EARLYNUTRITION

Long-term effects of early nutrition on later health

Placental Lipids and Fatty Acid Transfer in Maternal Overnutrition

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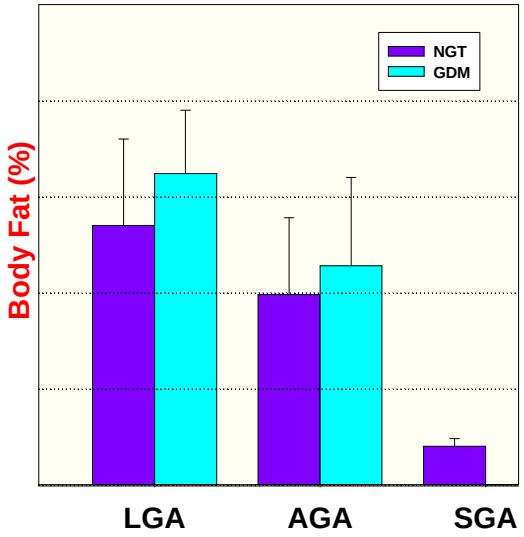
Fetal Phenotype in Diabesity

GDM



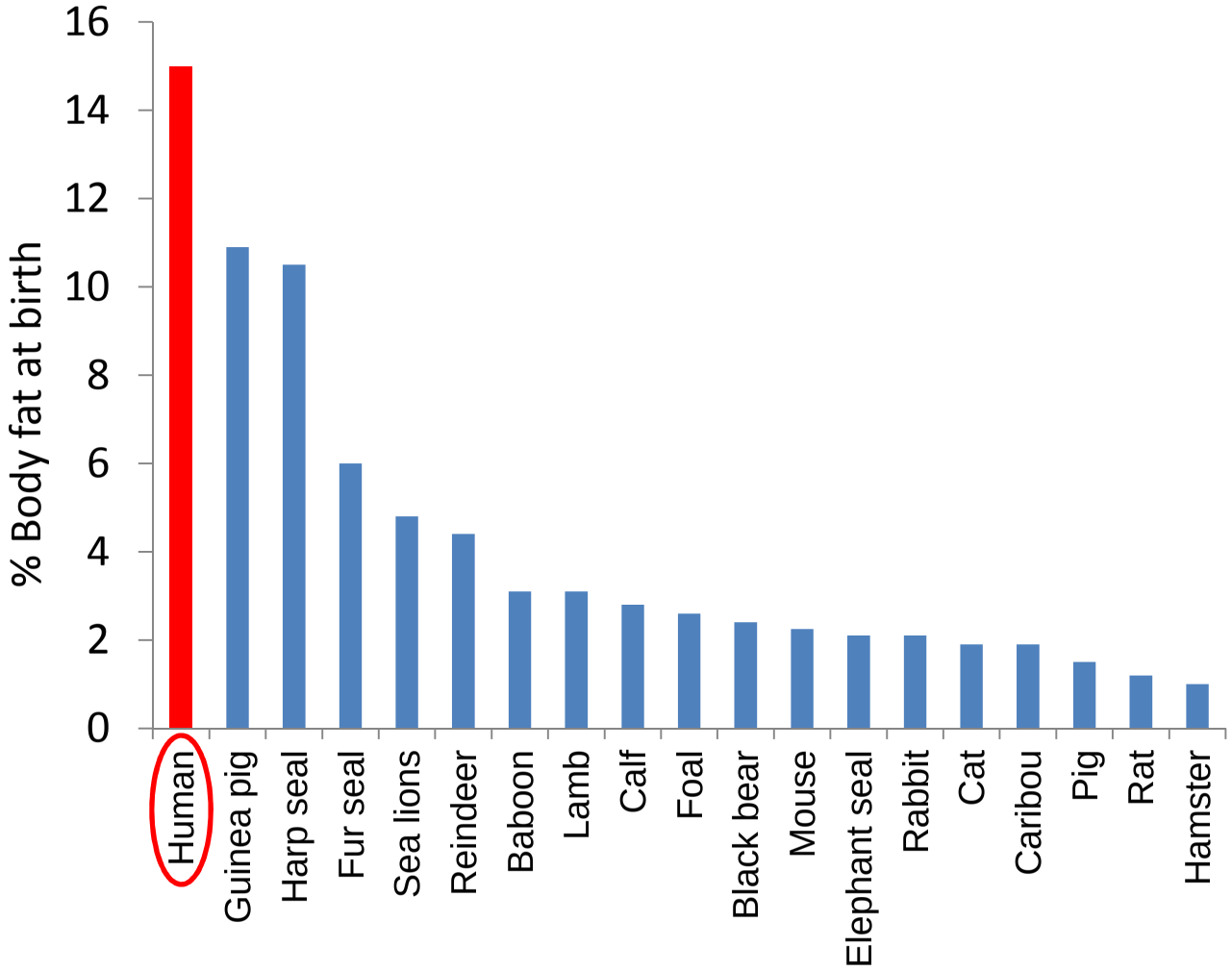
Obesity

Mean skinfold thickness
(sum of 8 skinfolds)

