

Obesity and inflammation

is the adipose tissue on fire?

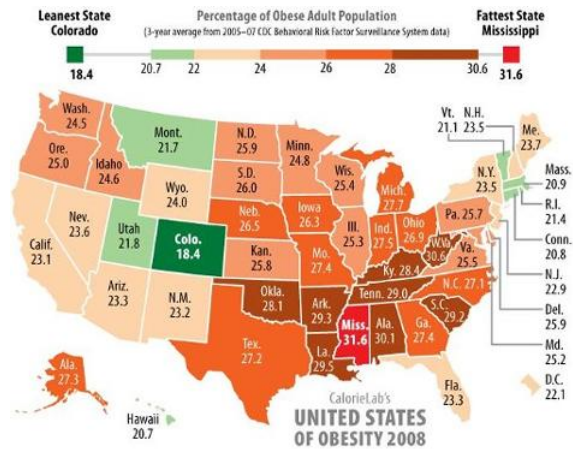
Jens M. Bruun, MD, PhD

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

Agenda

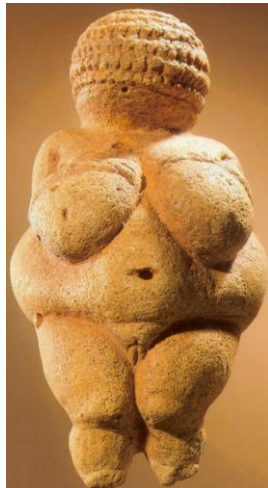
- **Obesity, adipose tissue and *low-grade inflammation*.**
- **Inflammation in adipocytes vs. stromal-vascular cells**
 - AT-macrophages – how did they get there and what are they doing.
- **Effects of weight loss.**
- **Conclusion and perspectives.**

Obesity in the US



Obesity – why care....

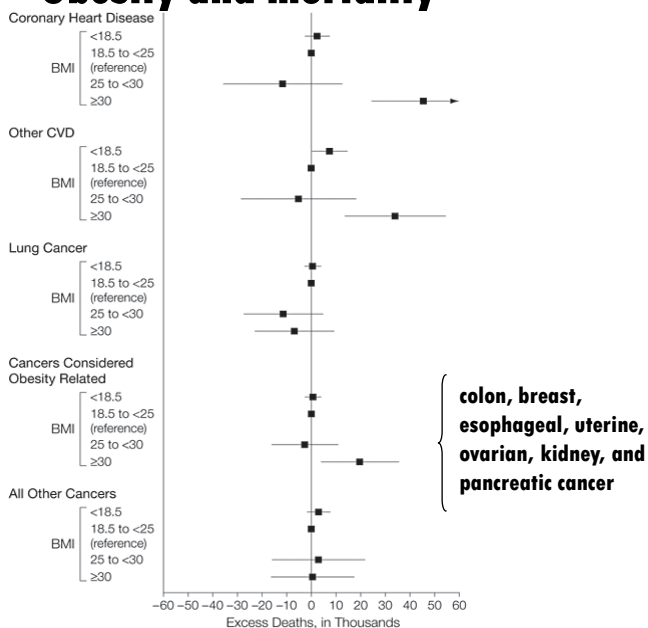
~20000 BC



~2005



Obesity and mortality



Flegal, JAMA 2007

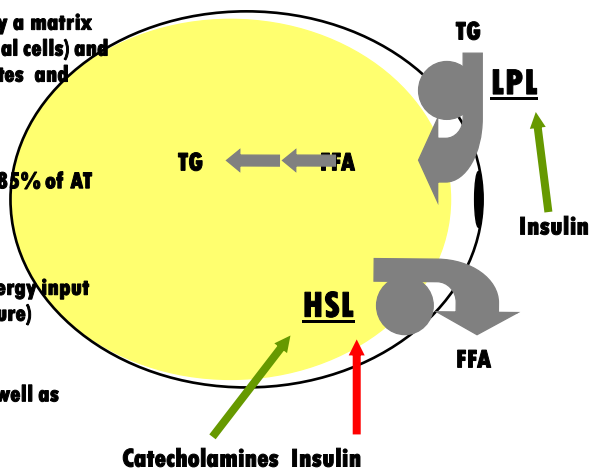
Adipose Tissue - a sophisticated container?

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.

