Obesity and Nutrigenomics

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Introduction

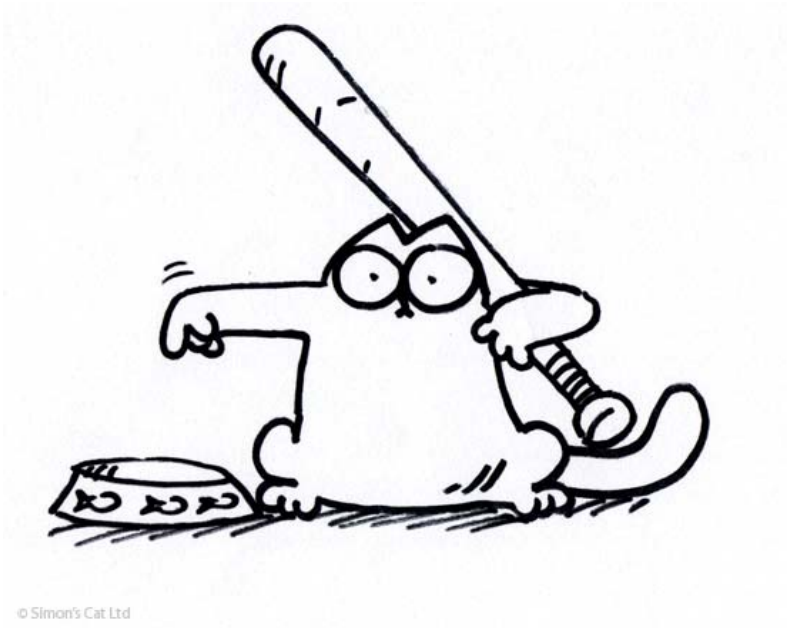
- Obesity
- Nutrigenetics and Nutrigenomics

Obesity

- Mortality:
  - Decreased lifespan
- Morbidity:
  - Endocrine, orthopedic, reproductive, urogenital, and neoplastic disorders
- Prevalence:
  - More than 50% of dogs and cats are at least 15 to 30% greater than their ideal BW.

Kealy et al., 2002; Larson et al., 2003; German, 2006; Calabash, 2011

Risk Factors

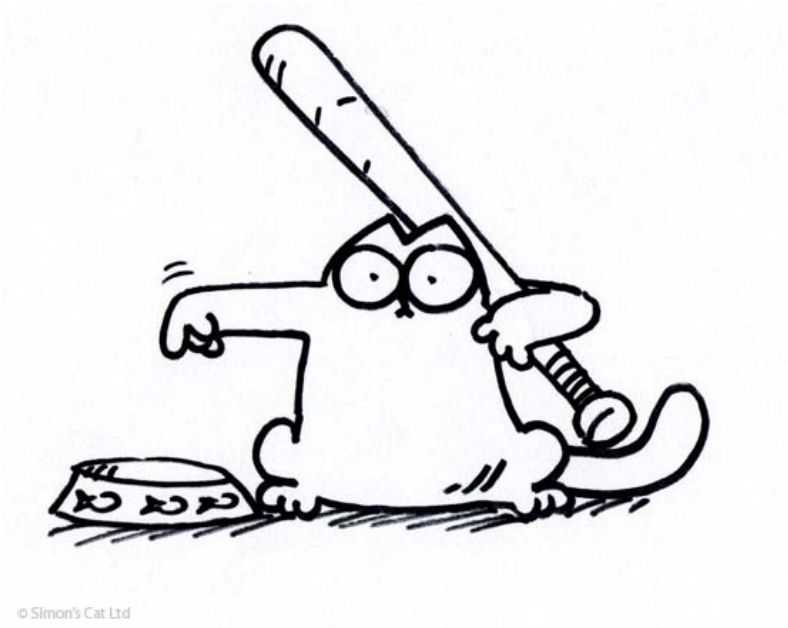


German, 2006

Risk Factors

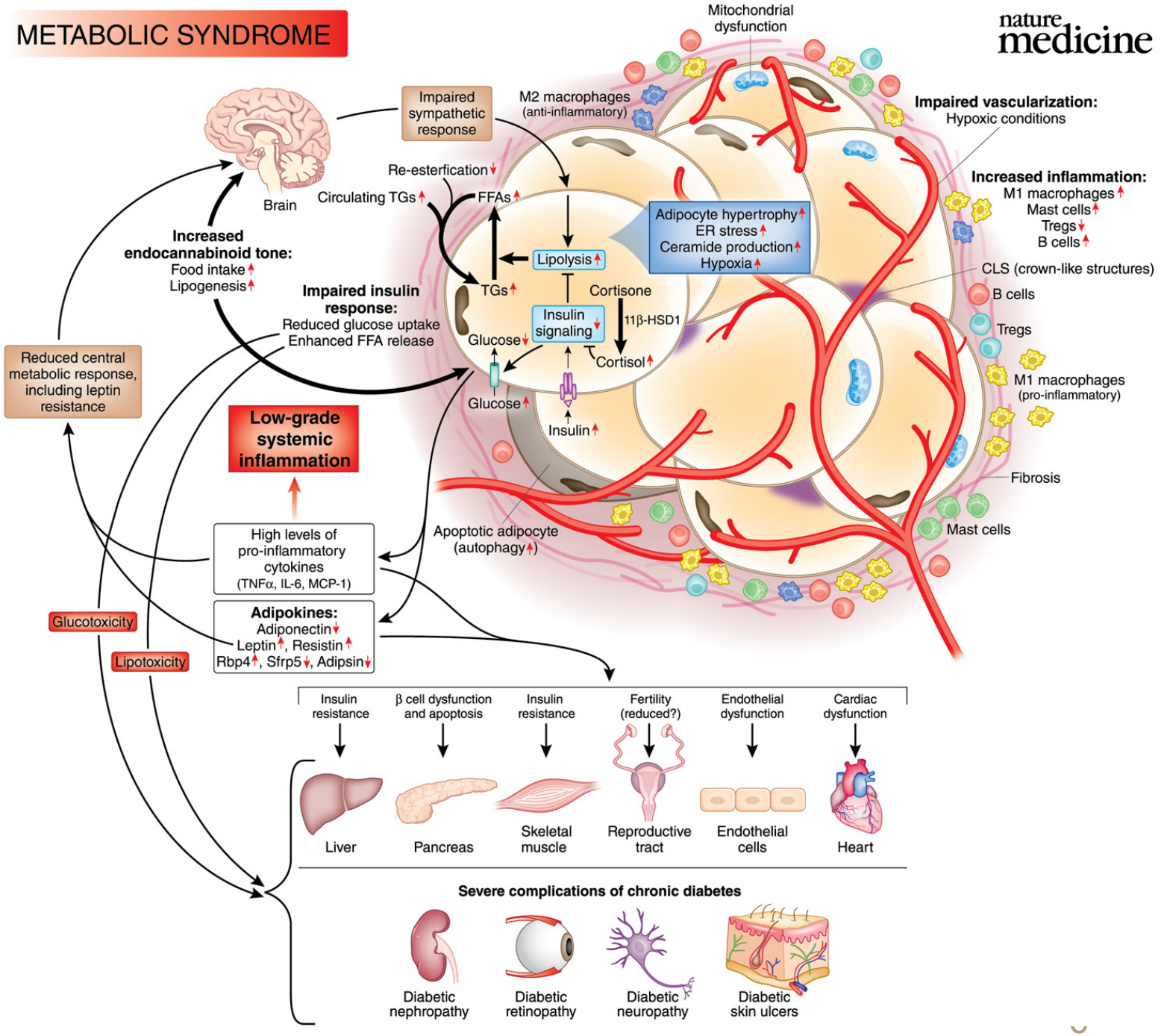
- Ad lib or free choice
- # of meals or snacks
- Inactivity and confinement
- Underestimation of BCS
- Spay / Neuter
- Age
- Breed
- Genetic defects
- Diseases
- Pharmaceuticals

