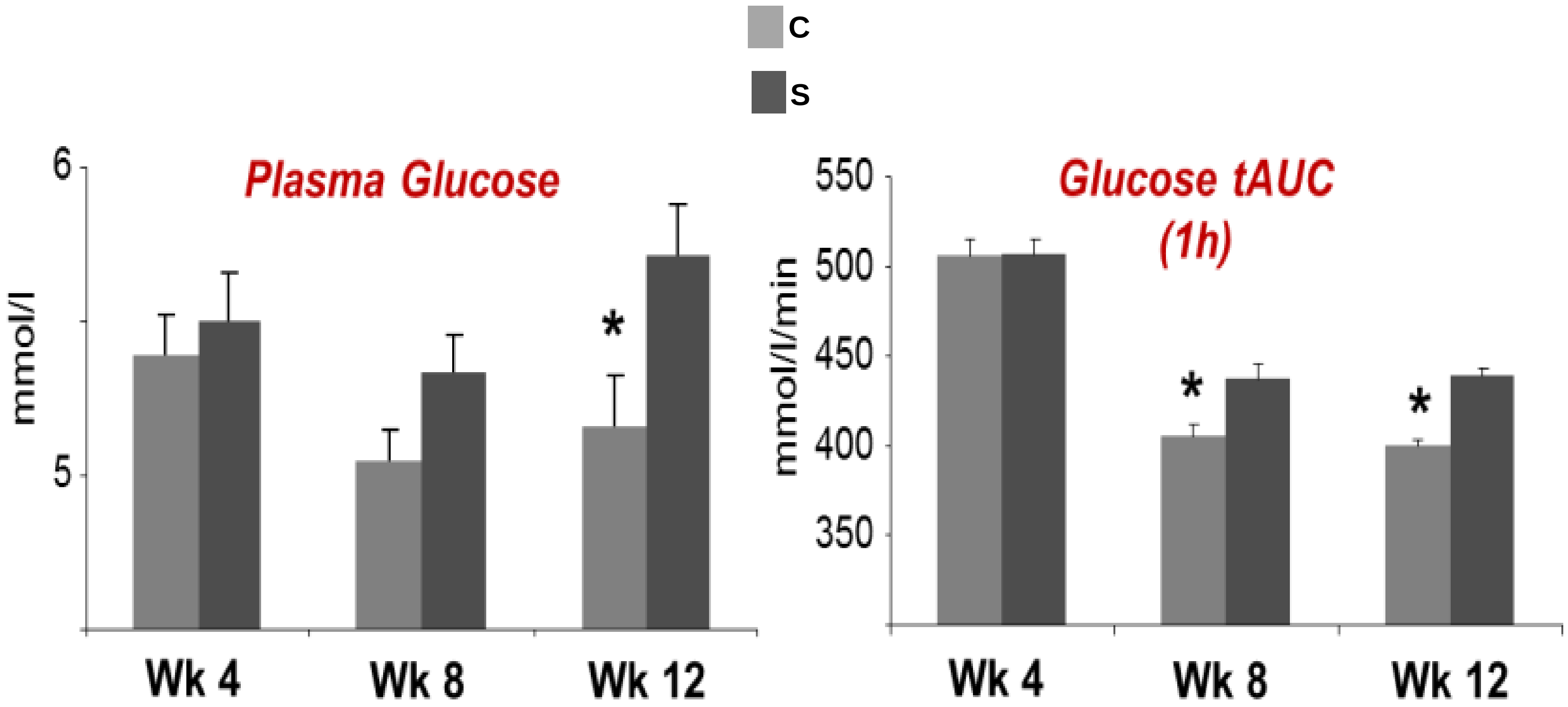
Blood Pressure



C: Gestational Casein Diet **S:** Soy Protein Casein Diet

Data are means ± SD, MIXED MODEL, Tukey's post hoc test; (n=12/group); * $p<0.05$

