

# ***Obesity and inflammation***

***is the adipose tissue on fire?***

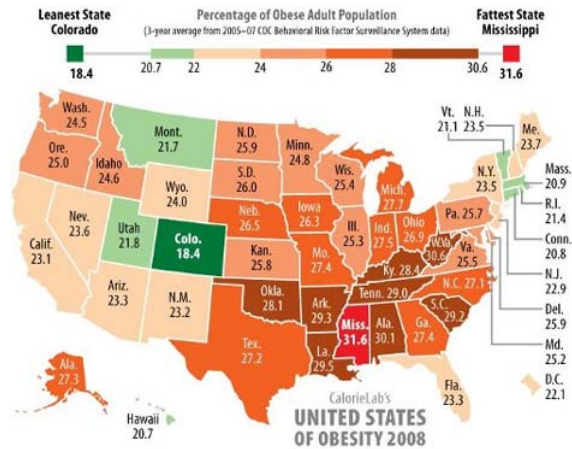
**Jens M. Bruun, MD, PhD**

**Dept. of Endocrinology and Metabolism C,  
Aarhus University Hospital, Aarhus Sygehus, Denmark.**

## **Agenda**

- **Obesity, adipose tissue and *low-grade inflammation*.**
- **Inflammation in adipocytes *vs.* stromal-vascular cells**
  - **AT-macrophages – how did they get there and what are they doing.**
- **Effects of weight loss.**
- **Conclusion and perspectives.**

# Obesity in the US



## Obesity – why care....

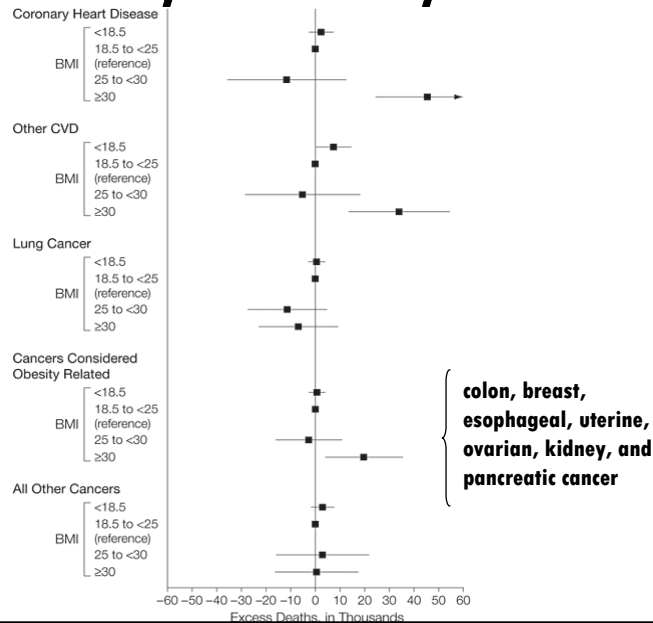
~20000 BC



~2005



## Obesity and mortality



Flegal, JAMA 2007

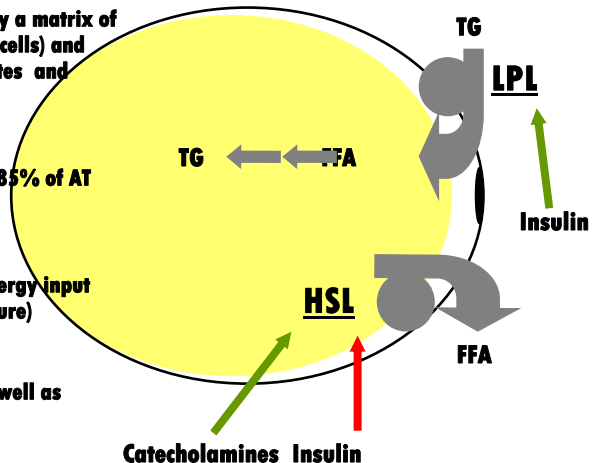
## Adipose Tissue - a sophisticated container?

Lipid-filled adipocytes surrounded by a matrix of collagen, blood vessels (endothelial cells) and cells of the immune system (monocytes and macrophages).

