



# L'organo adiposo, ruolo centrale nella sindrome metabolica

Claudio Pagano

Lab. Endocrino-Metabolico, Clinica Medica 3  
Dip. di Scienze Mediche e Chirurgiche  
Università di Padova



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## Medical Complications of Obesity



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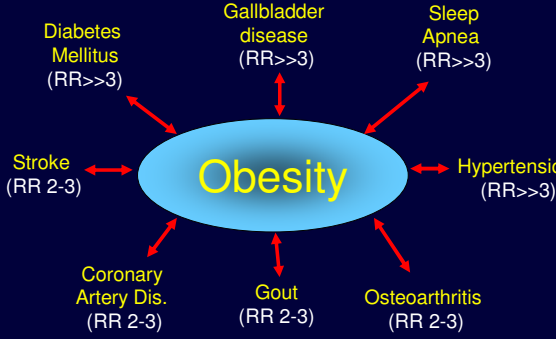
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## Conditions Associated With Obesity

(Relative Risk)



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## Clinical Identification of the Metabolic Syndrome\*: NCEP-ATP III

\*Diagnosis is established when  $\geq 3$  of these risk factors are present

| Risk Factor                                | Defining Level                   |
|--|----------------------------------|
| Abdominal obesity<br>(Waist circumference) |                                  |
| Men  | $>102$ cm ( $>40$ in)            |
| Women                                      | $>88$ cm ( $>35$ in)             |
| TG   | $\geq 150$ mg/dL                 |
| HDL-C                                      |                                  |
| Men  | $<40$ mg/dL                      |
| Women                                      | $<50$ mg/dL                      |
| Blood pressure                             | $\geq 130 / \geq 85$ mm Hg       |
| Fasting glucose                            | $>110$ ( $\geq 100^{**}$ ) mg/dL |

\*\* 2003 New ADA IFG criteria (Diabetes Care)

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. JAMA. 2001;285:2486-2497.

## The IDF consensus worldwide definition of the metabolic syndrome

Table 1: The new International Diabetes Federation (IDF) definition

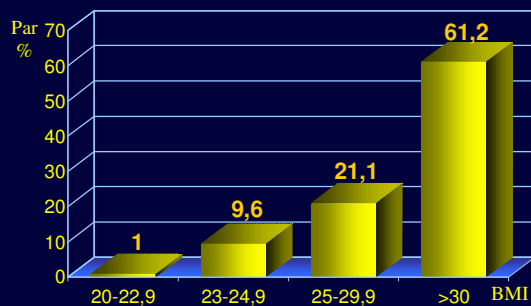
According to the new IDF definition, for a person to be defined as having the metabolic syndrome they must have:

**Central obesity** defined as waist circumference  $\geq 94$ cm for Europid men and  $\geq 80$ cm for Europid women, with ethnicity specific values for other groups)

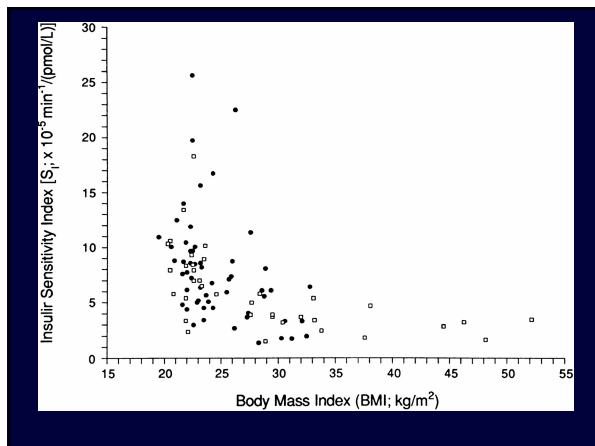
plus any two of the following four factors:

- **raised TG level:**  $> 150$  mg/dL (1.7 mmol/L), or **specific treatment for this lipid abnormality**
- **reduced HDL cholesterol:**  $< 40$  mg/dL (0.9 mmol/L) in males and  $< 50$  mg/dL (1.1 mmol/L) in females, or **specific treatment for this lipid abnormality**
- **raised blood pressure:** systolic BP  $\geq 130$  or diastolic BP  $\geq 85$  mm Hg, or **treatment of previously diagnosed hypertension**
- **raised fasting plasma glucose (FPG)**  $\geq 100$  mg/dL (5.6 mmol/L), or **previously diagnosed type 2 diabetes**  
If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