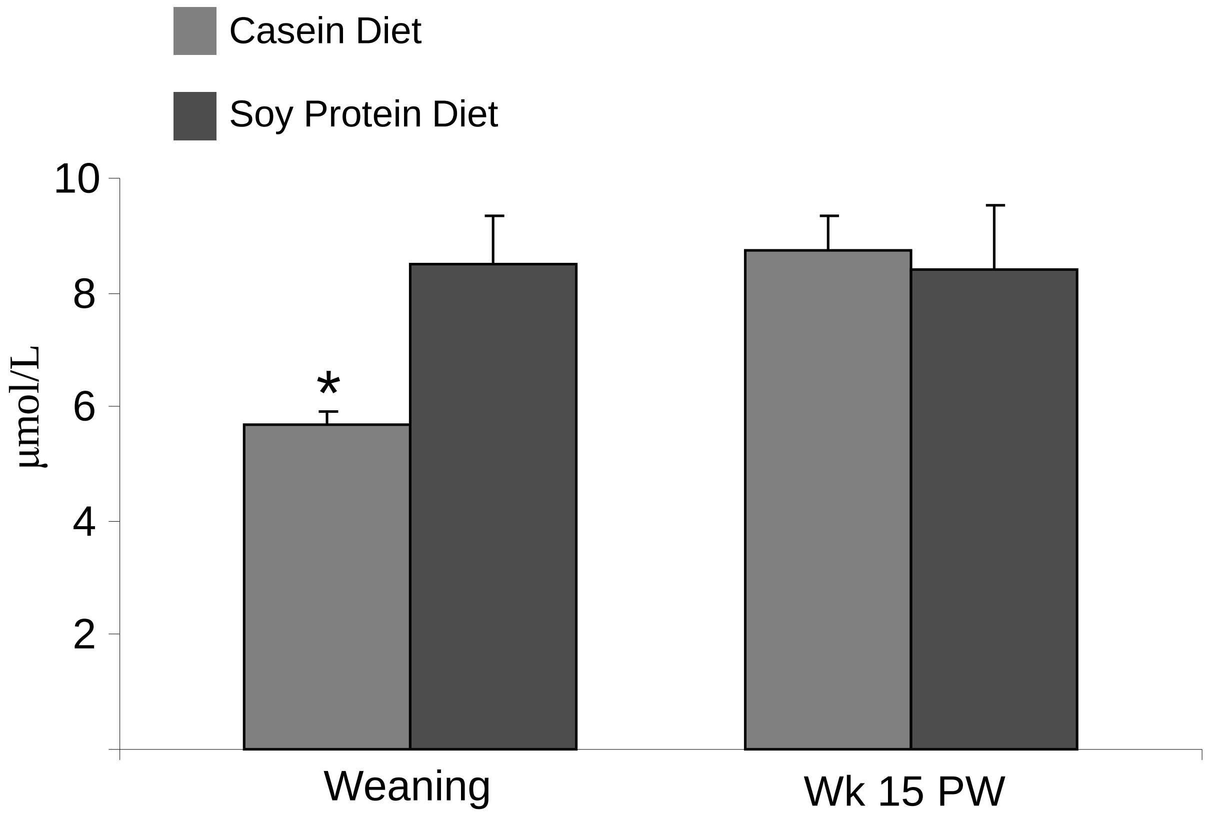
Glucose and Glucose Area Under the Curve (AUC)



C: Gestational Casein Diet **S:** Soy Protein Casein Diet

Data are means ± SD, MIXED MODEL, Tukey’s post hoc test; (n=12/group); * p<0.05

Plasma Homocysteine in Male Offspring



Hyperhomocysteinemia

Epigenetic regulation of gene expression:

Hypomethylation of the DNA[1]