Normal (10-90th centile)	Obese (> 90th centile)
28.6 ± 5.7	32.2 ± 6.1 p<0.001

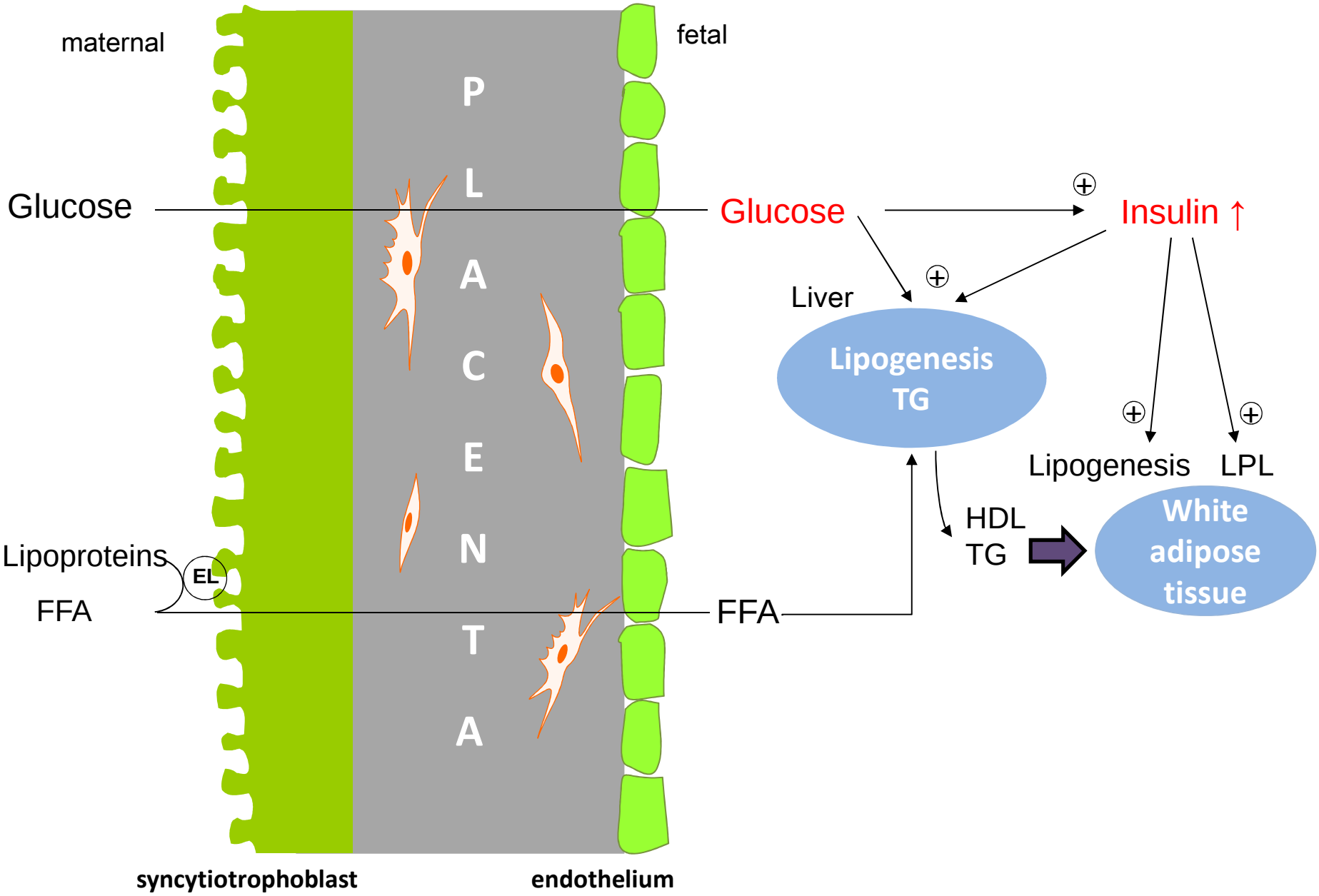
Catalano AJOG 2003; Durnwald AJOG 2004; Whitelaw AGL, 1976