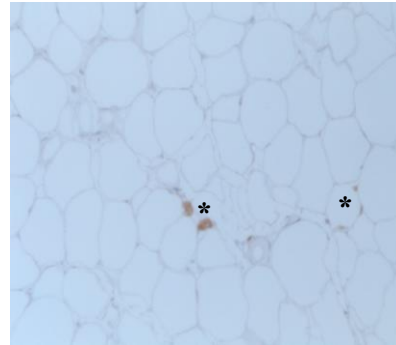


Cell-types in human AT

Table 1. Cellular components (%) of human AT

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

Adapted after Hauner H, Proc Nutr Soc 2005



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

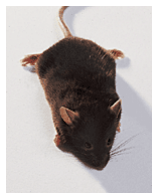
In the beginning....*there was leptin*

Positional cloning of the mouse obese gene and its human homologue

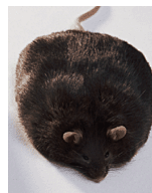
Yiying Zhang^{††}, Ricardo Proenca^{†}, Margherita Maffei[†], Marisa Barone^{**†},
Lori Leopold[†] & Jeffrey M. Friedman^{**††}**

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

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

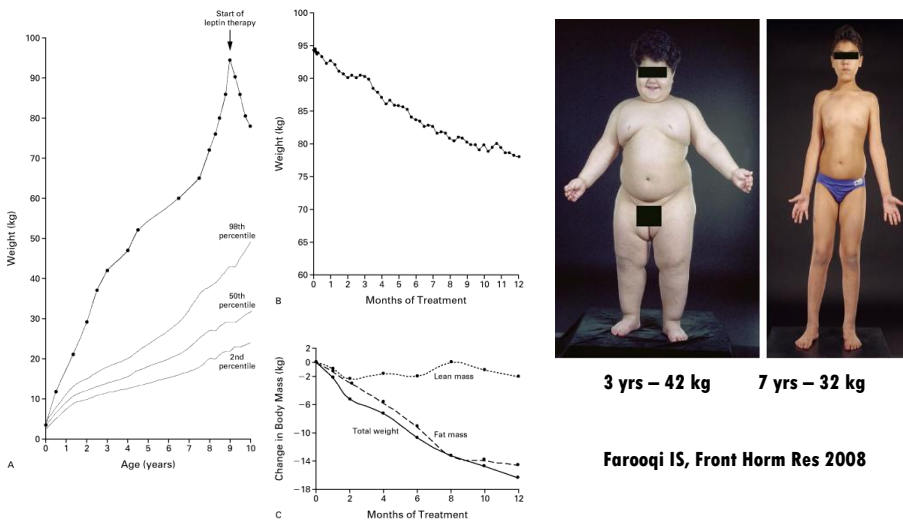


wildtype



ob/ob

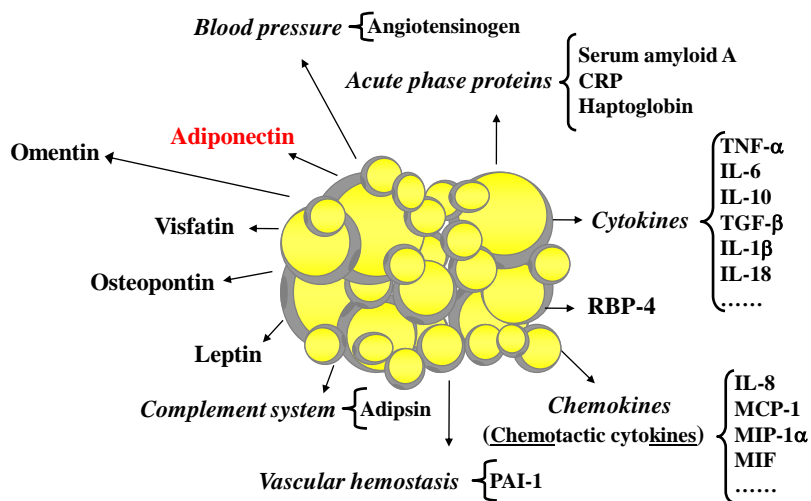
Leptin effects in humans (*ob/ob*)