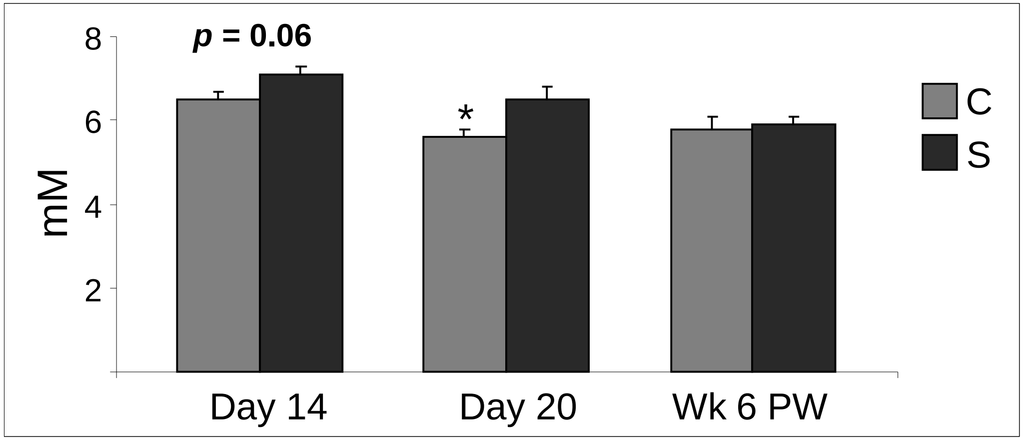
↓

Blood pressure and glucose metabolism [2, 3, 4]

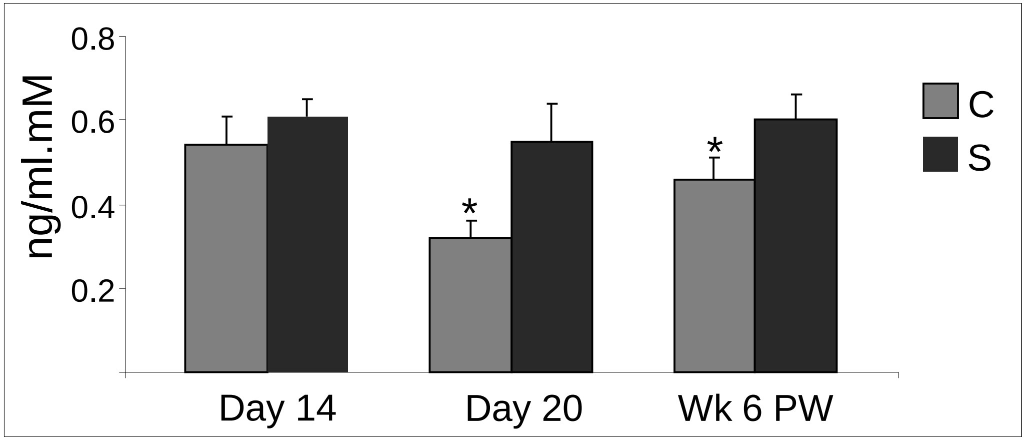
1- Jiang, 2007; 2- Petry, 1997; 3- McMillen & Robinson, 2005 ; 4- Petrie L, 2002 ; 5- McMillen, 2004;
6- Randeva, 2003

The Effect of Maternal Diet on Plasma Glucose and HOMA-IR Index in the Dams

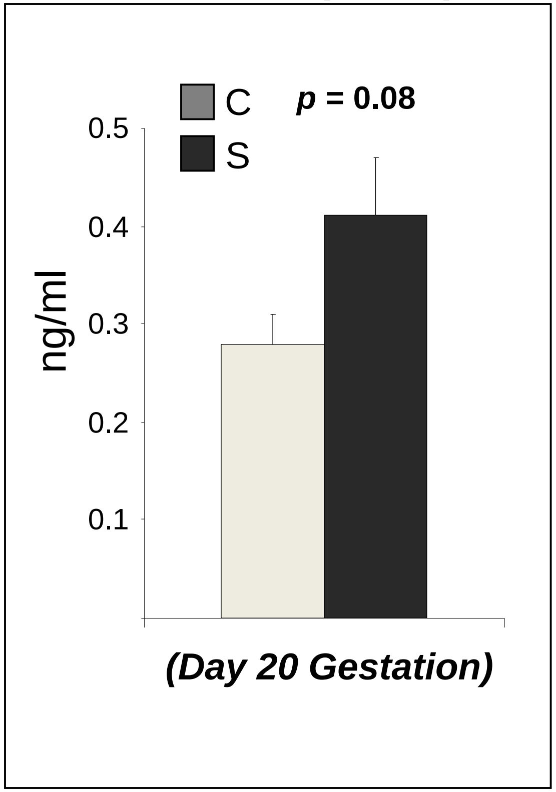
Plasma Glucose



HOMA-IR



Plasma Insulin (Fetus)