Human Newborns Have Highest % Body Fat Among Mammals

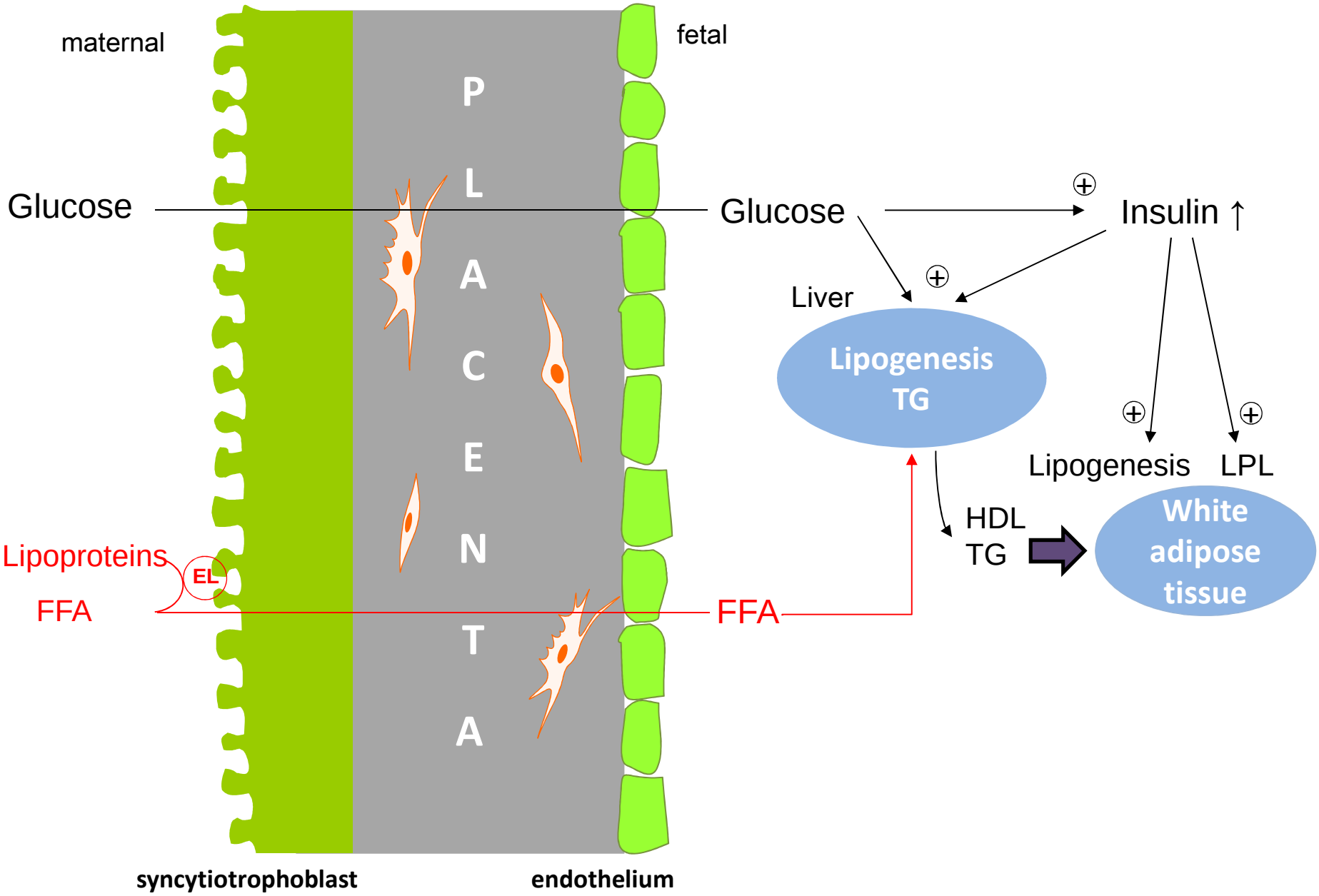


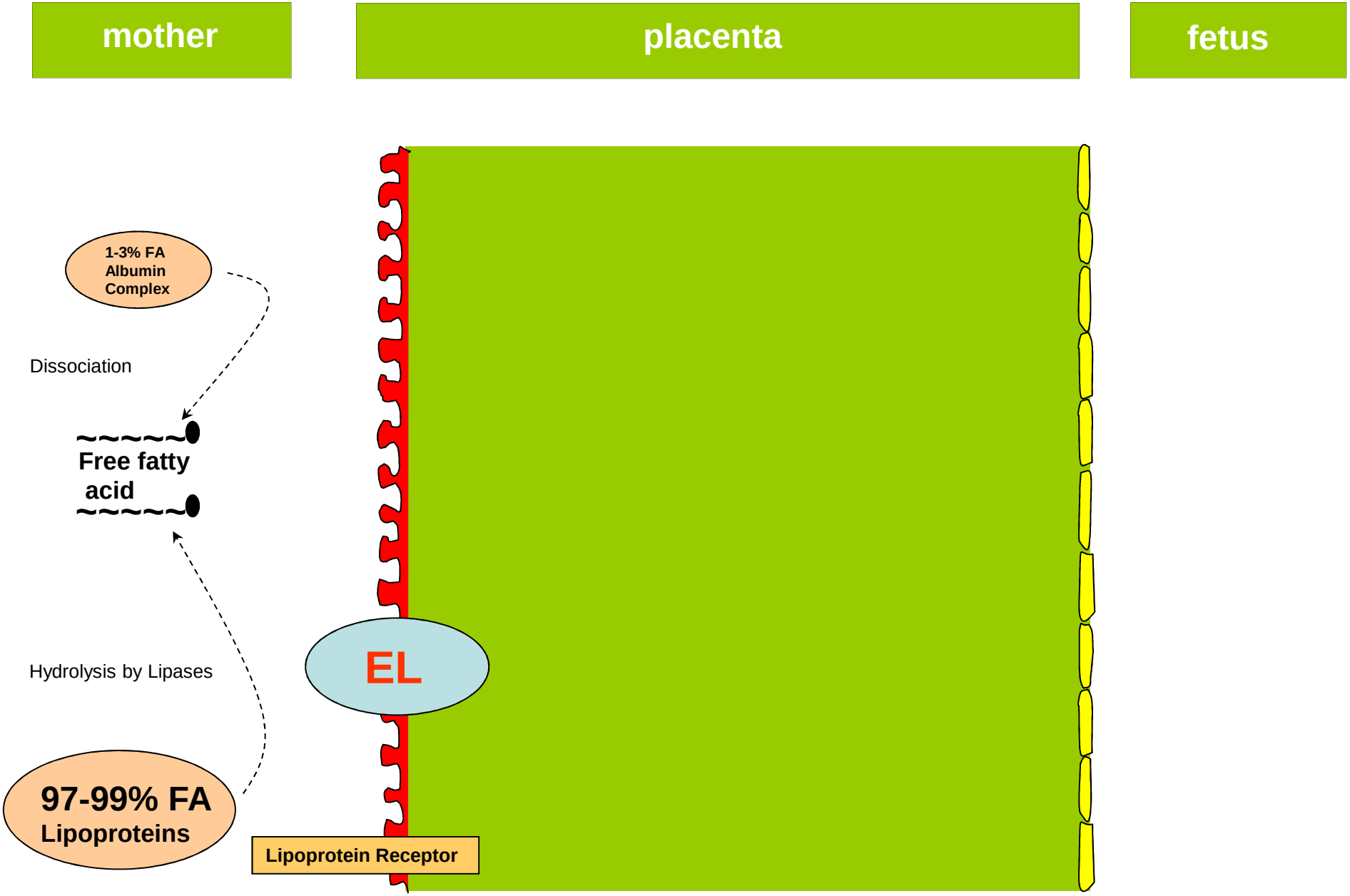
Kuzawa CW. Yearbook Physical Anthropol 41:177-209, 1998

Pedersen – Freinkel Concept Expanded



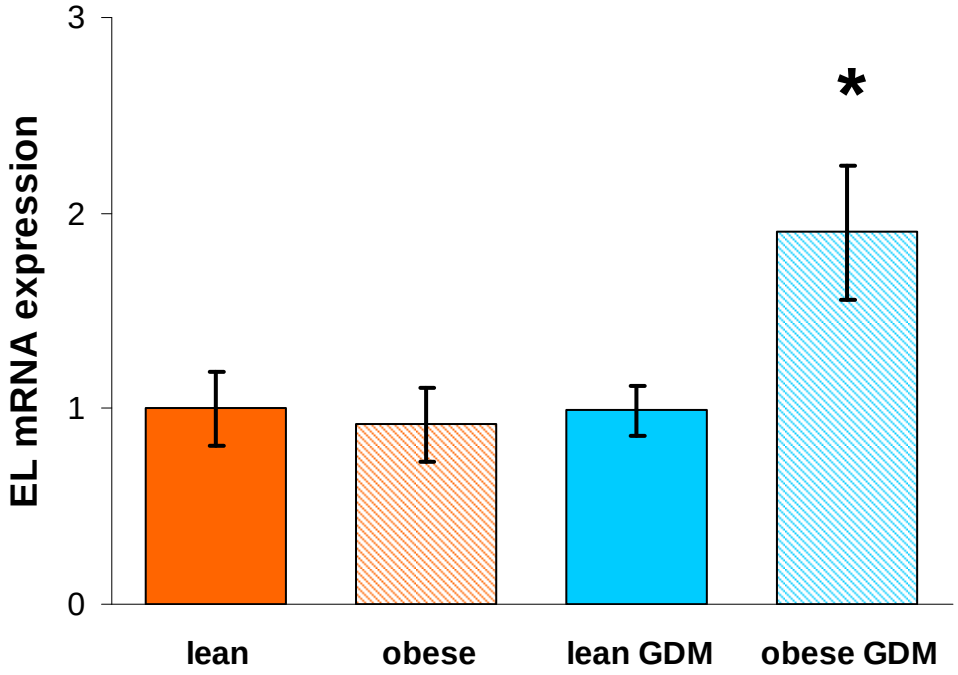
Pedersen – Freinkel Concept Expanded



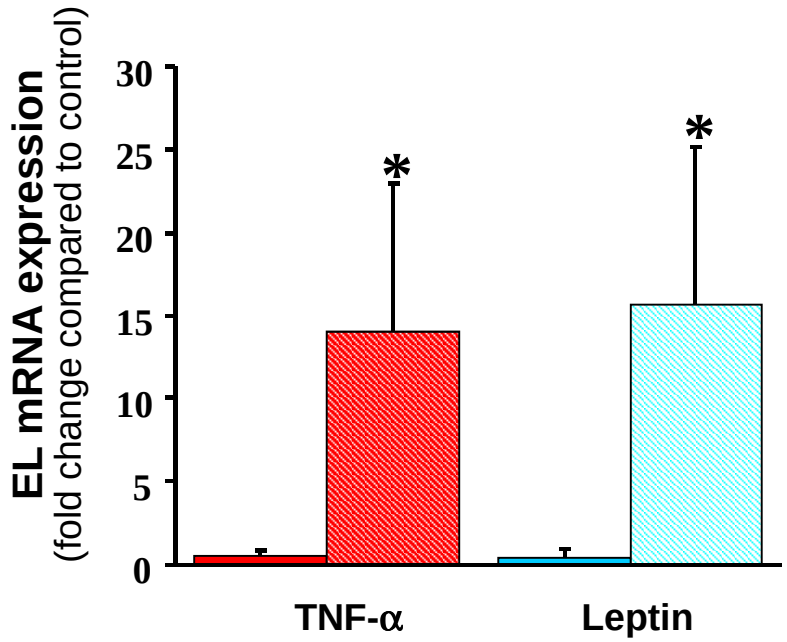

mother
placenta
fetus
1-3% FA
Albumin
Complex
Dissociation
Free fatty
acid
Hydrolysis by Lipases
EL
97-99% FA
Lipoproteins
Lipoprotein Receptor