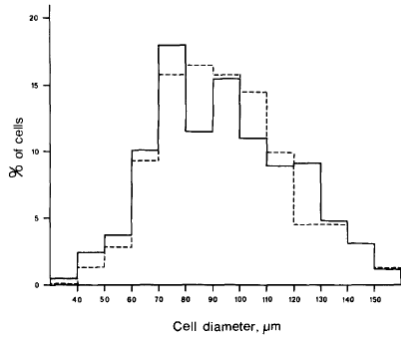
Farooqi IS, NEJM 1999

Farooqi IS, Front Horm Res 2008

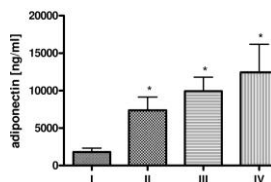
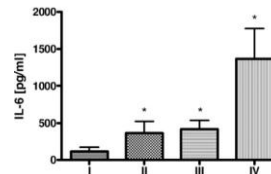
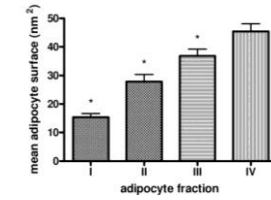
Adipose-secreted proteins - *adipokines*



The adipocyte



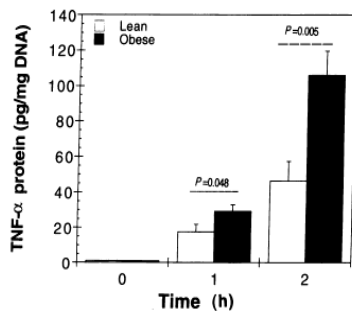
Smith U, J Lipid Res 1972



Skurk T, J Clin Endo Metab 2007

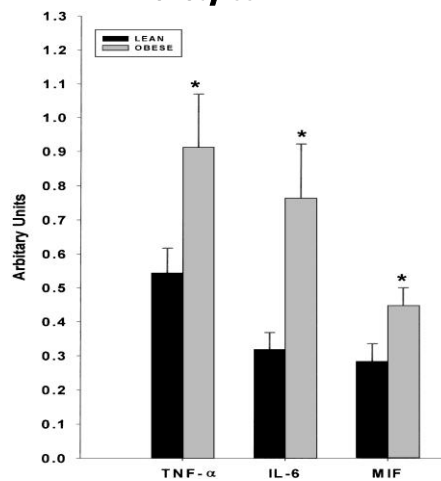
Obesity and low-grade inflammation

Adipocytes



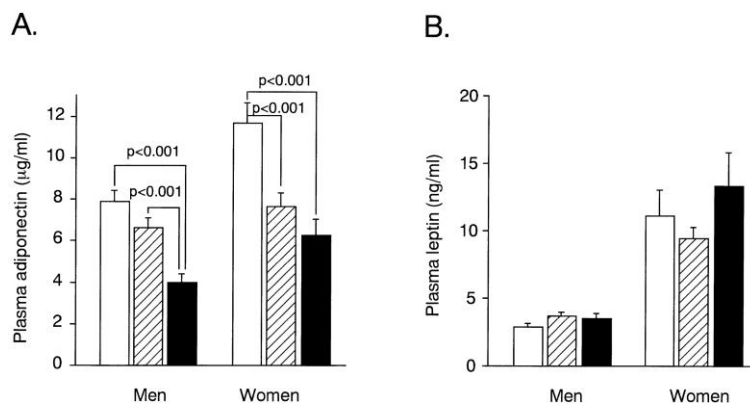
Hotamisligil GS, J Clin Invest 1995

Monocytes



Ghanim H, Circulation 2004

Obesity, low-grade inflammation and concomitant disease

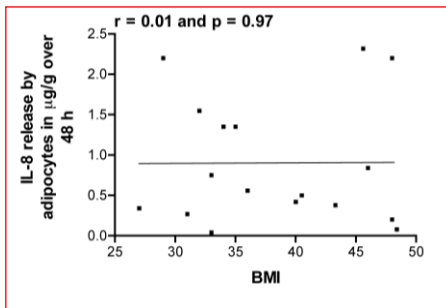
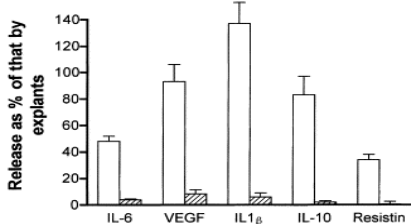
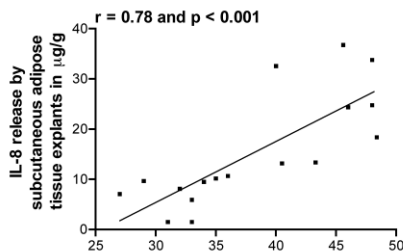
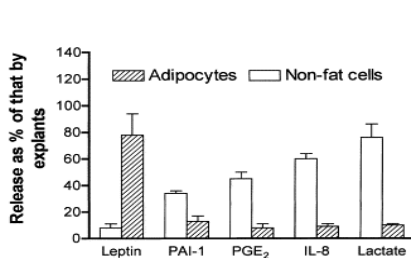