Percentuale di rischio popolazione-attribuibile (Par%) per diabete di tipo 2, per categorie di BMI vs BMI  $< 23$



Wolfe Colditz, 1996




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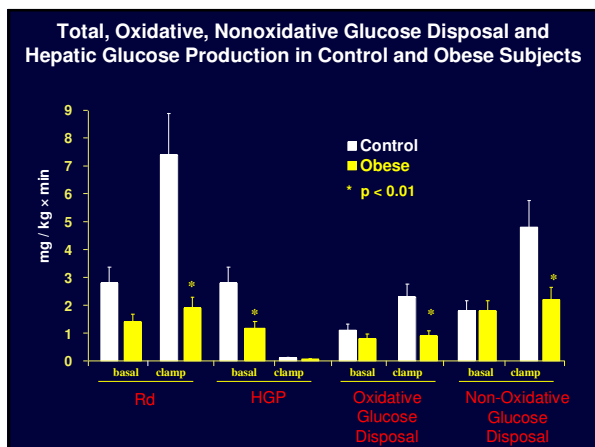
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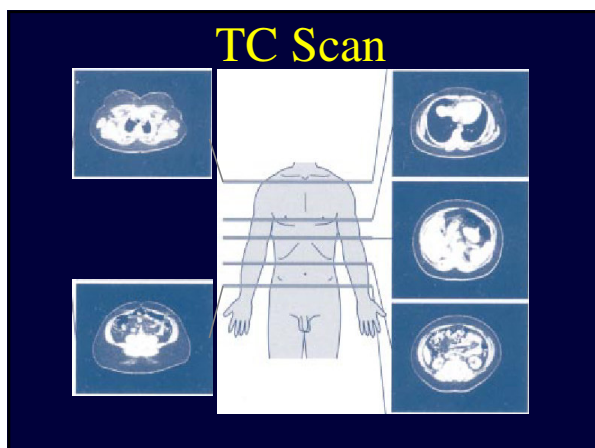
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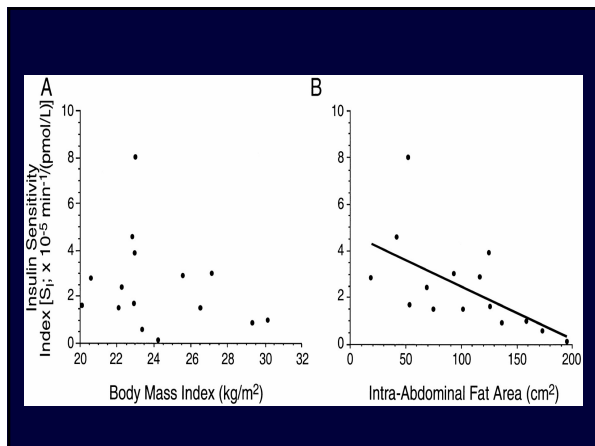
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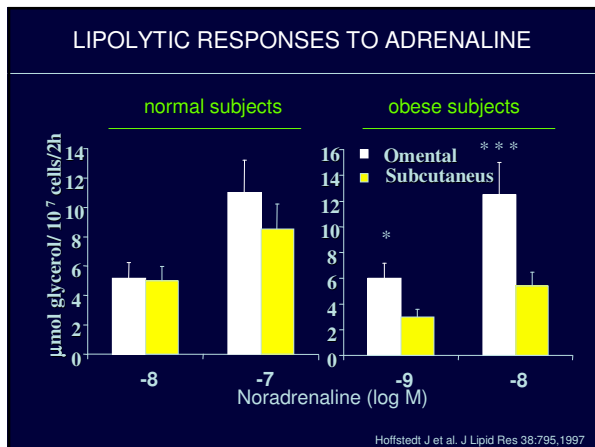
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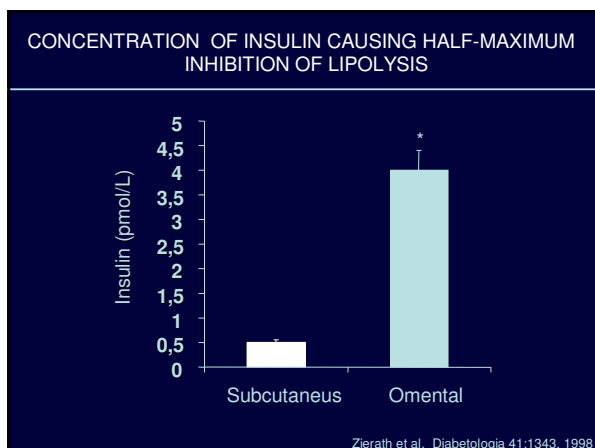
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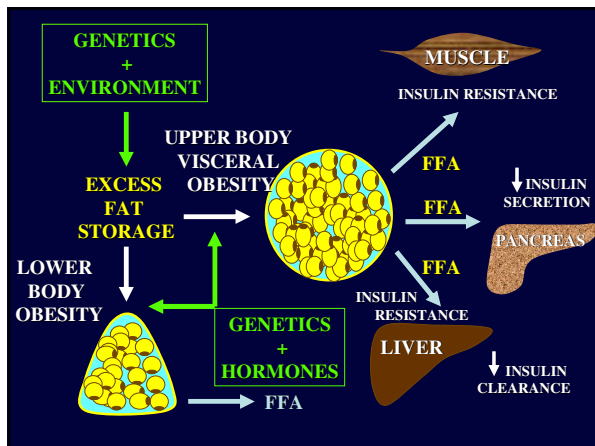