EL is Upregulated by GDM plus Obesity

Endothelial lipase is upregulated in obese GDM only



Inflammatory cytokines upregulate placental EL



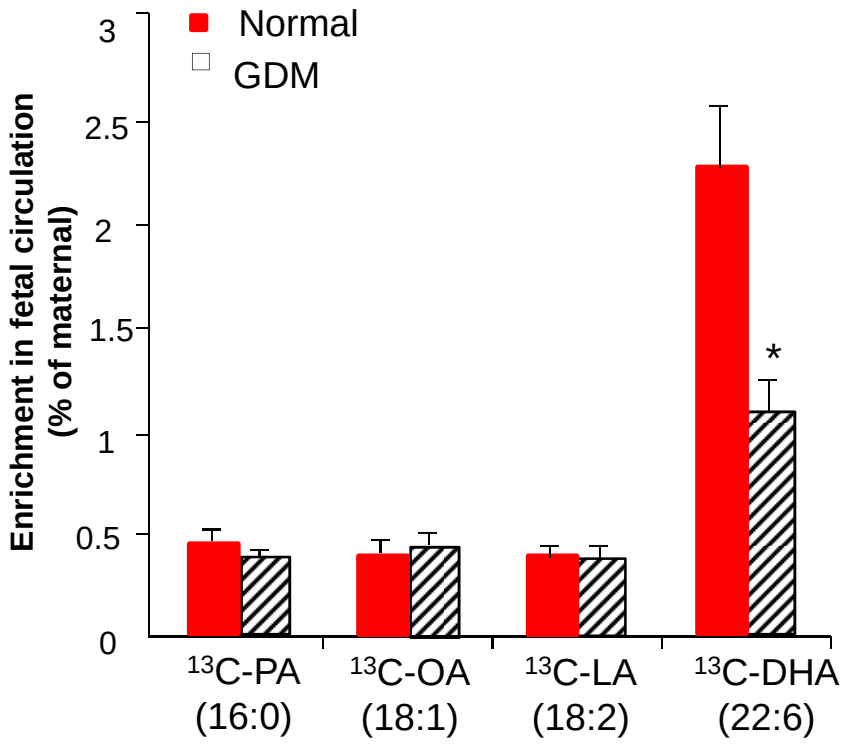
Gauster et al. Diabetes, 2011

Fatty Acid Transfer Across Term Human Placenta

Transfer characteristics:

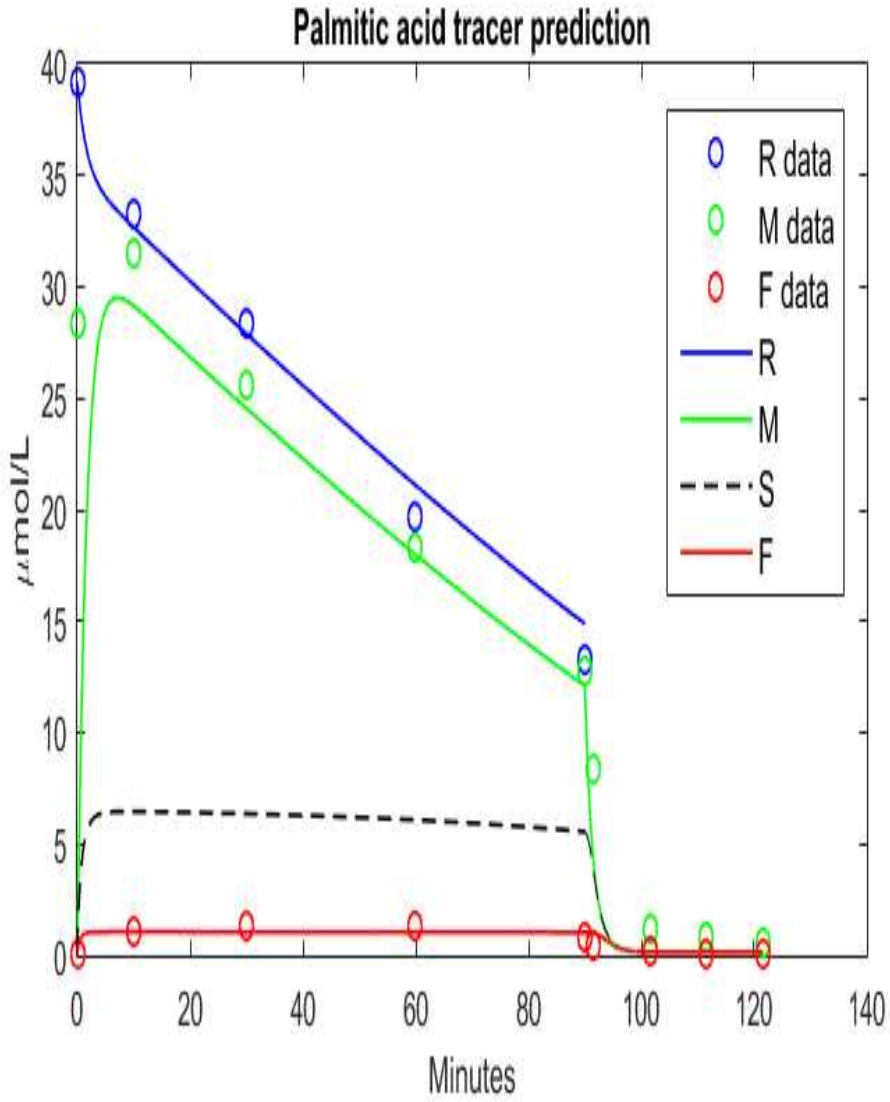
- Slow (3% clearance of H_20)
  Placenta 18: 635, 1997
- Inefficient
- Dependent on chain length
- Maternal FAs contribute to only ~ 70g (20%) of neonatal fat (normal pregnancy)
  Pediatr Res 7:192, 1973