Storage of energy as triglyceride (~85% of AT weight).

The size is mainly determined by energy input and energy output (energy expenditure)

The AT can undergo hypertrophy as well as hyperplasia.

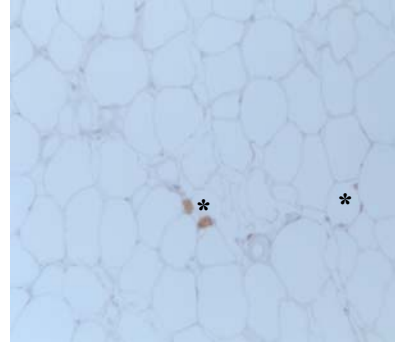


## Cell-types in human AT

**Table 1.** Cellular components (%) of human AT

<b>Mature adipocytes</b>	<b>50-70</b>
<b>Stromal "preadipocytes"</b>	<b>20-40</b>
<b>Endothelial cells</b>	<b>1-10</b>
<b>Macrophages</b>	<b>1-30</b>
<b>Other cell types</b>	<b>?</b>

*Adapted after Hauner H, Proc Nutr Soc 2005*



**\*CD68 positive cells**  
(with courtesy of Dr. Feigh)

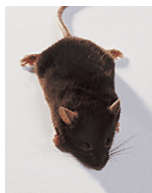
## In the beginning....*there was leptin*

### Positional cloning of the mouse *obese* gene and its human homologue

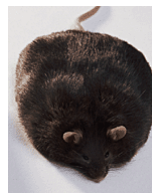
**Yiying Zhang<sup>\*,†</sup>, Ricardo Proenca<sup>\*,†</sup>, Margherita Maffei<sup>†</sup>, Marisa Barone<sup>\*,†</sup>,  
Lori Leopold<sup>†</sup> & Jeffrey M. Friedman<sup>\*,†,‡</sup>**

\* Howard Hughes Medical Institute, † The Rockefeller University, 1230 York Avenue, New York, New York 10021, USA