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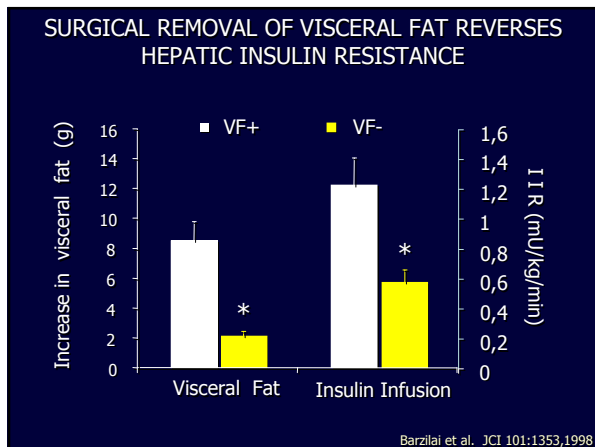
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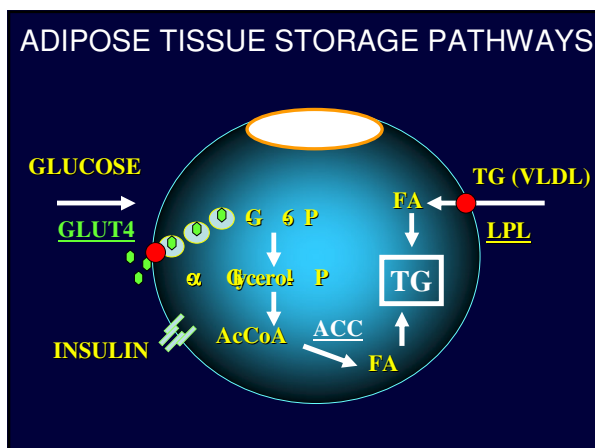
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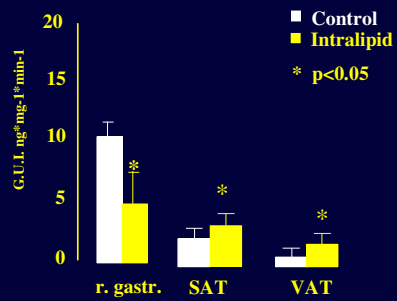
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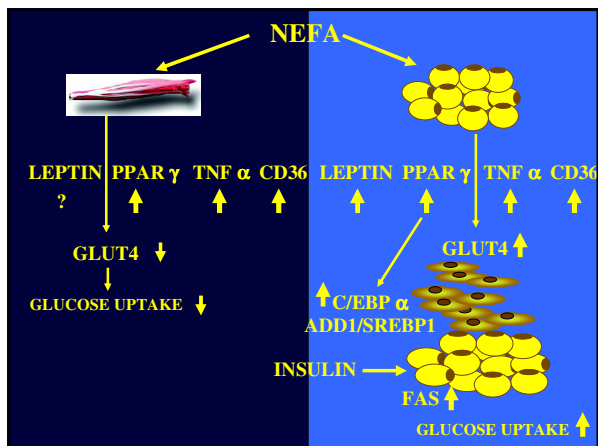
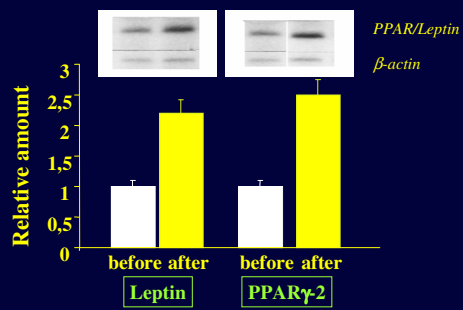
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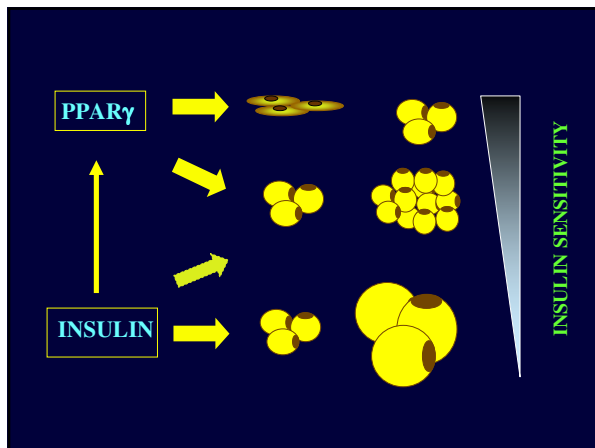
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Effect of 24 h Intralipid+heparin infusion on MUSCLE and ADIPOSE TISSUE glucose utilization.