In vivo stable isotopes



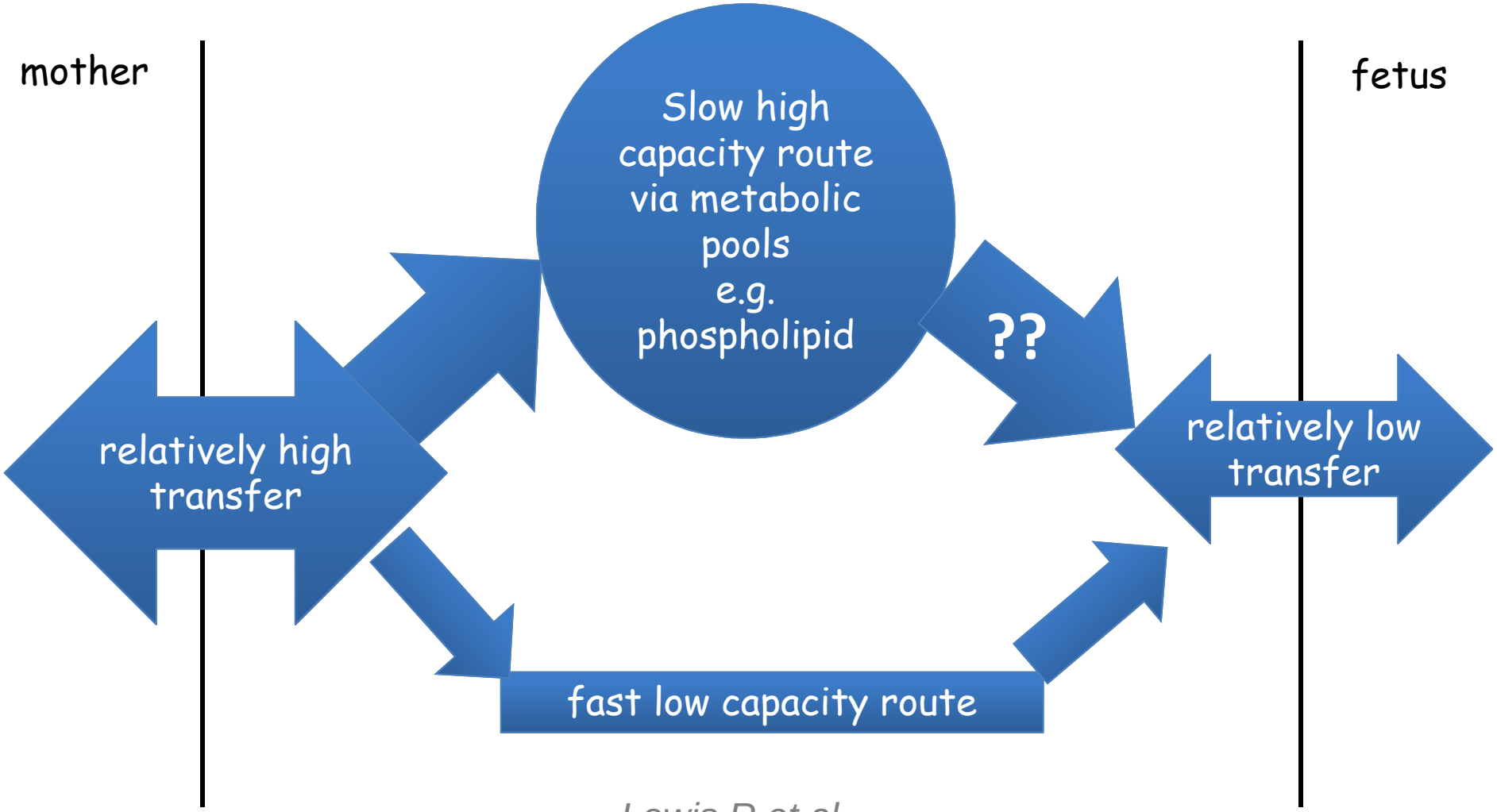
Pagán A et al, AJP-Endocr Metab 2013

Computer Model Predicts Transfer



Lewis R et al, Southampton, UK

Two Placental Fatty Acid Pools



Lewis R et al

Nature of the metabolic pool?

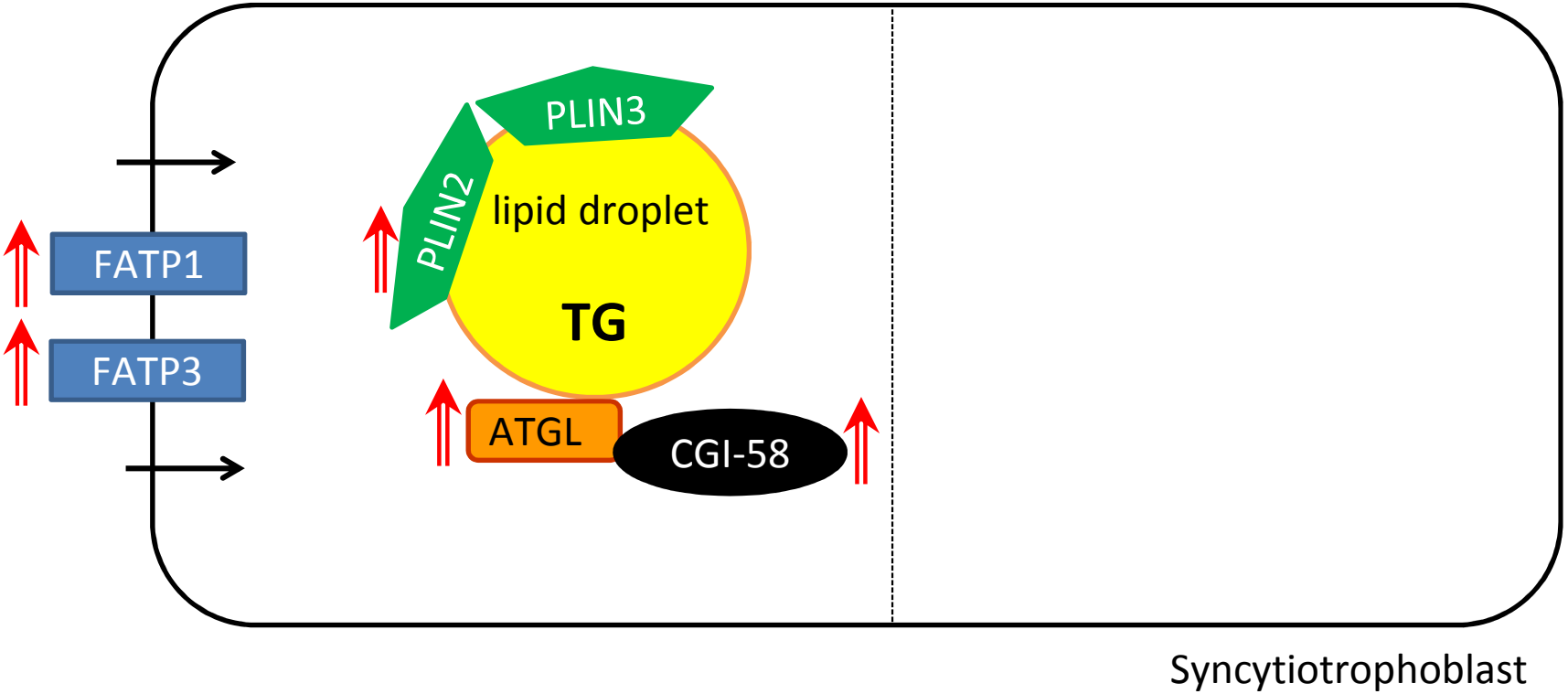
How does the placenta handle the fatty acid excess of GDM & obesity?