What about pet food itself?



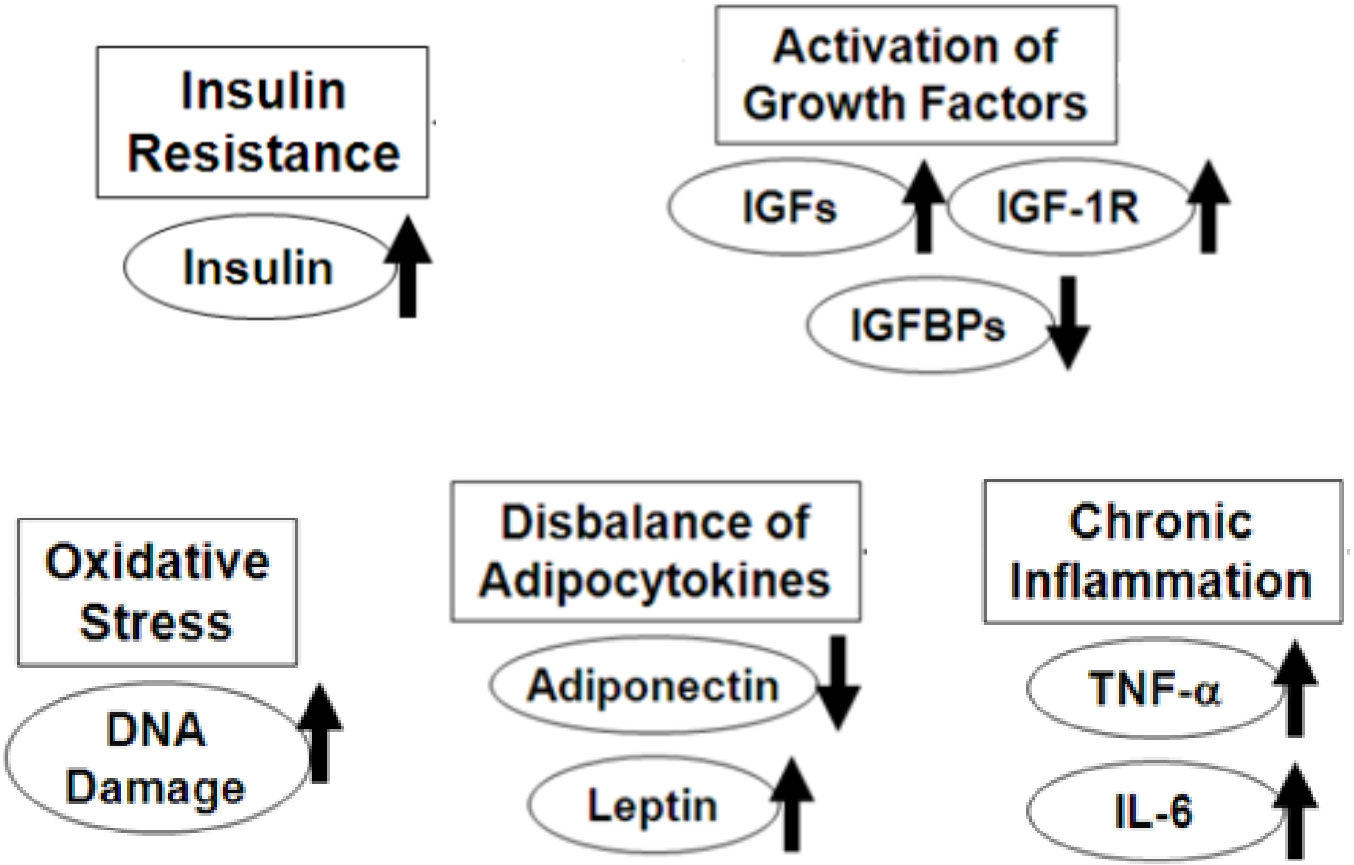
German, 2006

METABOLIC SYNDROME



Scherer, Nature Med.