PPAR $\gamma$ -2 AND LEPTIN mRNA LEVELS IN HUMAN ADIPOSE TISSUE BEFORE AND AFTER 5h INTRALIPID PLUS HEPARIN INFUSION






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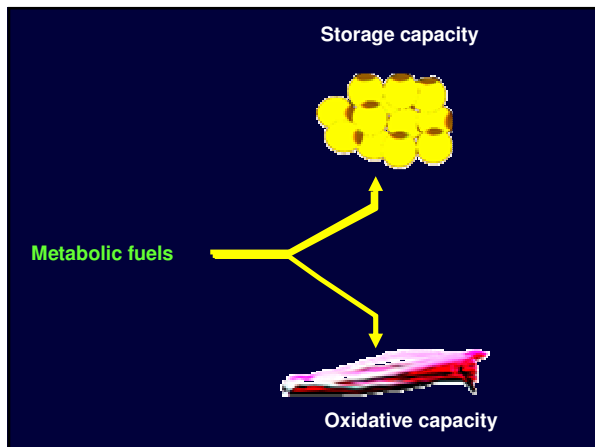
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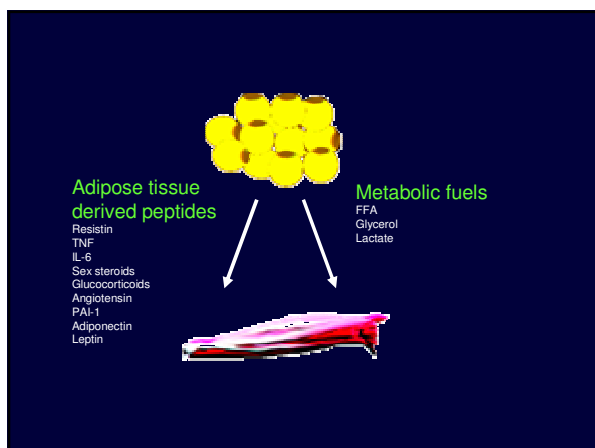
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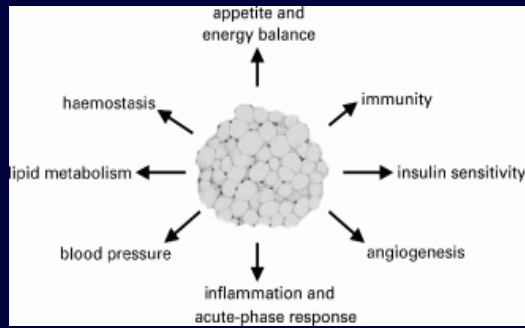
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## THE ADIPOSE ORGAN



Trayhurn P et al. Br J Nutr 2004.