*Nature*. 1994 Dec 1;372(6505):425-32

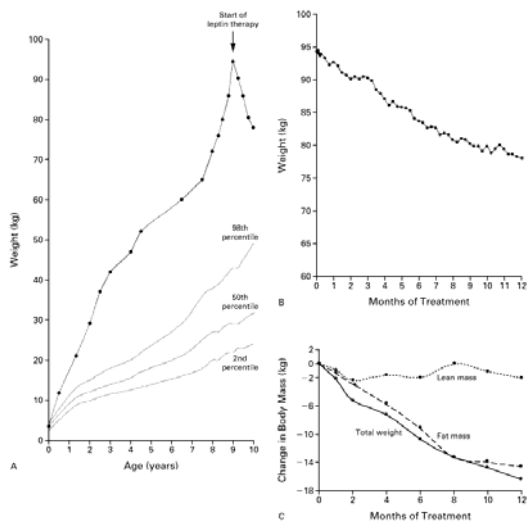


**wildtype**



***ob/ob***

## Leptin effects in humans (*ob/ob*)



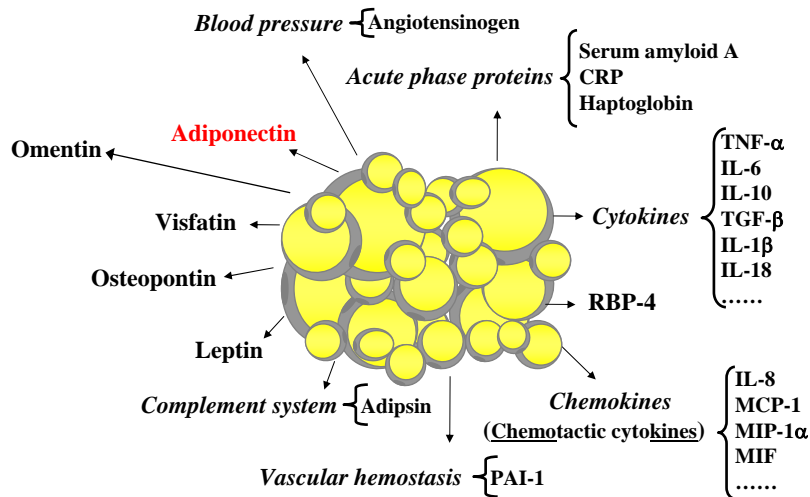
3 yrs – 42 kg

7 yrs – 32 kg

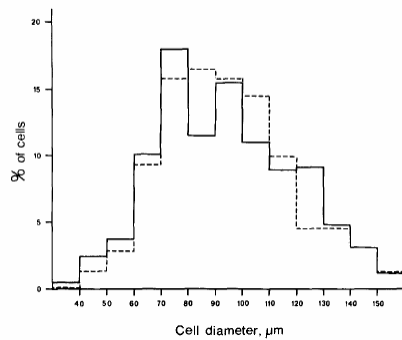
Farooqi IS, Front Horm Res 2008

Farooqi IS, NEJM 1999

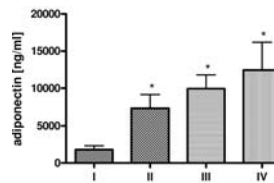
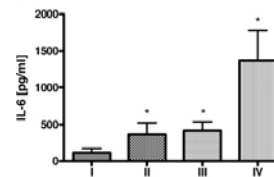
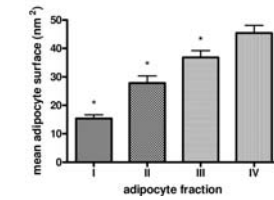
## Adipose-secreted proteins - *adipokines*