Some Obesity Related Metabolic Abnormalities

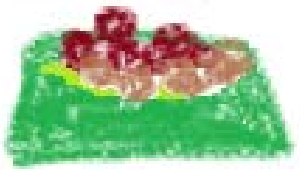


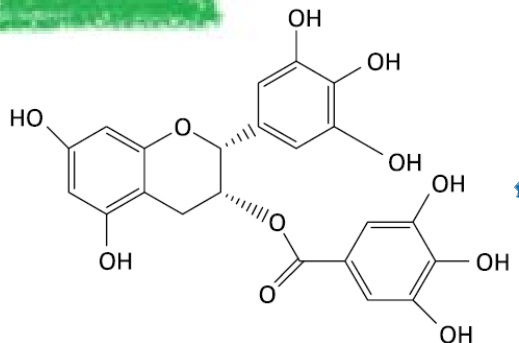
Nutrition and Obesity

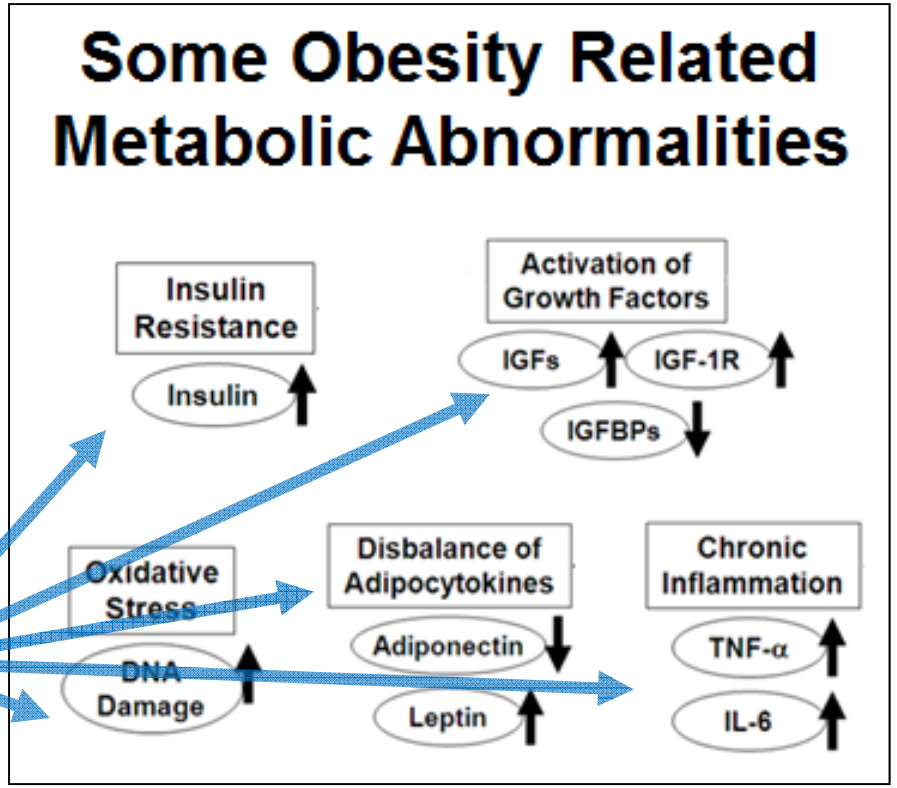
INTAKE
Calories From Foods

OUTPUT
Calories Used During Physical Activity

THE ENERGY BALANCE



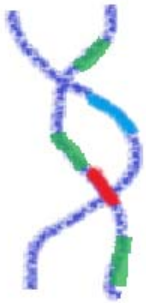




Petfood Industry

WATT

Individualized Nutrition



Genetics

Environment

=

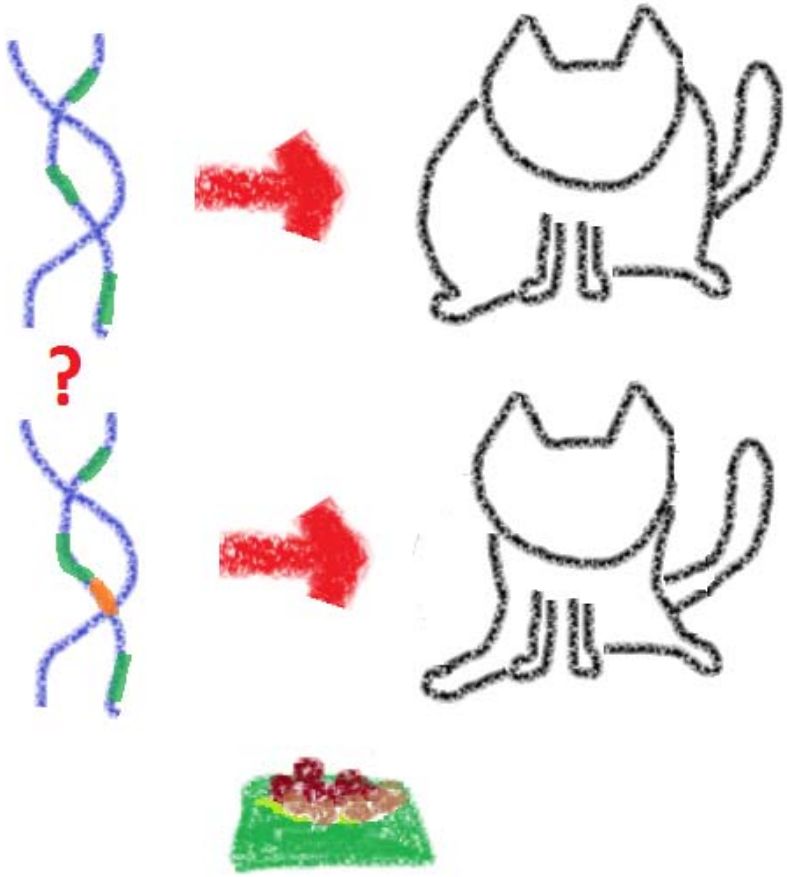
Nutritional Phenotype

Focused nutritional therapy:

- Species-based
- Breed-based
- Disease state
- Individual

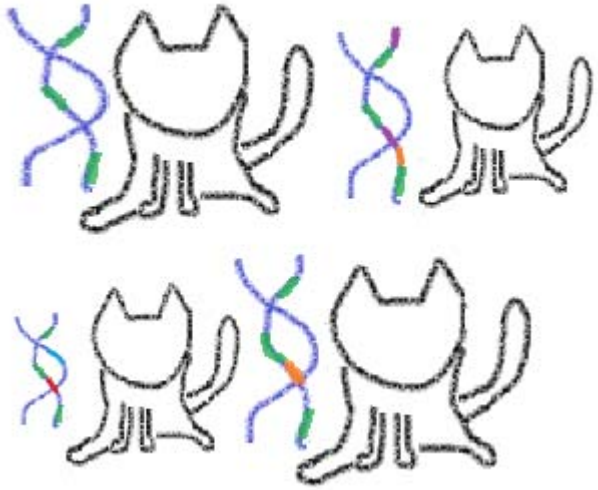
Nutrigenetics

What is the difference at the genetic level that determines a response?



Nutrigenomics

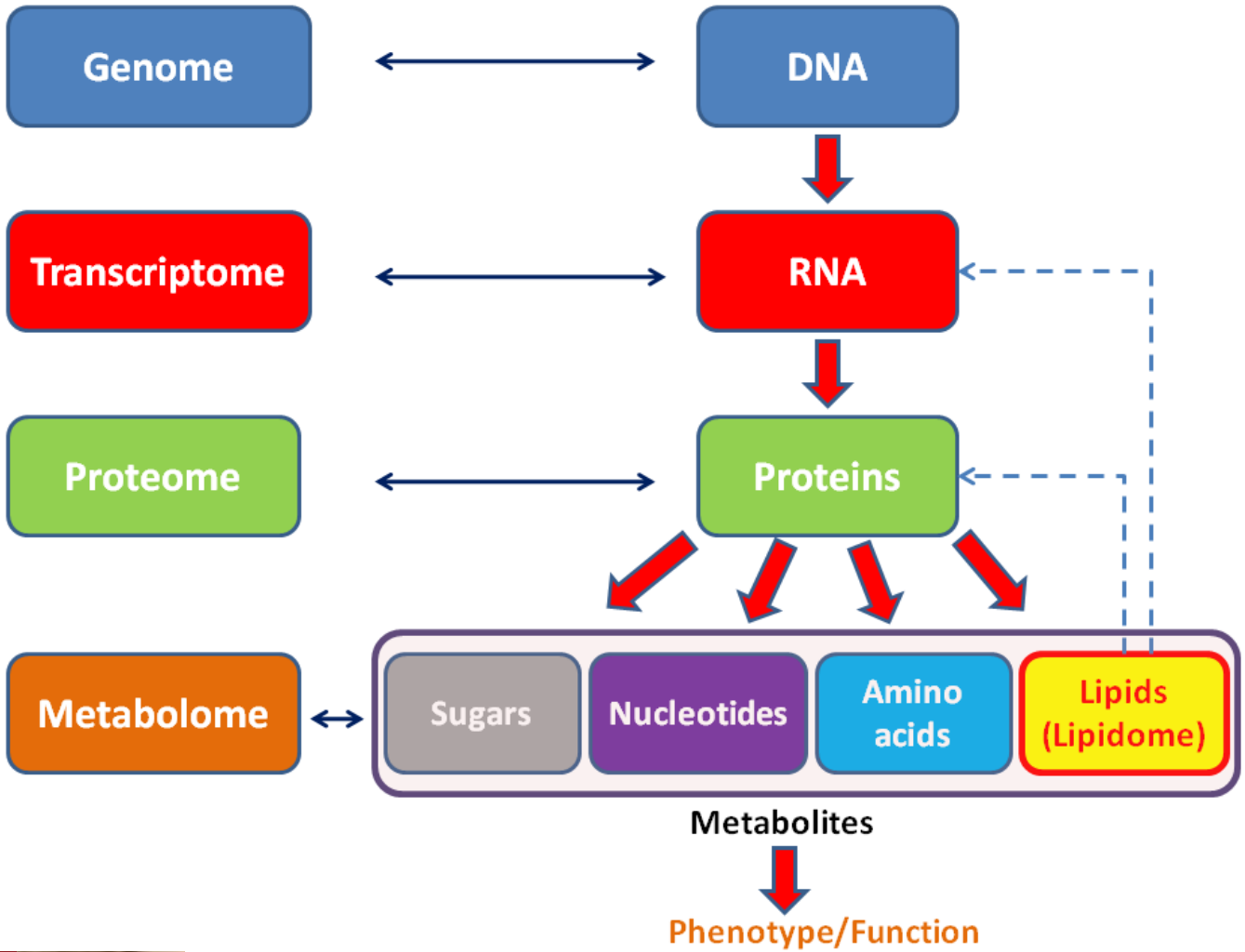
How does a nutritional factor influence genetic expression?



mRNA
Proteins
Metabolites

- Can we modify the system to prevent or delay the onset or severity of obesity, and optimize health?

Omics Cascade



Gene sequencing

Patterns of gene expression

Synthesis and structure of proteins

Profile and function of metabolites

Recent Advances = New Research Opportunities

- Sequencing
  - Cat and dog genome
  - High throughput sequencing techniques
- Transcriptome
  - RT-PCR
  - Dog microarray
  - RNA seq
- Proteome & Metabolome
  - Mass spectrometry

Research Questions

- Comparison to other species
  - Hormones, peptides, mechanisms similar?
- Obese vs. lean
  - Identify potential targets
- Biomarkers of obesity and obesity related disease
  - Prevention and treatment

Research Questions

- Nutrition-based
  - Requirements the same in obesity?
    - Ameliorate
    - Exacerbate
  - Appetite regulation
  - Mechanisms of functional foods
- Musts
  - Correlate changes to physiology
  - Determine mechanisms