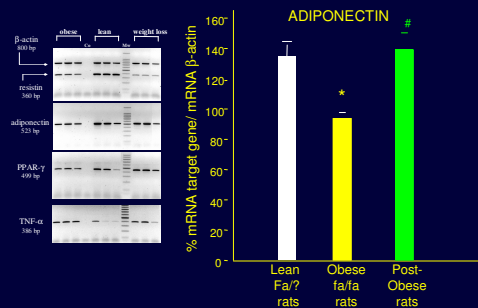


August 2001 Volume 7 Number 8 pp 941 - 946

The fat-derived hormone adiponectin reverses insulin resistance associated with both lipodystrophy and obesity

T. Yamauchi et al.

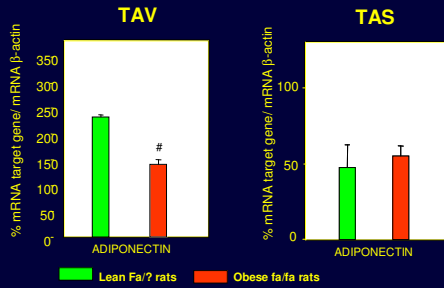
## adiponectin expression in obese rats: effect of weight loss



Milan G et al. Obesity Research 2002

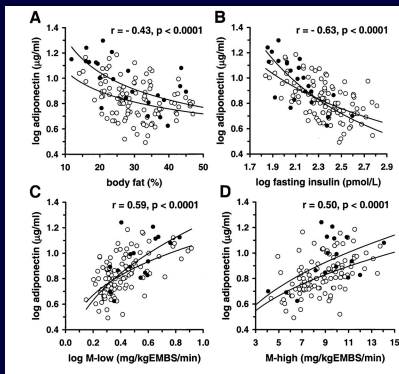


## Regional differences in adiponectin expression



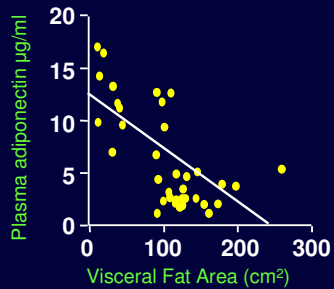
Milan G et al. Obesity Res 2002

## Adiponectin is Reduced in Obese Humans

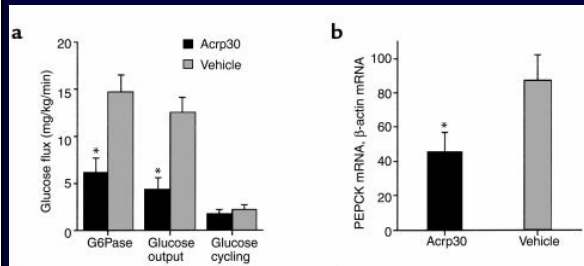


Weyer et al JCEM 86:1930,2001

## Decreased Plasma Adiponectin in Visceral Obesity



(a) Effect of Acrp30 on glucose production, G6Pase flux, and glucose cycling.  
 (b) Effect of Acrp30 on hepatic mRNA expression of PEPCK.



Combs TP et al. J Clin Invest 2001

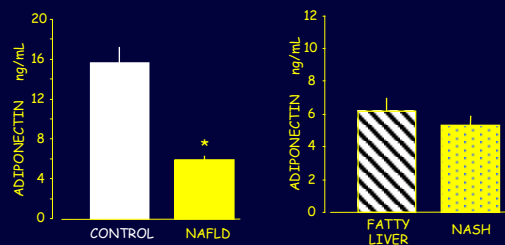
European Journal of Endocrinology (2005) 152 1-7