## The adipocyte



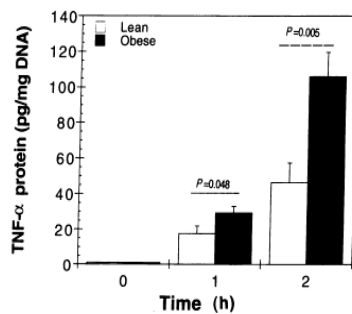
Smith U, J Lipid Res 1972



Skurk T, J Clin Endo Metab 2007

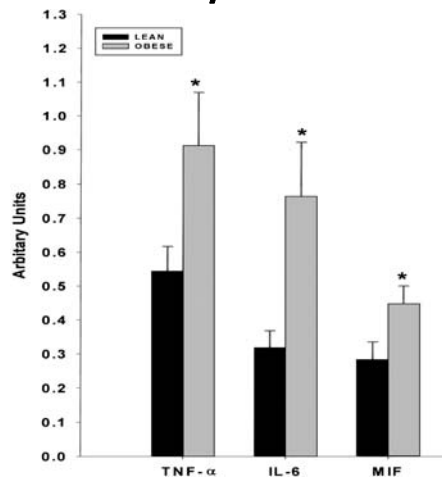
## Obesity and low-grade inflammation

### Adipocytes



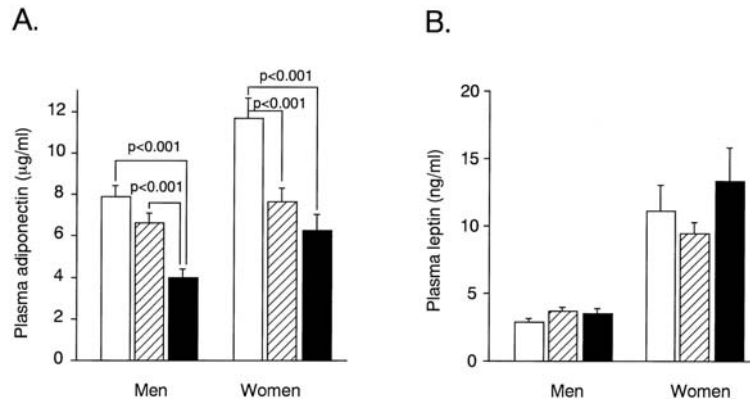
Hotamisligil GS, J Clin Invest 1995

### Monocytes



Ghanim H, Circulation 2004

## Obesity, low-grade inflammation and concomitant disease

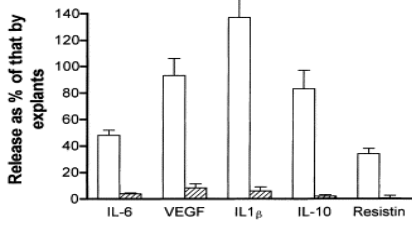
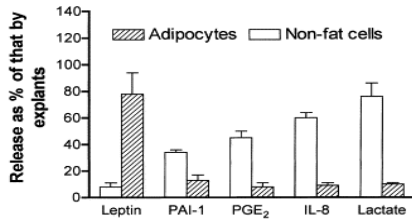


Hotta K, Arterioscler Thromb Vasc Biol 2000

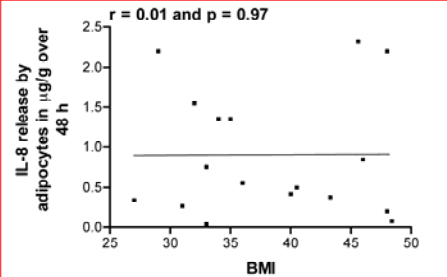
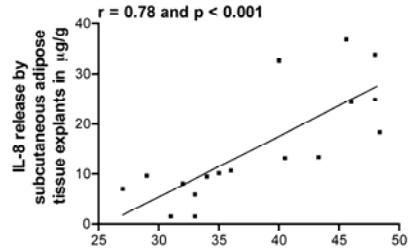
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- Effects of weight loss.
- Conclusion and perspectives.

## Adipocytes vs. SV-cells



Fain JN, BBRC 2003

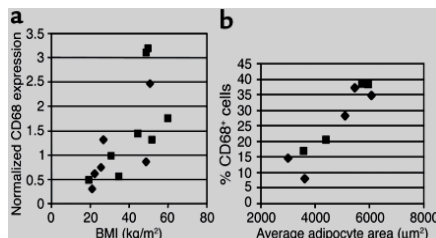
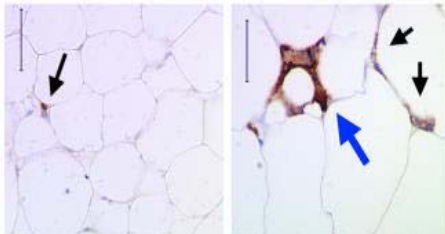
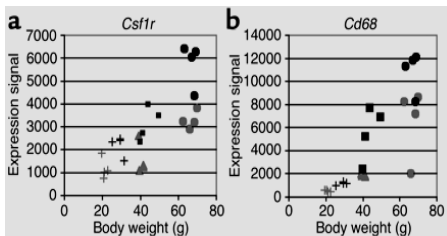