Risk Factors

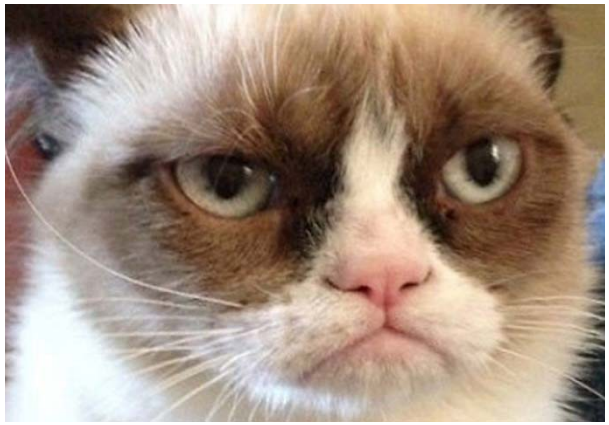
- Ad lib or free choice
- # of meals or snacks
- Inactivity and confinement
- Underestimation of BCS
- Spay / Neuter
- Age
- Breed
- Genetic defects
- Diseases
- Pharmaceuticals

German, 2006

Characteristics of our pets
~~Risk Factors~~

- Ad lib or free choice
- # of meals or snacks → Appetite regulation
- Inactivity and confinement → Exercise mimetic
- Underestimation of BCS
- Spay / Neuter → Estrogenic Flavonoids
- Age → Carnitine
- Breed
- Genetic defects
- Diseases
- Pharmaceuticals

German, 2006



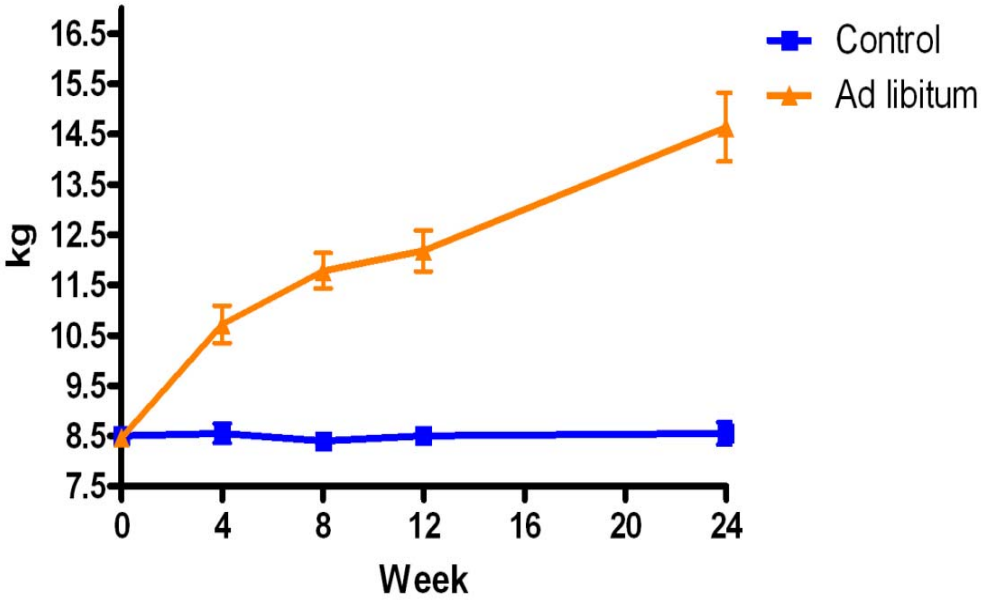
A few examples….