ISSN 0804-4643

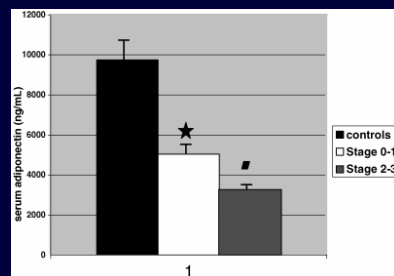
#### CLINICAL STUDY

### Plasma adiponectin is decreased in nonalcoholic fatty liver disease

Claudio Pagano, Giorgio Soardo, Walter Esposito, Francesco Fallo, Lorenza Basan, Debora Domini, Giovanni Federspil, Leonardo A Sechi and Roberto Vettor  
 Endocrine-Metabolic Laboratory, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy and Liver Unit, Internal Medicine, Department of Pathology and Experimental and Clinical Medicine, University of Udine, Udine, Italy  
 (Correspondence should be addressed to Claudio Pagano, Department of Medical and Surgical Sciences, University of Padova, Via ospedale 105, 35100 Padova, Italy; Email: claudio.pagano@unipd.it)

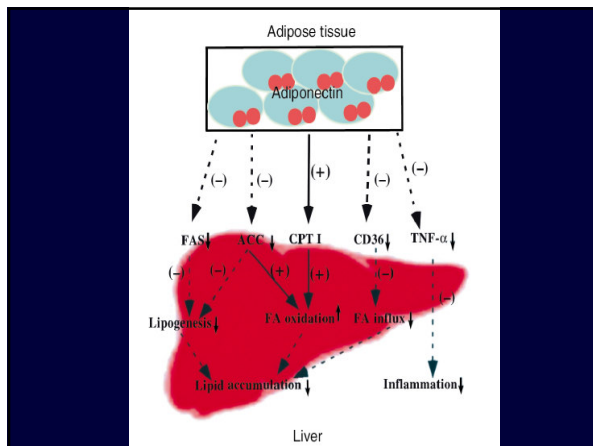


### Serum adiponectin in NASH patients, according to fibrosis stage, and of insulin-sensitive controls



Stage 0-1:absent-mild fibrosis  
 Stage 2-3:moderate-severe fibrosis

Musso G et al. Am J Gastroent 2005




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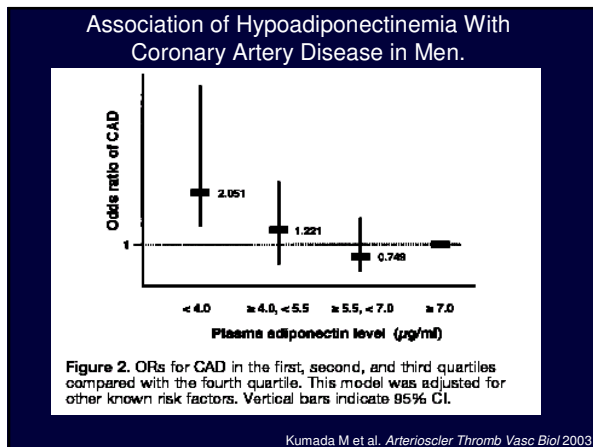
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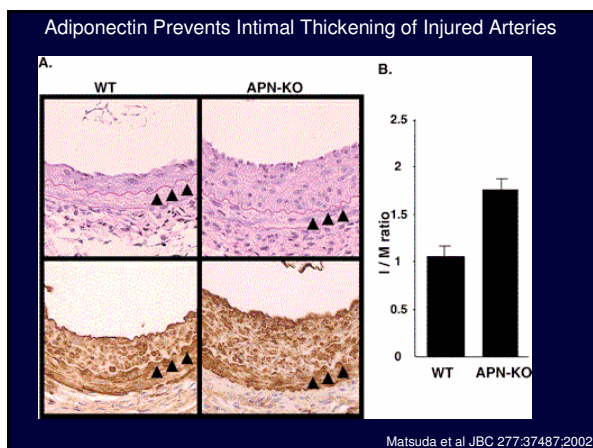
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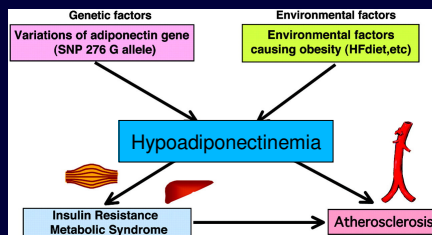
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## Adiponectin hypothesis for insulin resistance, metabolic syndrome, and atherosclerosis