C: Casein diet; ***S:*** Soy protein diet

Maternal Glucose Metabolism and Fetal Programming

Plasma insulin ↑

↓

Insulin in immature hypothalamus ↑

↓

- Neuronal hypotrophy in PVN and VMN
- Increased activity of Galanine and NPY [1]

↓

Permanent alterations in metabolism, blood pressure and BW [2, 3, 4]

1 Plageman, 1999
2 Conover KL, 1987.
3 Contreras RJ, 2000.
4 Cherif H, 2001.

Effect of Intact Protein vs. Amino Acid-based Maternal Diets on Dams' Body Weight

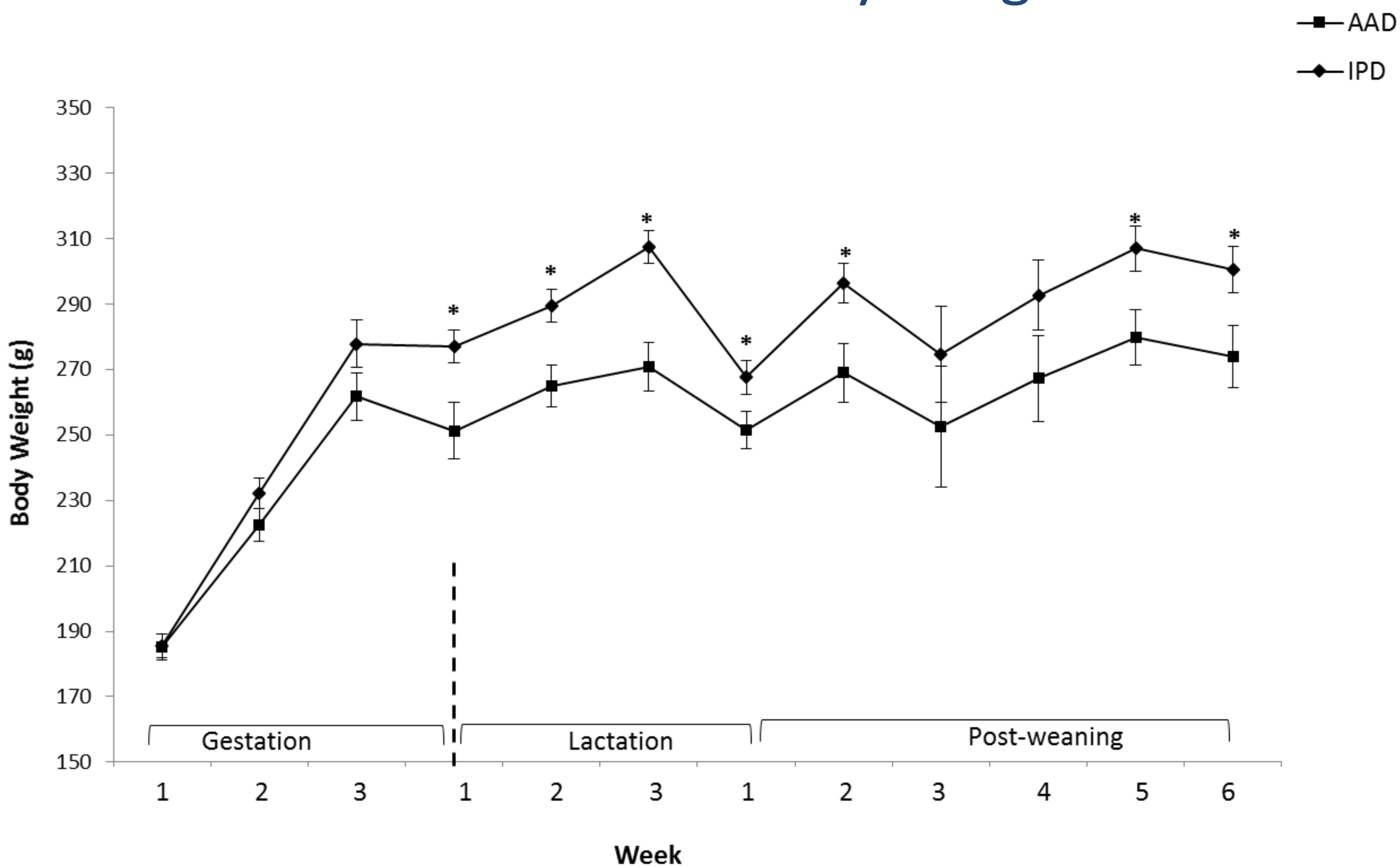


Fig. 1. Effect of maternal diet on dams' body weight (n = 12/group). Data are means ± SEM; BW was analyzed one-way ANOVA. * $p < .05$; AAD: Amino Acid-based Diet; IPD: Intact Protein Diet