- Diet induced obesity
- Obese vs. lean dogs
- Green tea extract

Diet Induced Obesity

Diet Induced Obesity

- Obesity



Grant et al., 2011

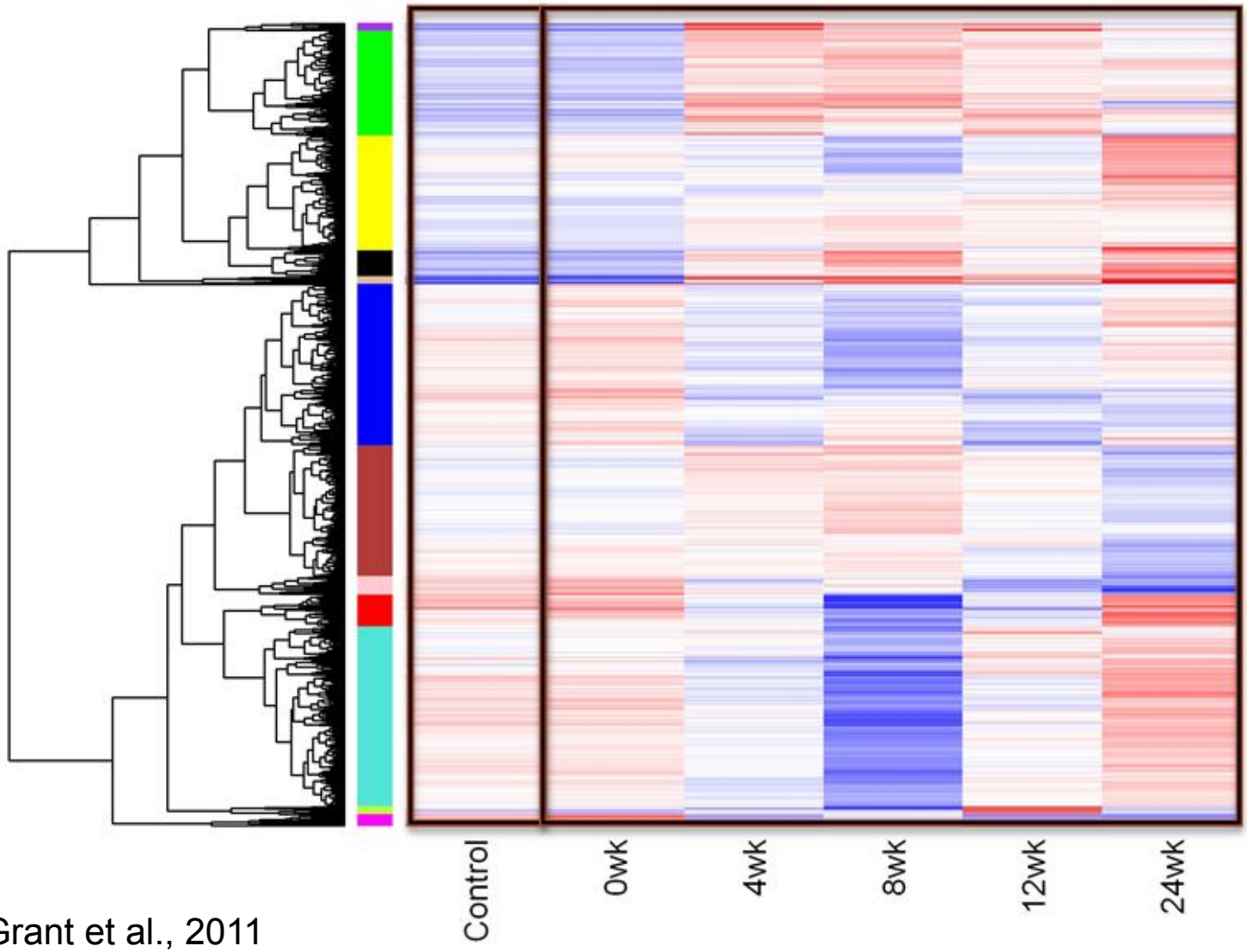
Diet Induced Obesity

- Obesity
  - Increased in blood:
    - Leptin
    - Triglycerides
    - Non-esterified fatty acids
    - Insulin

  - Subcutaneous fat biopsy
    - mRNA expression

Grant et al., 2011

Diet Induced Obesity



Grant et al., 2011

Diet Induced Obesity

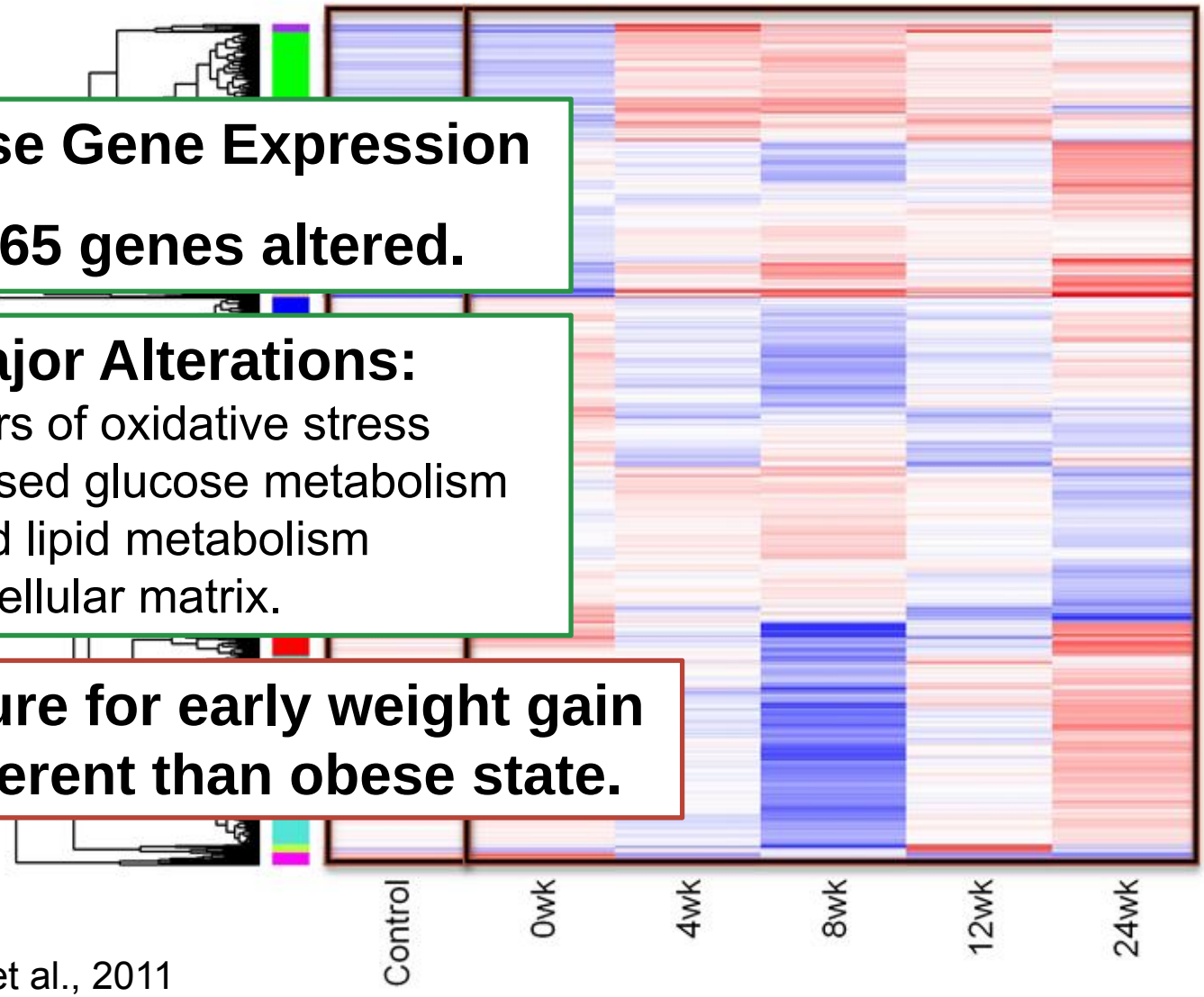
Adipose Gene Expression

- 1,665 genes altered.

Major Alterations:

- Markers of oxidative stress
- Increased glucose metabolism
- Altered lipid metabolism
- Extracellular matrix.

Signature for early weight gain is different than obese state.