Kadowaki T et al. Endocr Rev 2005

## The hormone resistin links obesity to diabetes

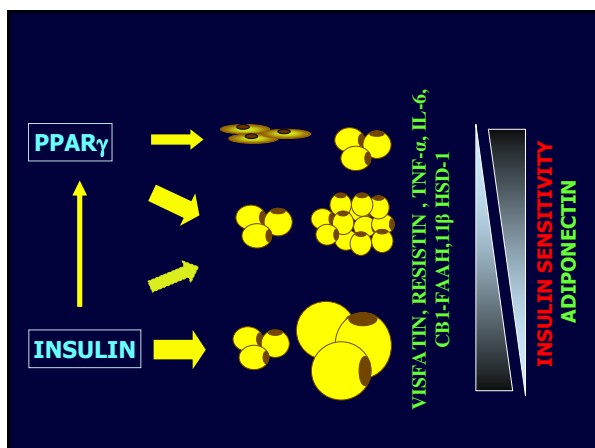
Claire M. Steppan, Shannon T. Bailey, Savitha Bhat, Elizabeth J. Brown, Ronadip R. Banerjee, Christopher M. Wright, Hiralben R. Patel, Rexford S. Ahima & Mitchell A. Lazar

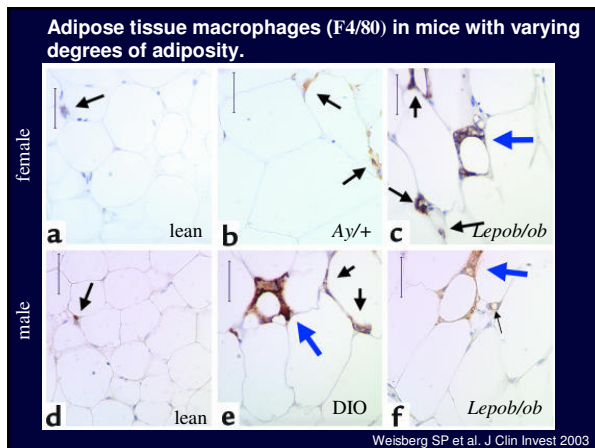
Division of Endocrinology, Diabetes, and Metabolism, Departments of Medicine and Genetics, and The Penn Diabetes Center, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania 19104, USA

Diabetes mellitus is a chronic disease that leads to complications including heart disease, stroke, kidney failure, blindness and nerve damage. Type 2 diabetes, characterized by target-tissue resistance to insulin, is epidemic in industrialized societies and is strongly associated with obesity; however, the mechanism by which increased adiposity causes insulin resistance is unclear. Here we show that adipocytes secrete a unique signalling molecule, which we have named resistin (for resistance to insulin). Circulating resistin levels are decreased by the anti-diabetic drug rosiglitazone, and increased in diet-induced and genetic forms of obesity. Administration of anti-resistin antibody improves blood sugar and insulin action in mice with diet-induced obesity. Moreover, treatment of normal mice with recombinant resistin impairs glucose tolerance and insulin action. Insulin-stimulated glucose uptake by adipocytes is enhanced by neutralization of resistin and is reduced by resistin treatment. Resistin is thus a hormone that potentially links obesity to diabetes.

Nature 409:307-12, 2001

1. Resistin expression is adipose specific
2. Resistin is present in blood and increased in obese mice
3. Neutralization of resistin improves hyperglycemia and insulin resistance
4. Resistin impairs glucose tolerance in mice
5. Resistin antagonizes insulin-stimulated glucose uptake in 3T3-L1 cells