Effect of Intact Protein vs. Amino Acid-based Maternal Diets on Pups' Body Weight

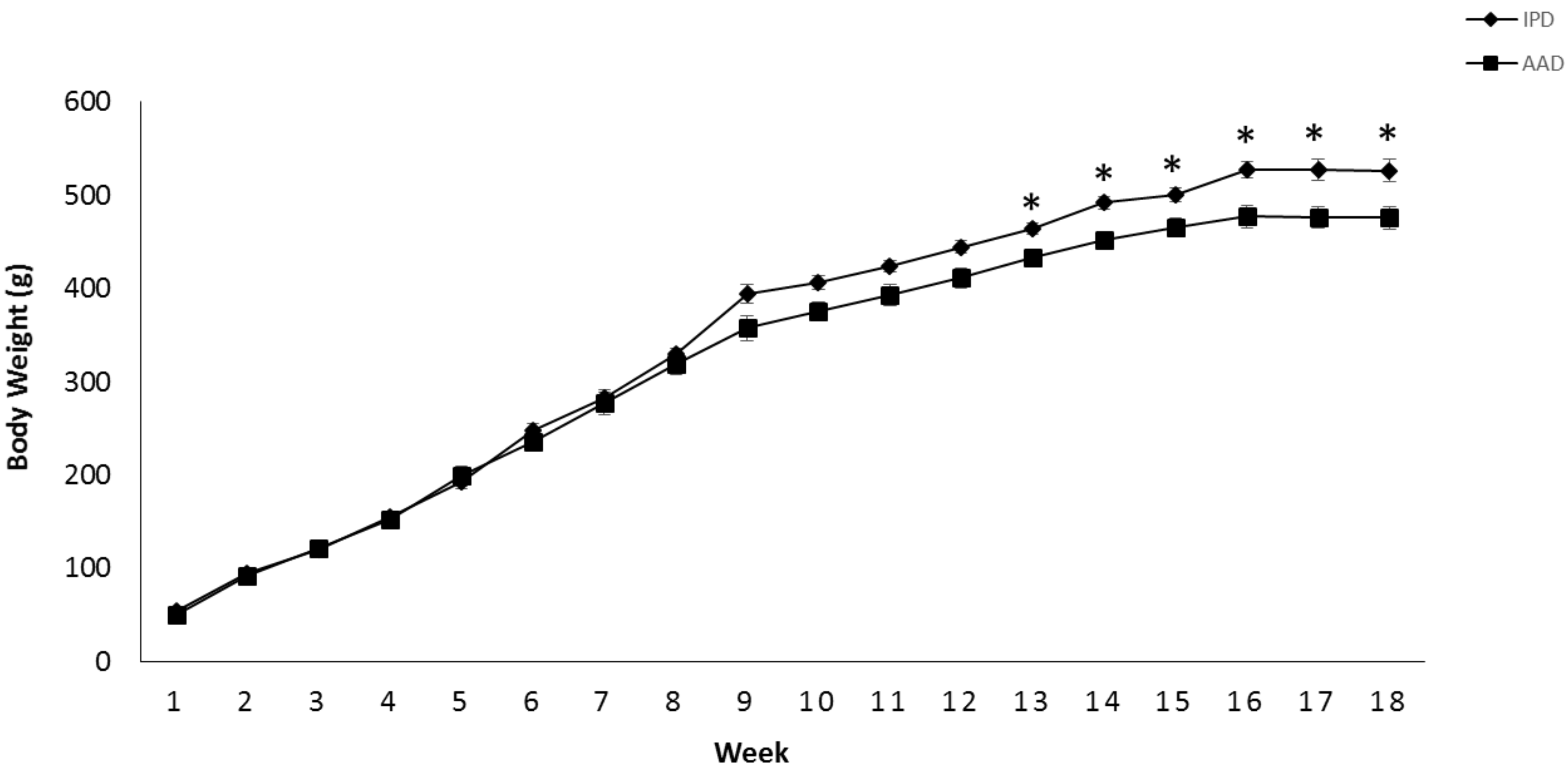
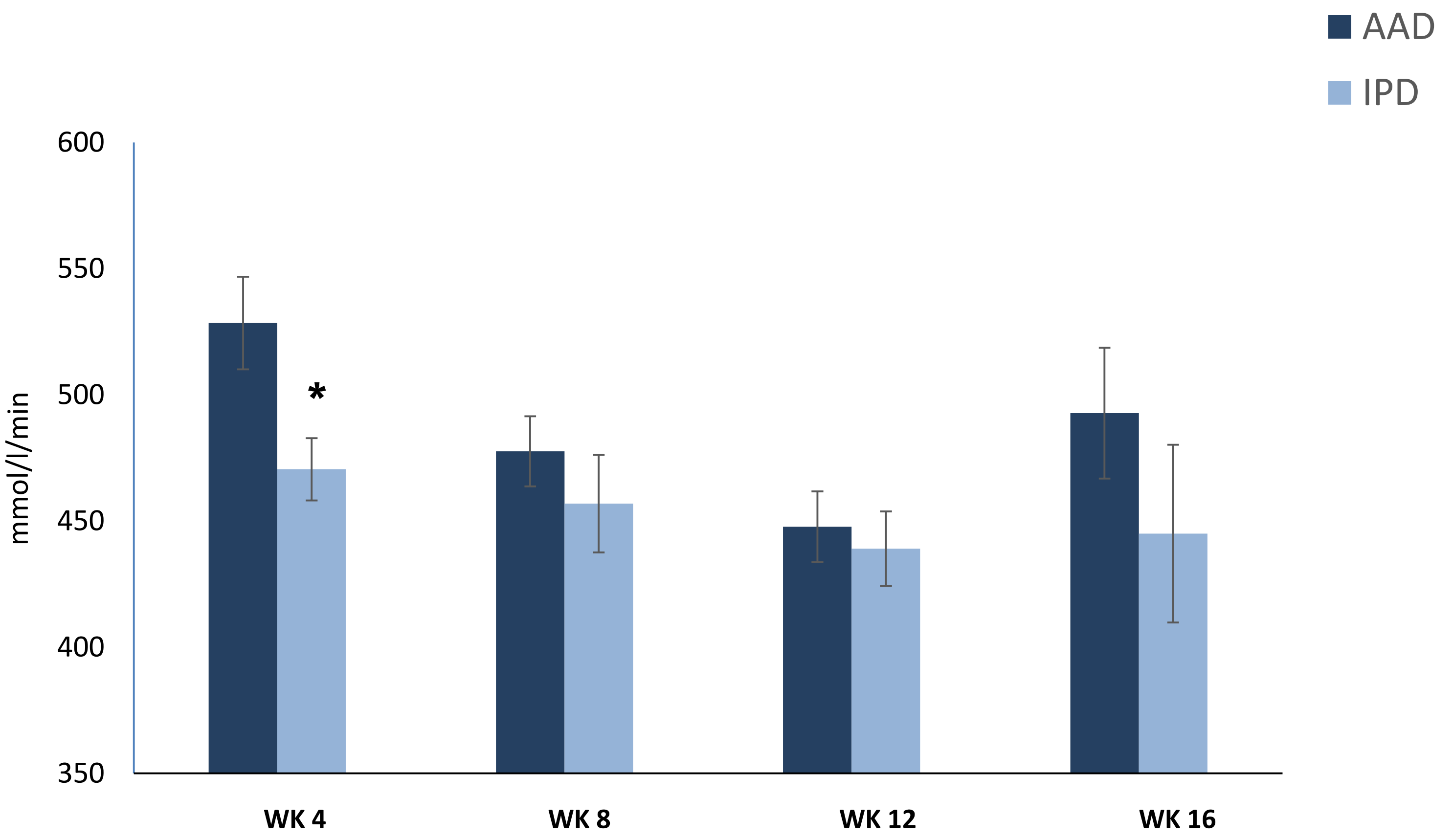
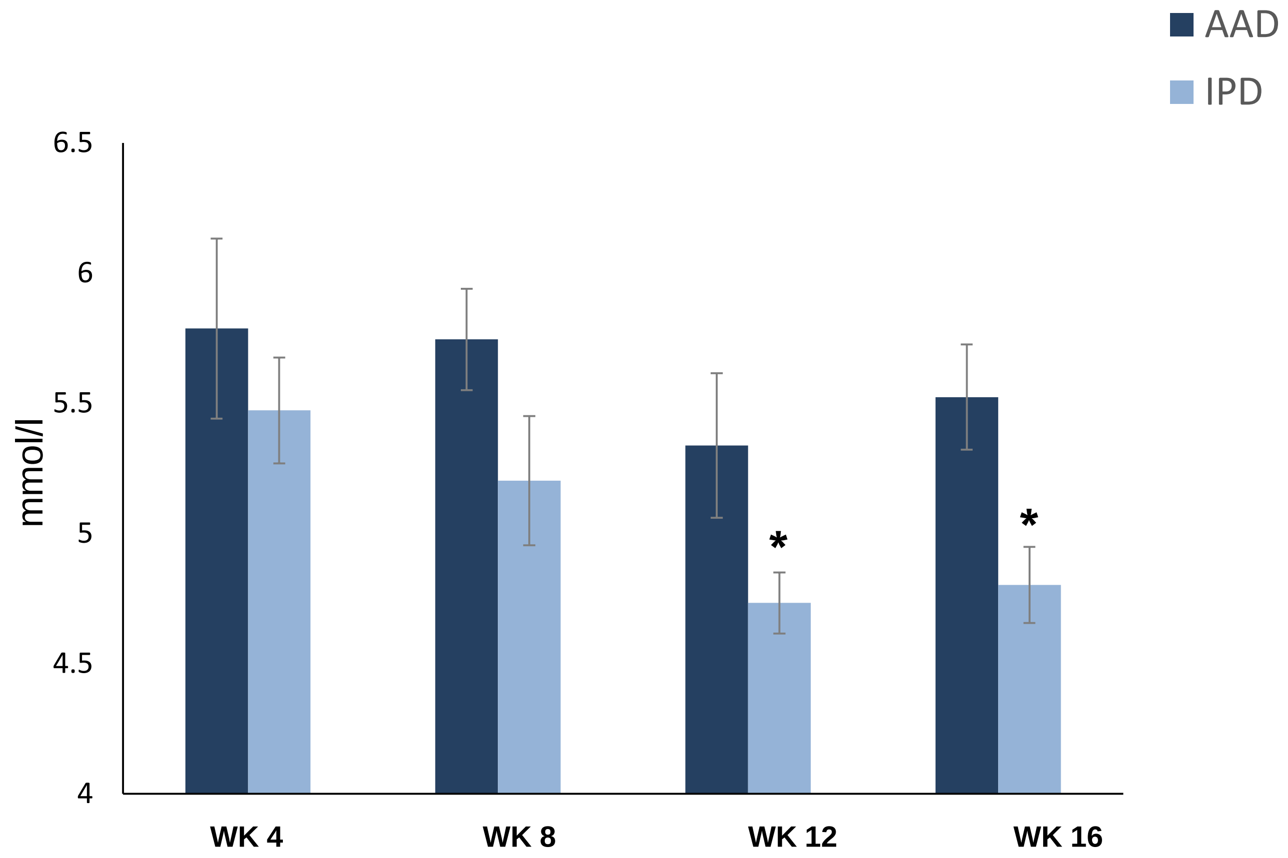


Fig. 3. Effect of maternal diet on post-weaning body weight of male offspring (n = 12/group). Data are means ± SEM; BW was analyzed by MIXED model with maternal diets and time as main factors. Time: $p < .0001$; maternal diet: $p < .009$; weaning diet: $p = .06$. AAD: Amino Acid-based Diet; IPD: Intact Protein Diet

Glucose Area Under the Curve (AUC)



Fasting Plasma Glucose



Summary

- Proteins elicit physiological and biological properties beyond their nutritional role
- Their effect is source, time and dose-dependent!
- Protein quantity, source and also characteristics of proteins fed during gestation and lactation influence body weight and also glucose metabolism of offspring

Questions?