Grant et al., 2011

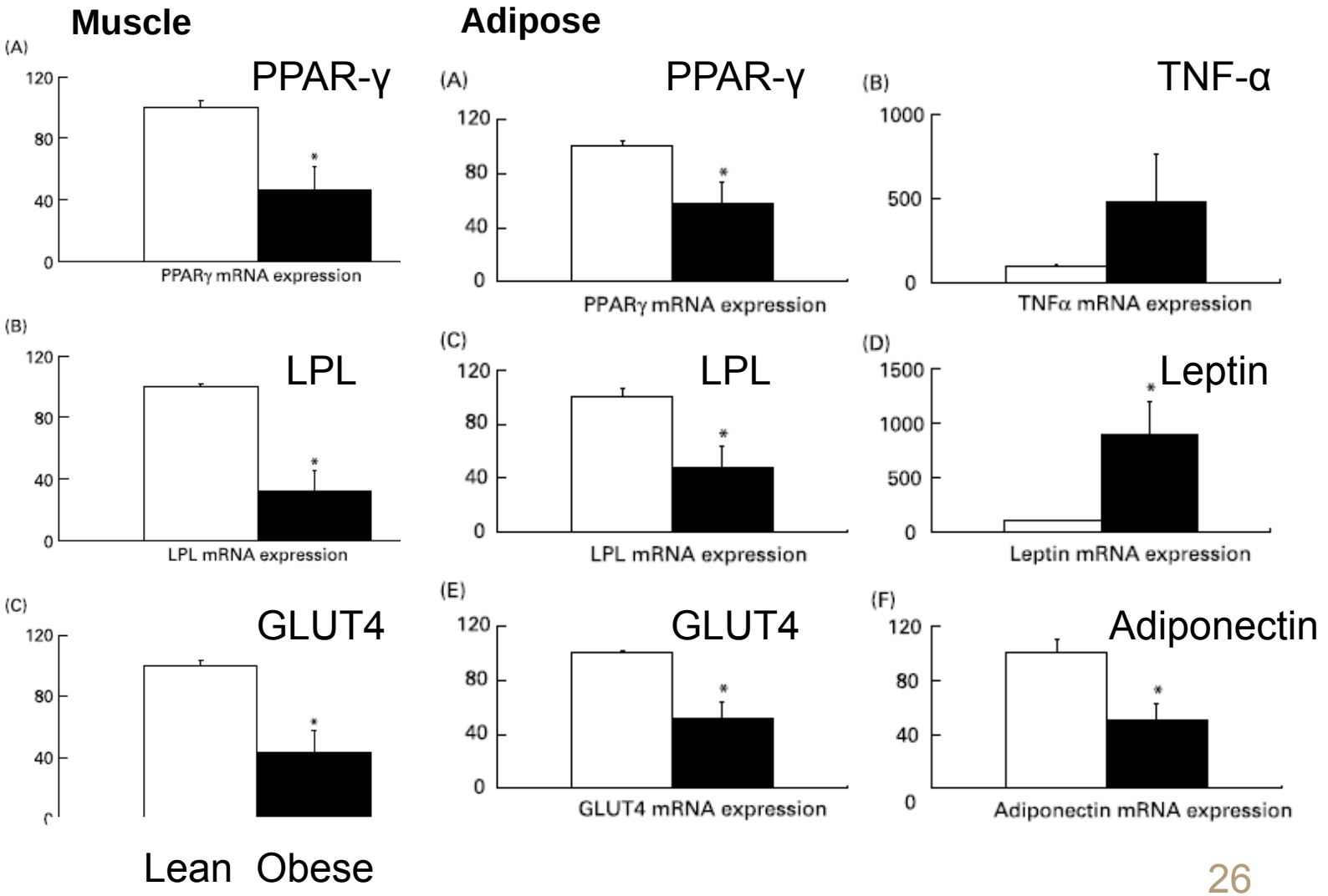
Obese vs. Lean Dogs

Obese vs. Lean Dogs

- 7 neutered female beagles
- Obese dogs
  - Fed at 1.4 times NRC recommendation
  - 140% starting BW
  - Increased blood triglycerides, leptin, insulin
  - Decreased blood adiponectin
  - Decreased insulin sensitivity

Gayet et al., 2007

Obese vs. Lean Dogs

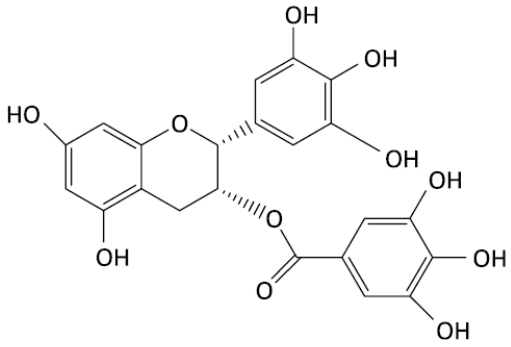


Gayet et al., 2007

Green Tea Extract

Green Tea Extract

- Monomeric polyphenols = catechins
  - Epigallocatechin-3-gallate (EGCG)



(–)-Epigallocatechin gallate

- Potential role in obesity
  - Increased insulin sensitivity
  - Lower adipose tissue weight
  - Decreased hepatic lipid deposition
  - Decreased inflammatory markers

Green Tea Extract
Data from other species

- Enhanced:

Lipolysis, B-oxidation, and thermogenesis (adipose)
- CPT-1
- Uncoupling protein 1
- Uncoupling protein 2
- HSL
- Adipose triglyceride lipase

Insulin Sensitivity
- Adiponectin
- CD36
- IRS1
- IRS2
- GLUT1
- GLUT4
- Glycogen synthase 1

B-oxidation of fats (liver)
- Acyl-CoA oxidase
- Medium chain acyl-CoA dehydrogenase

Green Tea Extract
Data from other species

- Inhibited:

Adipogenic genes (Adipose)
- C/EBP-α
- SREBP-1c (also liver)
- Adipocyte fatty acid-binding protein
- FAS (also liver)
- SCD-1 (also liver)

Inflammation
- TNF-α
- IL-6

FA synthesis (Liver)
- FAS
- Glycerol-3-phosphate acyltransferase
- SCD-1
- G6PDH