Hotta K, Arterioscler Thromb Vasc Biol 2000

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Adipocytes vs. SV-cells



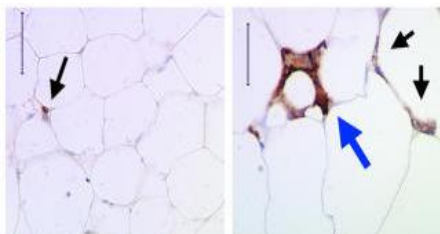
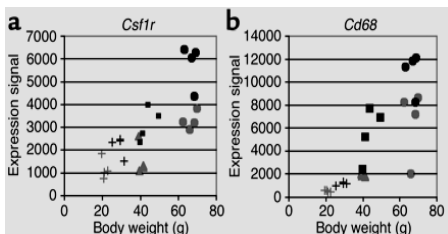
Fain JN, BBRC 2003

Bruun JM, AJP Endo Metab 2004

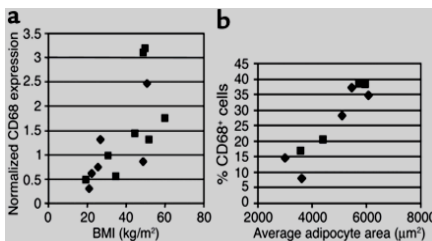
Obesity and ATM

Lean

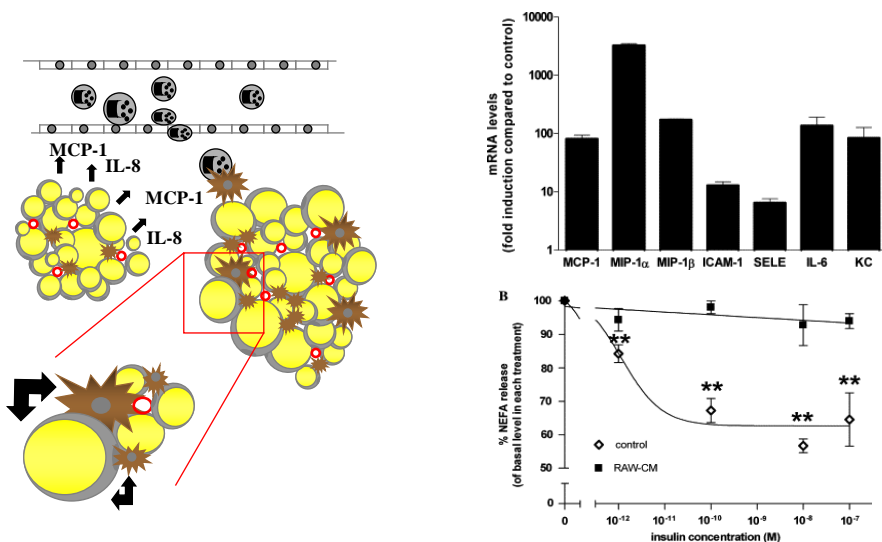
DIO



Weisberg SP, J Clin Invest 2003

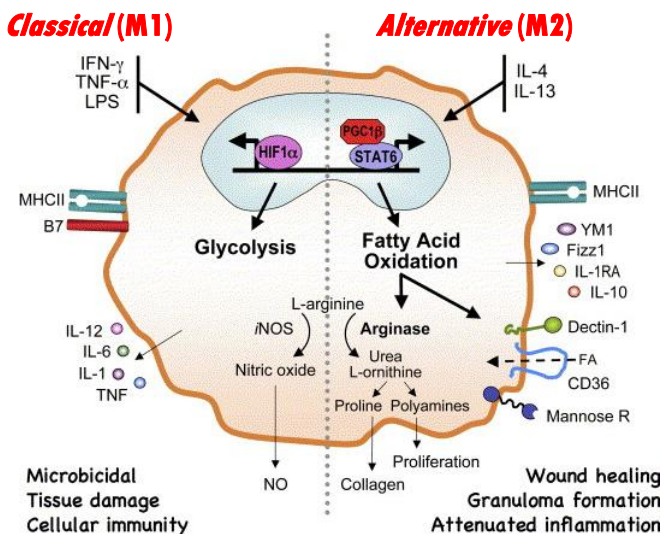


Adipocyte and ATM –cross talk?