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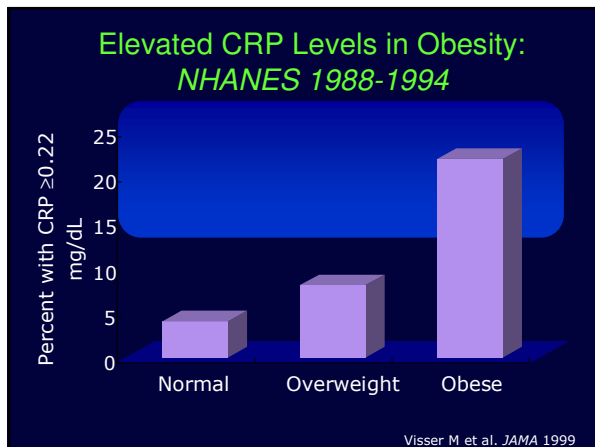
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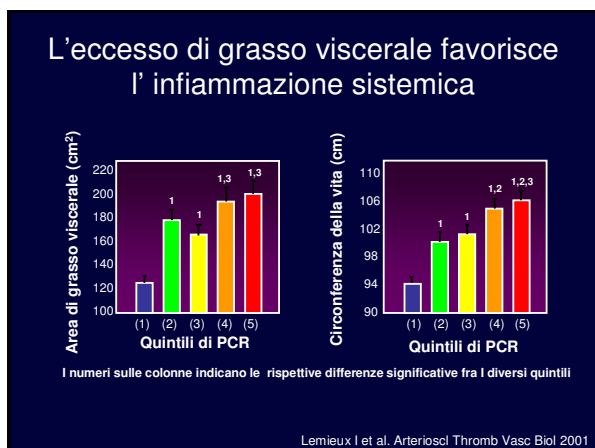
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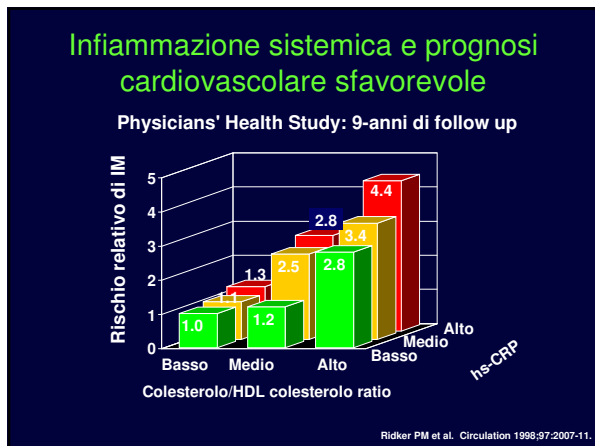
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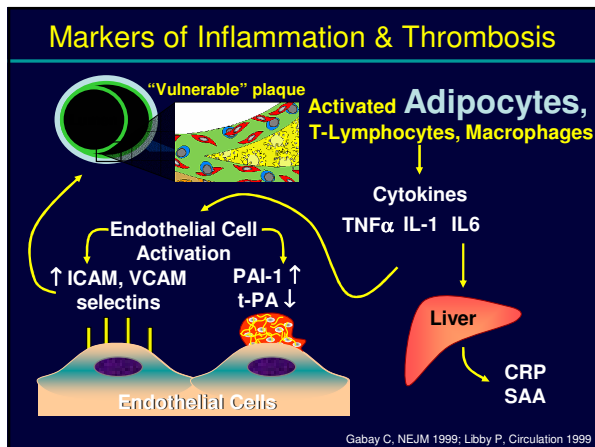
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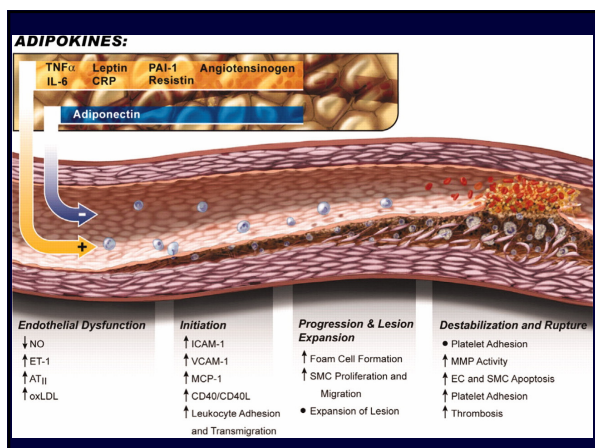
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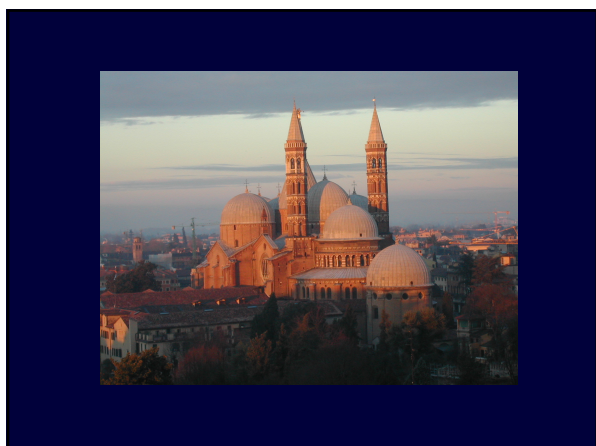
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