Green Tea Extract

- Obese female dogs - BCS: 7 – 8
- 12 wk treatment
  - Green Tea (n = 6)
  - Control (n = 4)

- Green Tea Extract (80 mg/kg BW)
  - 35.7 mg/g epicatechin
  - 64.8 mg/g epicatechin gallate
  - 20.2 mg/g epigallocatechin
  - 153.1 mg/g EGCG

Serisier et al., 2008

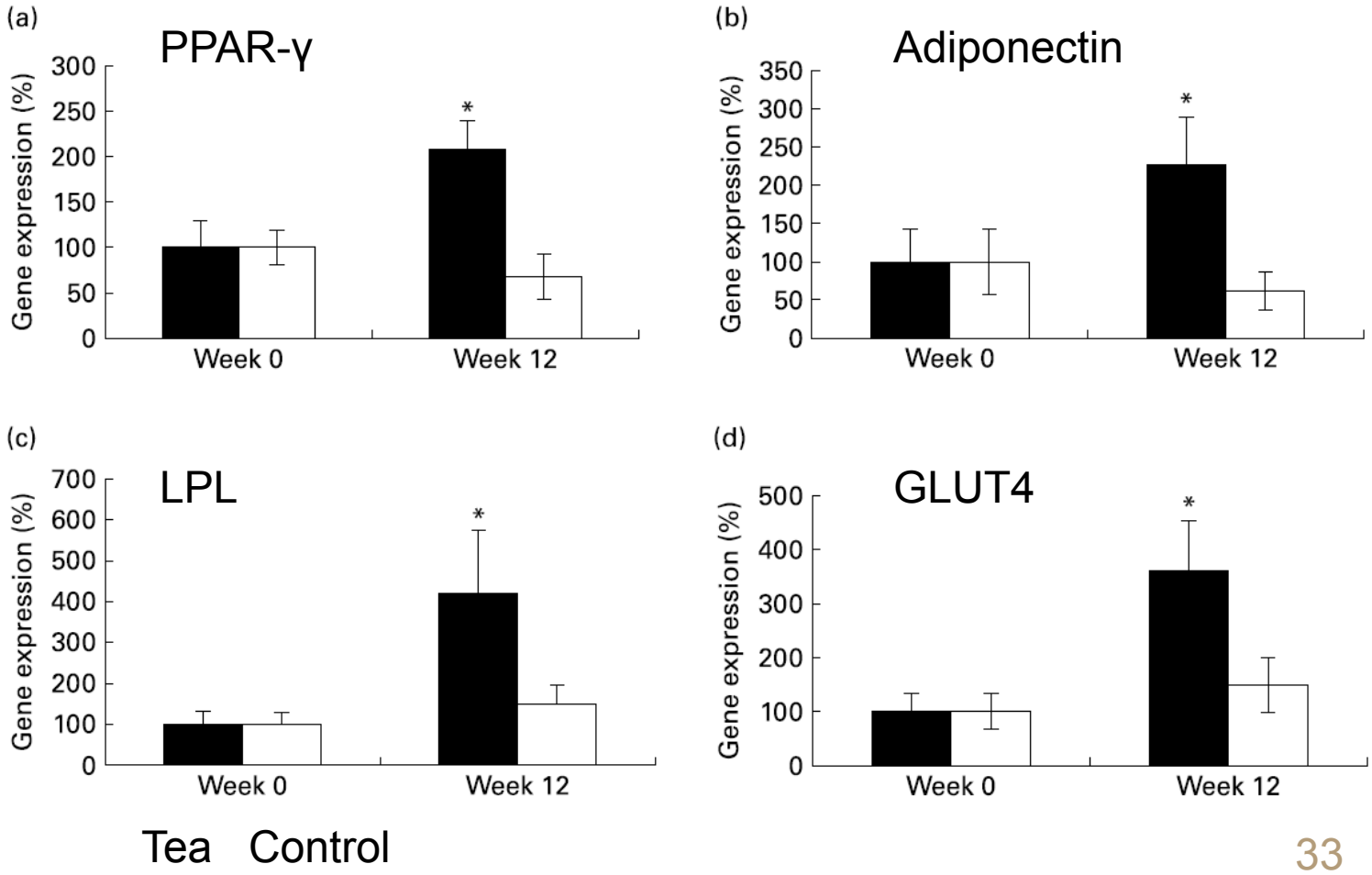
Green Tea Extract

- No change in BW
- Increased insulin sensitivity
- Decreased plasma TAG

Serisier et al., 2008

Green Tea Extract

- Visceral adipose



Serisier et al., 2008

Some other studies:

- Dogs
  - Nicotinic acid supplementation in obese dogs (Le Bloc'h et al., 2010)
  - scFOS supplementation in obese dogs (Respondek et al., 2008)
  - High fat vs. low fat diet (Kabir et al., 2005, 2011)
  - Weight loss – (Leray et al., 2008; Wakshlag et al., 2011; Tvarijonaviciute et al., 2012)

Some other studies:

- Cats
  - Polyphenols and curcumin in obese cats (Leray et al., 2011)
  - High protein vs. moderate protein (Vester et al., 2009b)
  - Lean vs. obese (Hoenig et al., 2006; Mori et al., 2009; Lee et al., 2011)
  - Spay/neuter induced obesity (Belsito et a., 2009; Vester et al., 2009a)
- Recent Review:
  - de Godoy and Swanson, 2013

Summary

- Management of obesity will require an understanding of diet, genetics, obesity, and their interaction.
- Recent developments in genomic research have improved understanding at cell, tissue, and body level.
- Huge potential impact.

- Potential for application to pet food
  - Need more research
  - Identify species differences
  - Identify targets
    - Tissue
    - Disease
    - Physiological state
  - Interaction with microbiota?
  - Dietary interventions

Substances that may be of interest:

- Fibers (scFOS)
- Green tea
- Curcumin
- Isoflavones
- Dried beans
- n-3 PUFA
- CLA
- L-Carnitine
- Carotenoids

Thank You

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