Cleveland Cohort with Various Degrees of Obesity

BMI		Number of samples
Lean:	20-24.9	20
Obese:	30.0-33.9	24
	34.0-39.9	16
	≥ 40.0	20

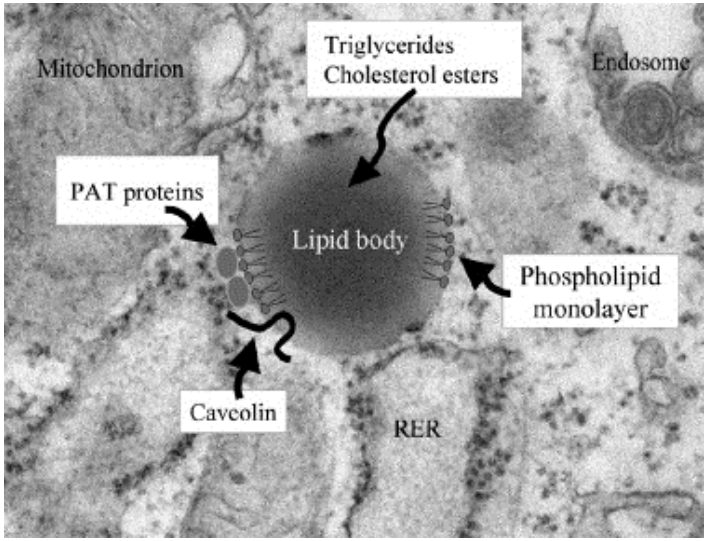
RNA extracted
Quality control on bioanalyzer, RIN>7.5
Gene expression measured by Nanostring technology