Bruun JM, AJP Endo Metab 2004

## Obesity and ATM

Lean

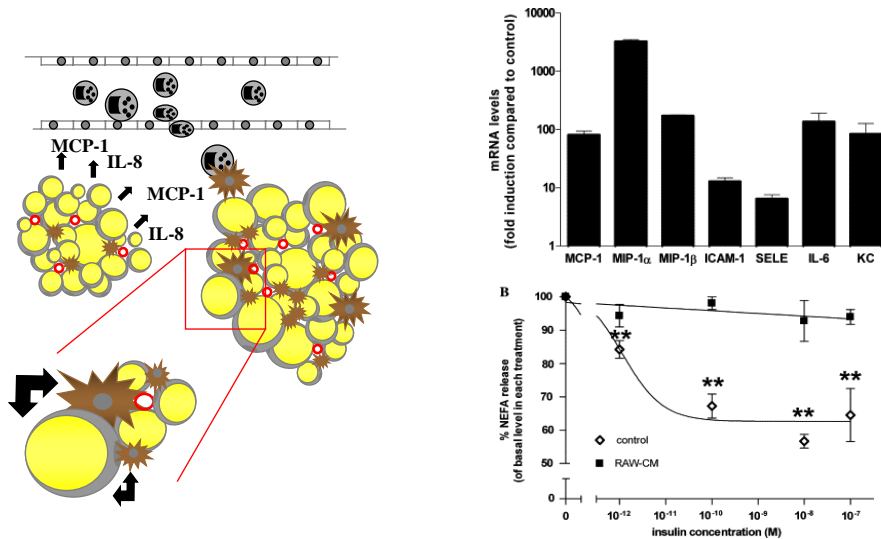
DIO



Weisberg SP,  
J Clin Invest 2003

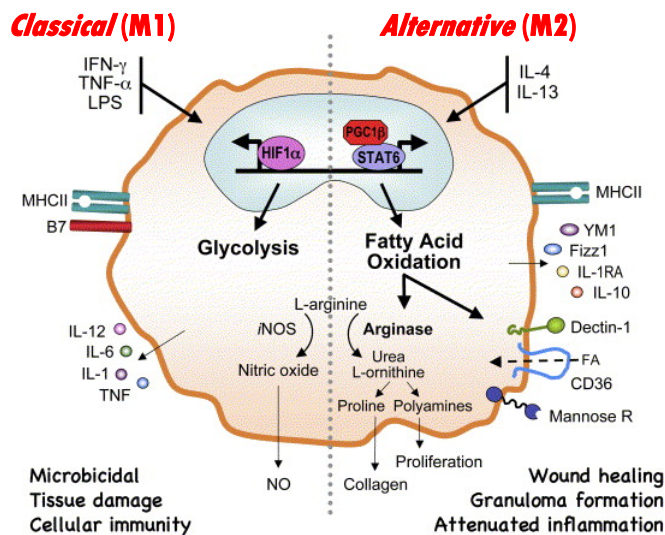


## Adipocyte and ATM –cross talk?



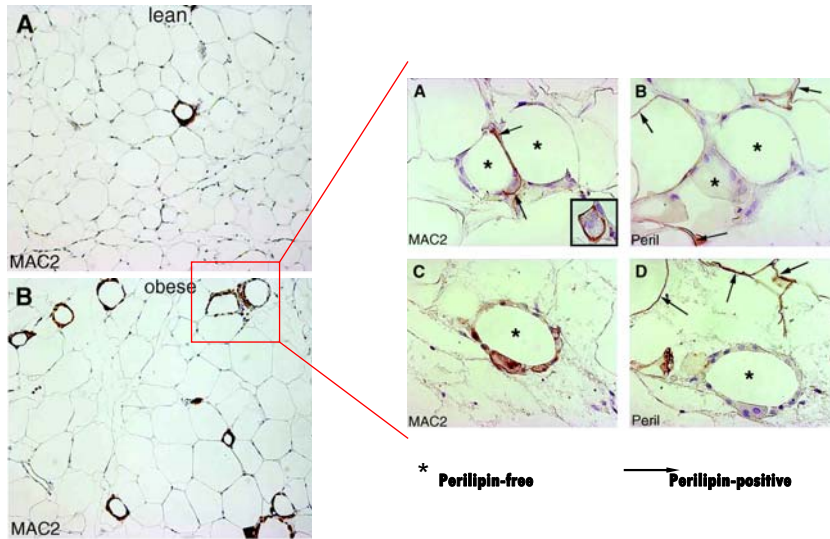
Permana PA, BBRC 2006

## Macrophages



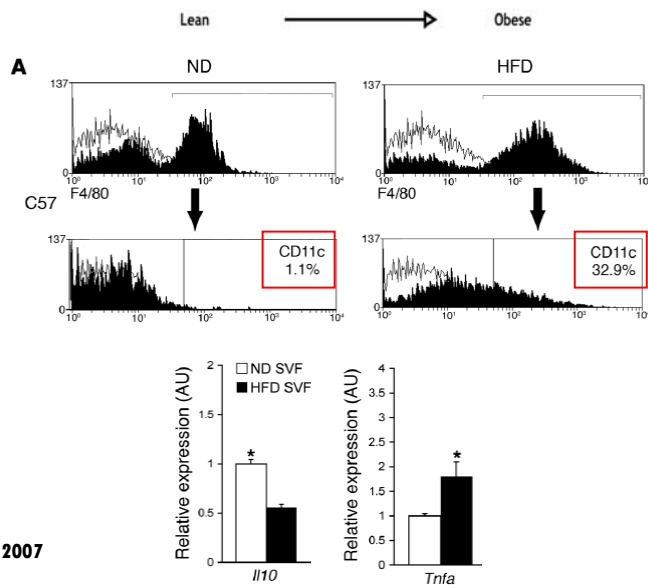
Lacy-Hulbert and Moore, Cell Metab 2006

## What are ATM doing?



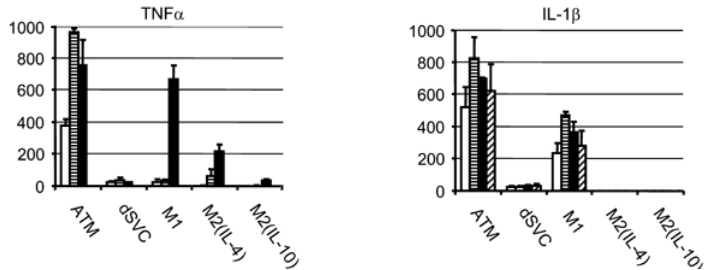
Cinti S, *Lipid Res.* 2005

## ATM and obesity



Lumeng CN,  
*J Clin Invest* 2007

## ATM, activation and inflammation



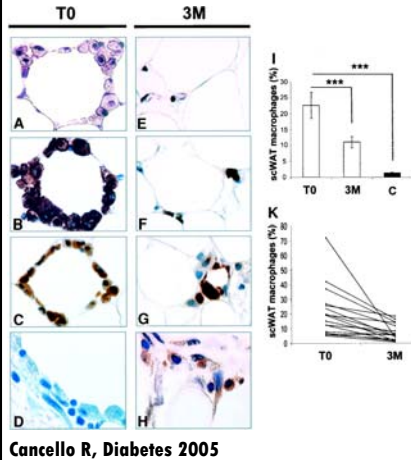