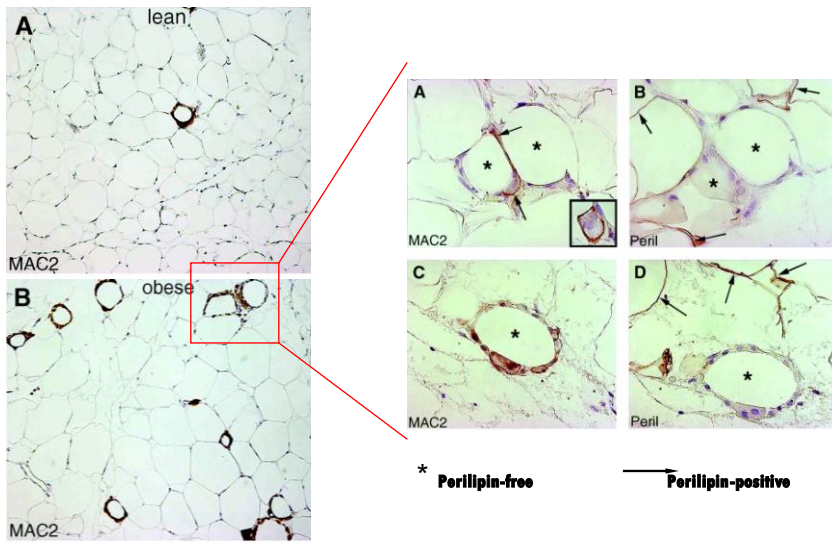
Permana PA, BBRC 2006

Macrophages



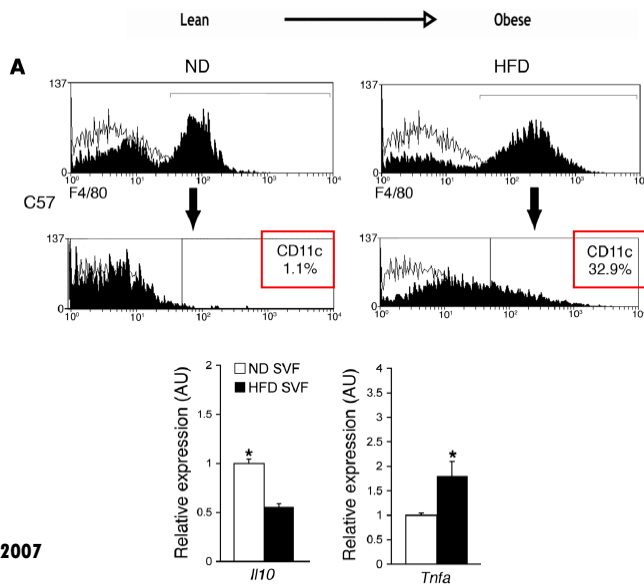
Lacy-Hulbert and Moore, Cell Metab 2006

What are ATM doing?