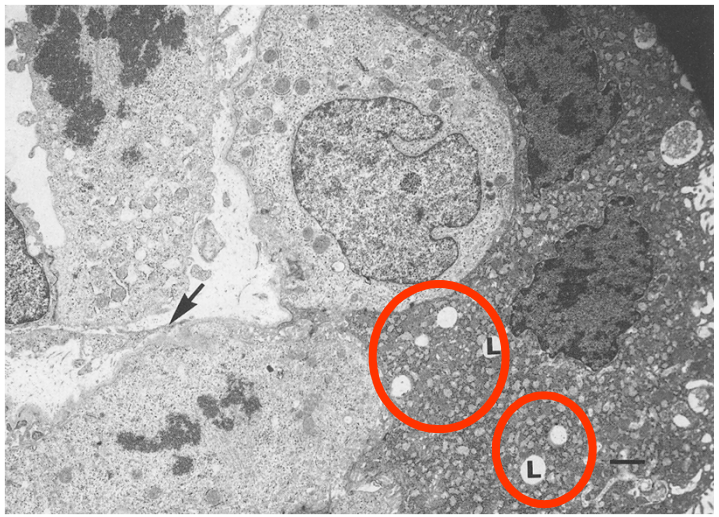
Summary mRNA

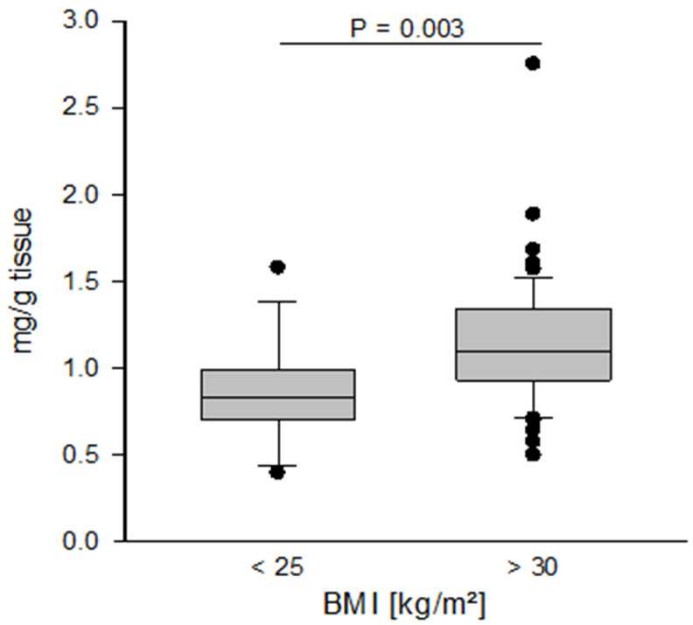


Hirschmugl B et al, Int J Obes, in press

In Maternal Obesity the Human Placenta Stores More Triglycerides



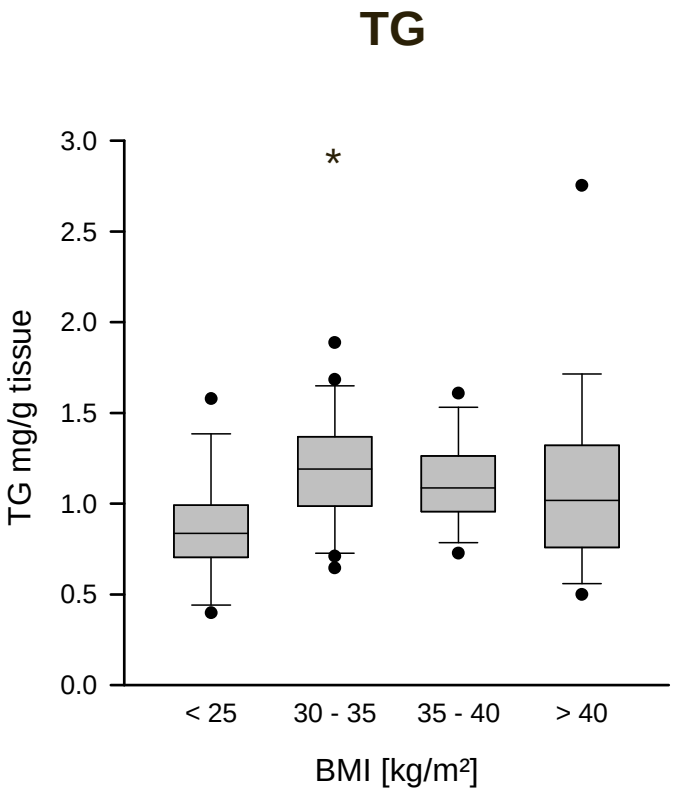


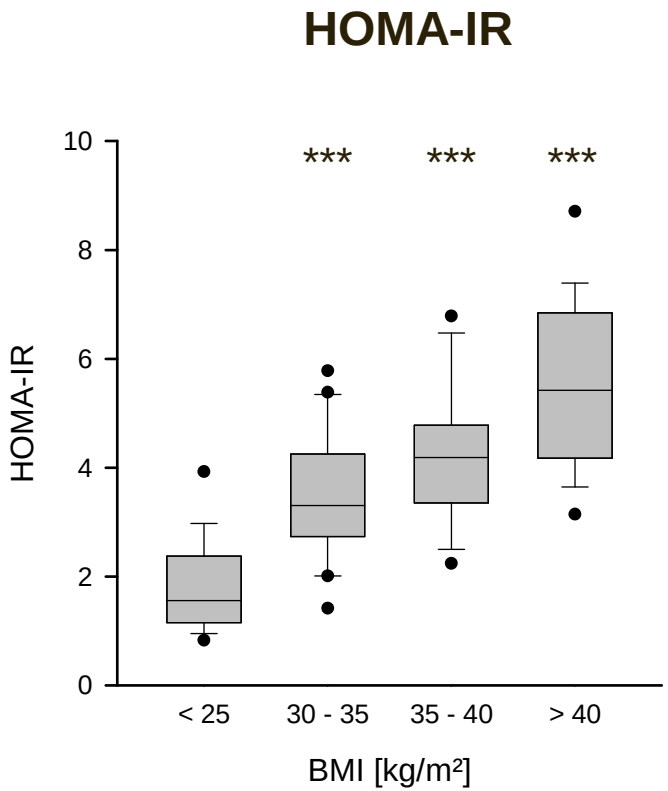


Jones & Fox, Electron Microsc Res 4: 129, 1991

Hirschmugl B et al, Int J Obes, in press

Triglycerides in Placental Tissue

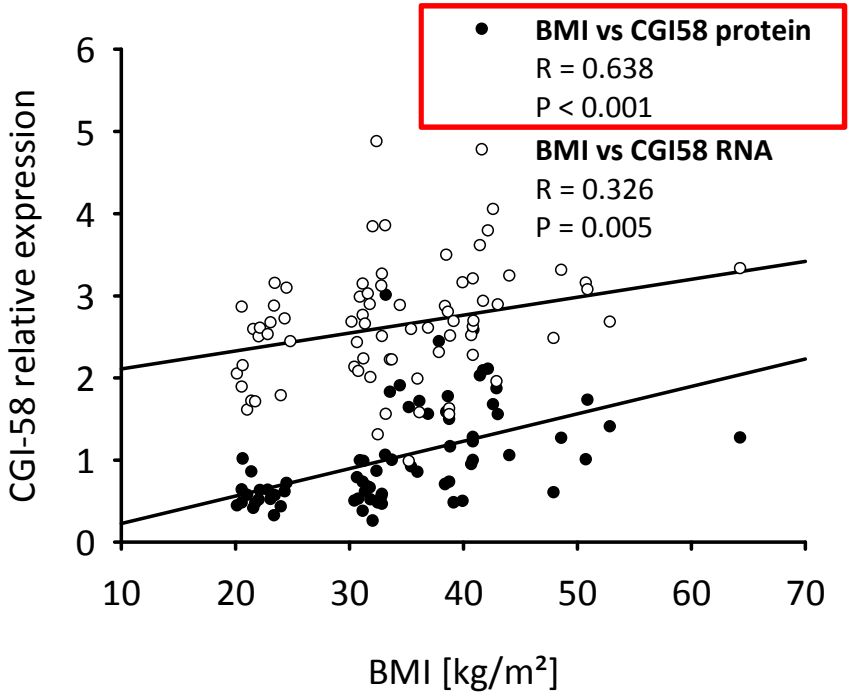


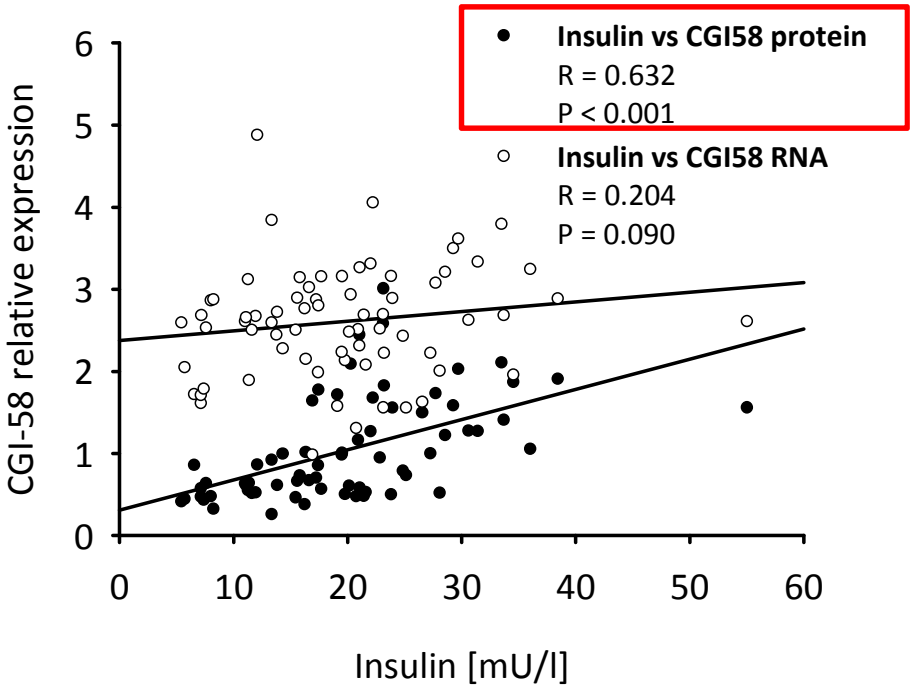


lean (20-25 kg/m^2 n=18) vs. obese (30-64 kg/m^2 n=55), placenta specimen collected in Cleveland (USA)
* P <0.05, *** P <0.001