Zeyda M, I J Obes (Lond) 2007

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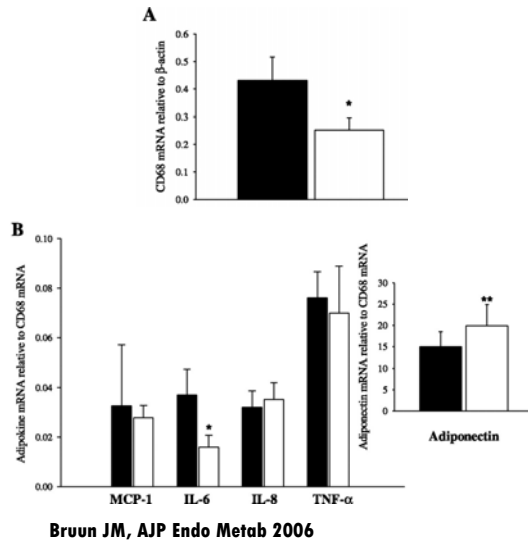
# Weight loss – ATM and inflammation

## *Surgery*



Cancello R, Diabetes 2005

## *Diet and exercise*



Bruun JM, AJP Endo Metab 2006

## Agenda

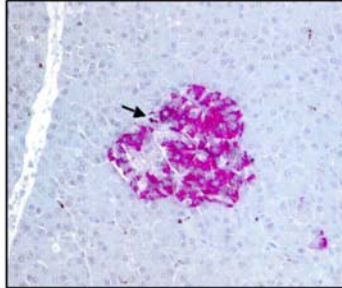
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## Perspectives – *Inflammation and T2D*

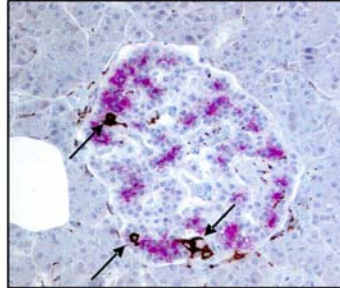
**A**

CD68/**INSULIN**: Human Control



**B**

CD68/**INSULIN**: Type 2 Diabetic



Ehses JA, Diabetes 2007