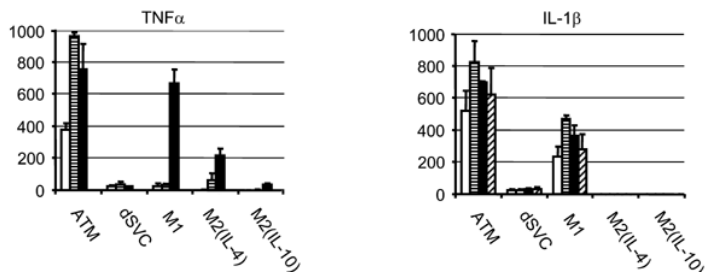
Cinti S, *Lipid Res.* 2005

ATM and obesity



Lumeng CN, *J Clin Invest* 2007

ATM, activation and inflammation



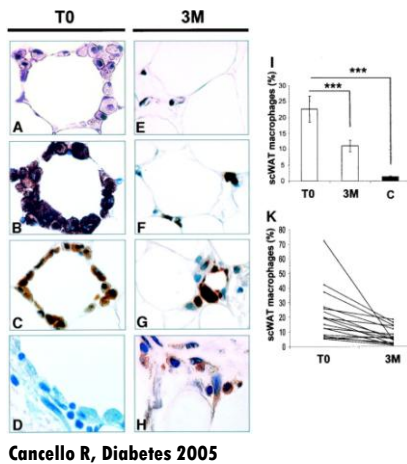
Zeyda M, I J Obes (Lond) 2007

Agenda

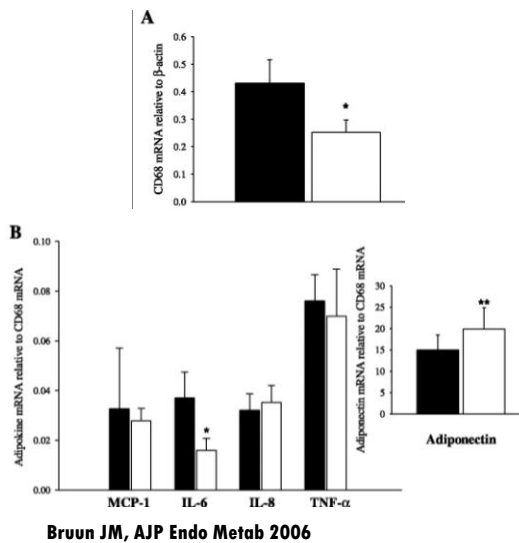
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Weight loss – ATM and inflammation

Surgery



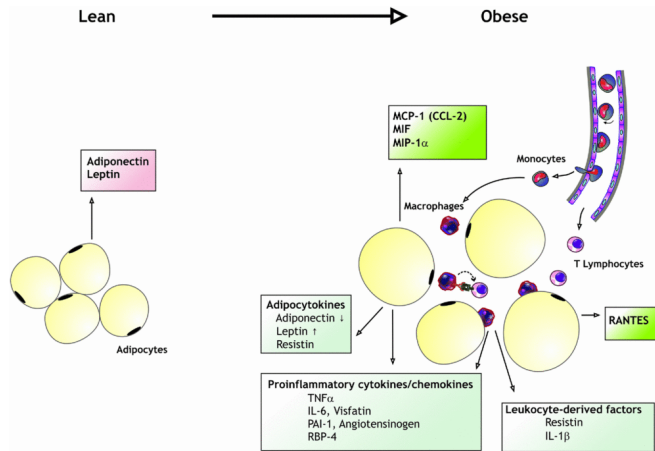
Diet and exercise



Agenda

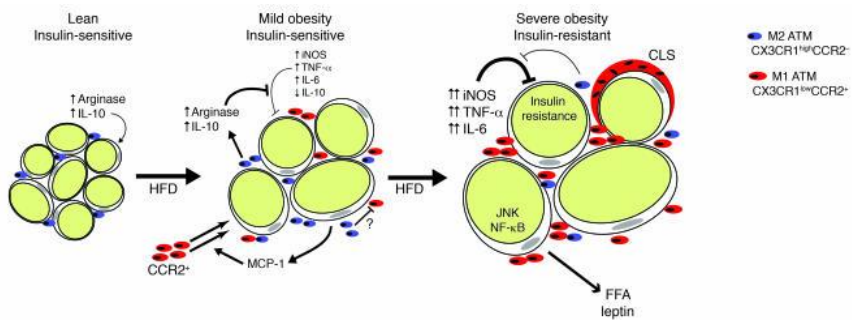
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Summary



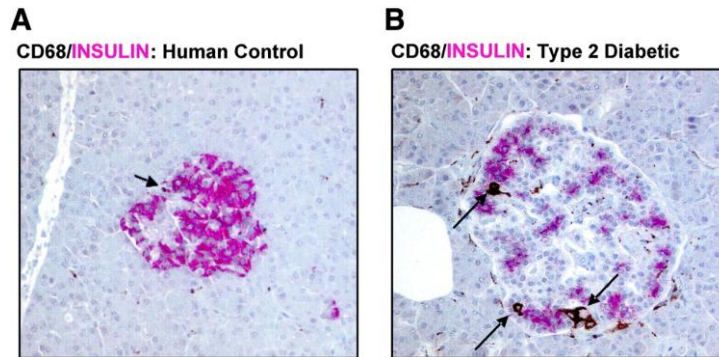
Tilg H, Clin Sci (London) 2008

Summary (part 2)



Lumeng CN, J Clin Invest 2007

Perspectives – *Inflammation and T2D*



Ehes JA, Diabetes 2007