Hirschmugl B et al, Int J Obes, in press

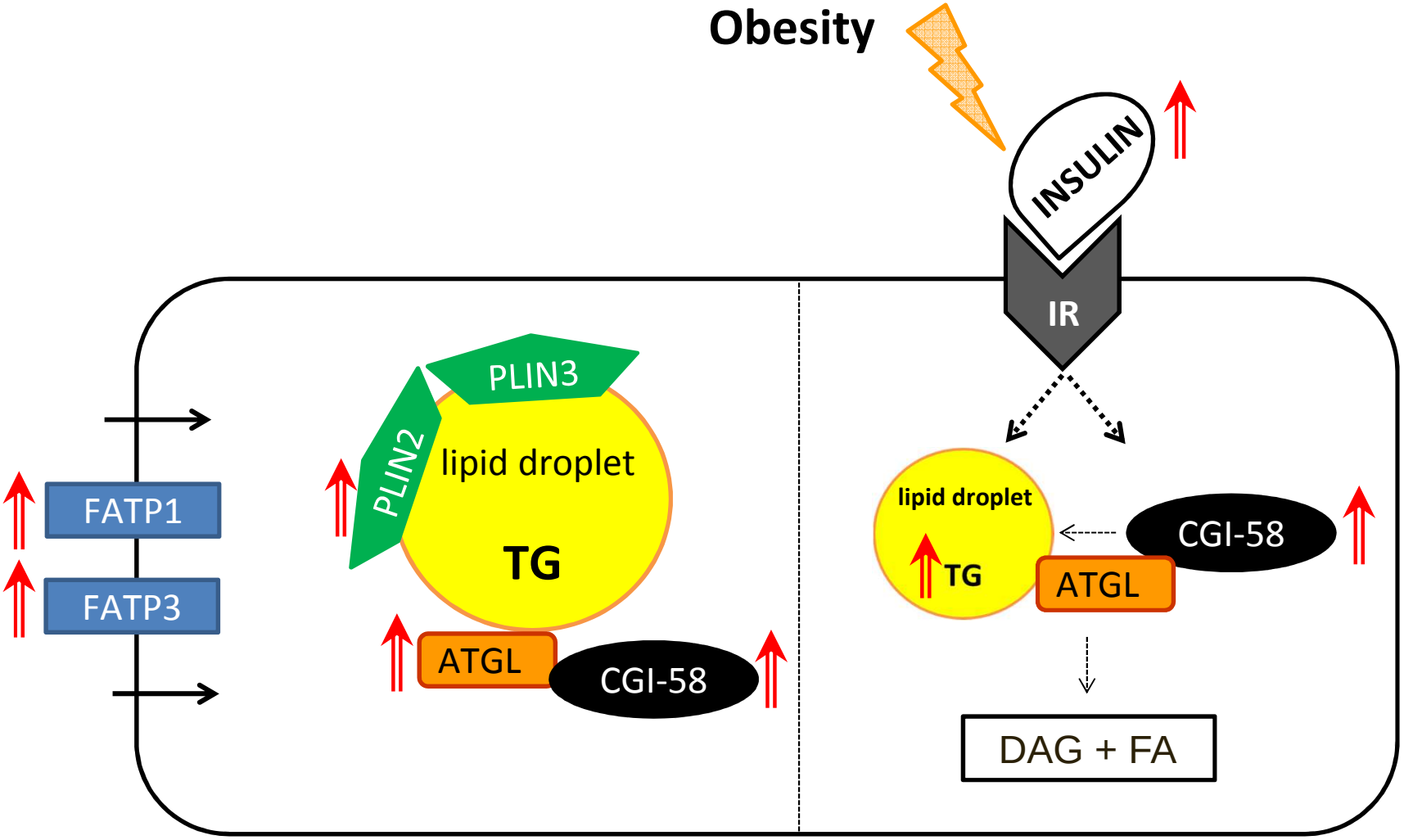
Maternal BMI and Insulin Associate with Placental CGI-58



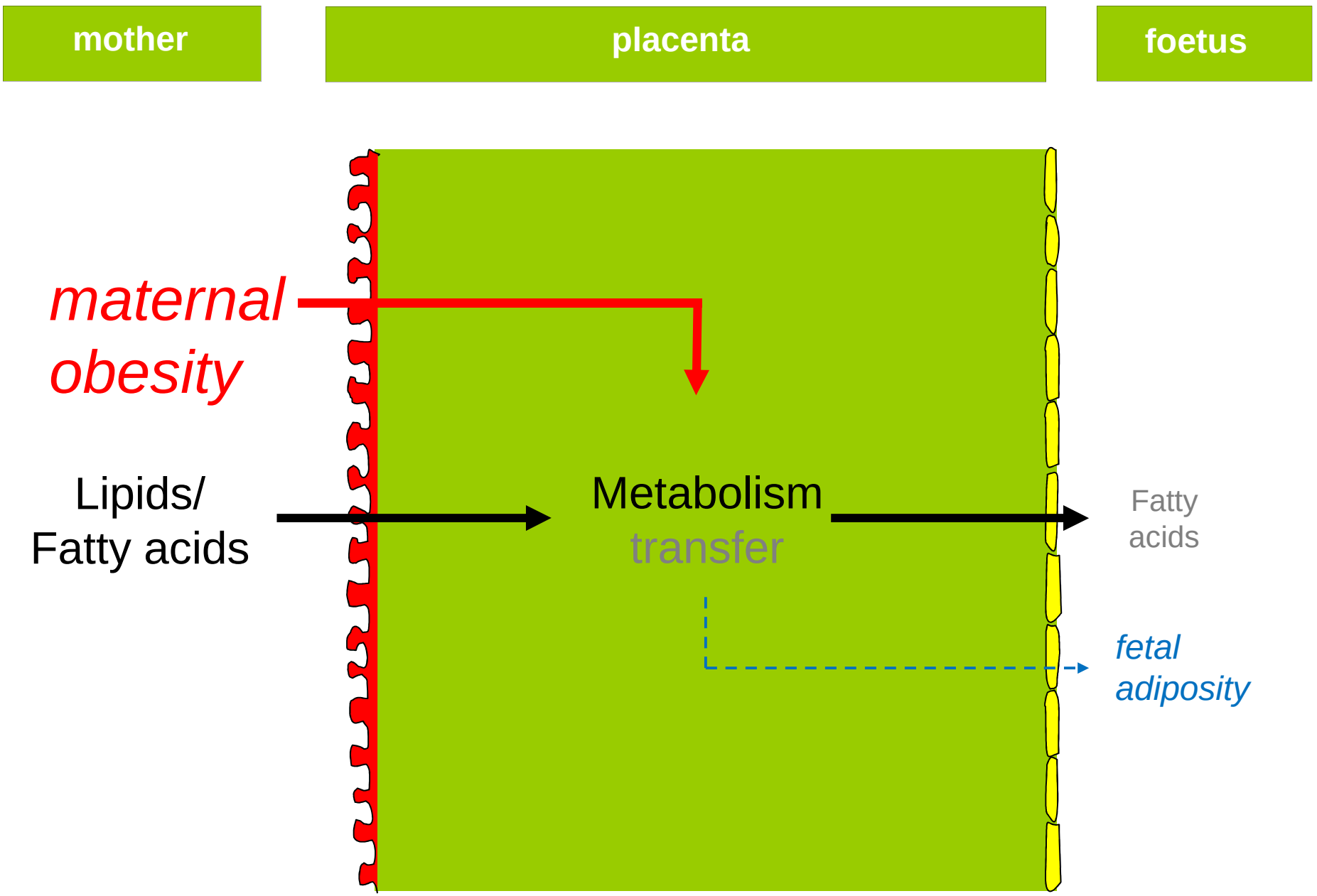


Hirschmugl B et al, Int J Obes, in press

Summary



Syncytiotrophoblast


mother
placenta
foetus
maternal obesity
Lipids/ Fatty acids
Metabolism
transfer
Fatty acids
fetal adiposity

Summary and Conclusion

Maternal-fetal transfer of non-essential fatty acids is unaltered in GDM

Fatty acids are stored as TG in the placenta (trophoblast) in lipid droplets; more TG stored in GDM and obesity

Activity of TG synthesis and lipolysis determine the net amount of TG stored

It is unclear what happens in extreme conditions of maternal overnutrition

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Thank you for your attention!

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