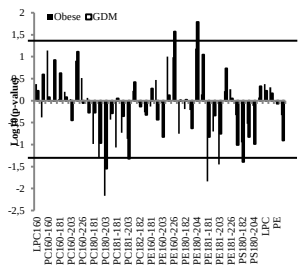
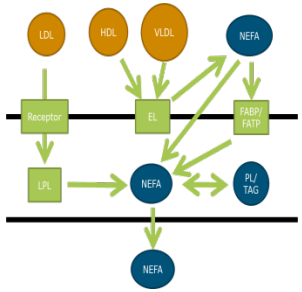
LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

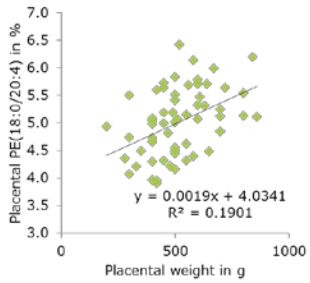
EARLYNUTRITION Long-term effects of early nutrition on later health

MATERNAL GESTATIONAL DIABETES MELLITUS AND PLACENTAL LIPIDS

Olaf Uhl

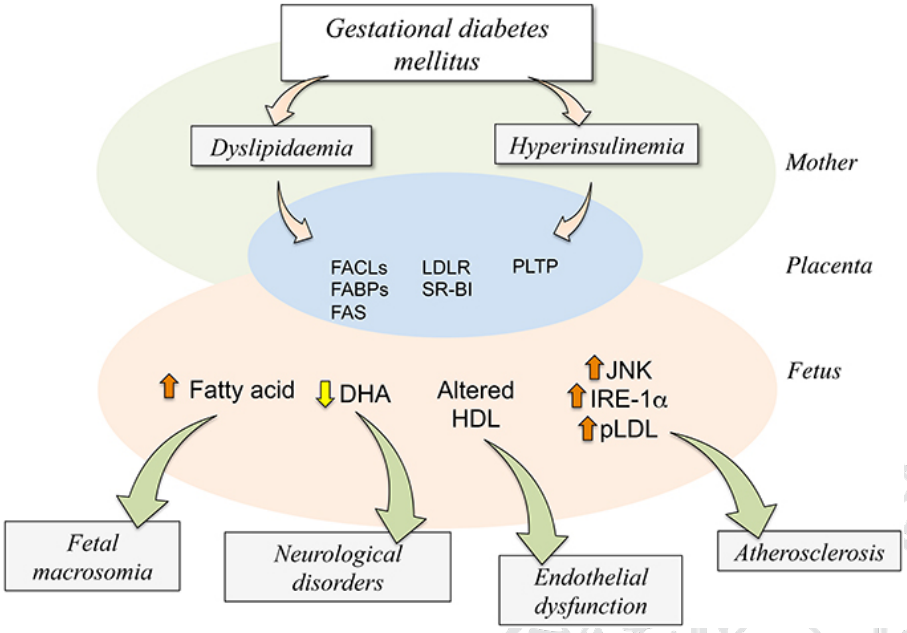






EPIDEMIOLOGICAL OBSERVATIONS

- Gestational diabetes mellitus (GDM) is the most common form of diabetes in pregnancies
- Maternal glucose status is linked to higher risk for perinatal mortality [1] and offspring macrosomia [2]
- Despite of glycemic control in T2DM mothers, infants are still at higher risk for macrosomia [3] and various deviations in the lipid status were observed
- Macrosomia and dyslipidemia might be induced by other factors than glucose →Lipids?



Sobrovia,FrontPhys,2016

[1] Balsells, JCEM, 2009
[2] Najafian, ISRN Obstet Gynecol, 2012
[3] Evers, Diabetologia, 2002

METABOLISM OF PREGNANT WOMEN

- First trimester →adipose tissue accumulation
  - ↑ Lipoprotein lipase activity (LPL)

- Last trimester →enhanced lipolysis
  - ↓ FA synthesis of AT
  - ↓ LPL activity
  - ↑ Lipolytic activity of AT

} Results of IR? [1]

[2] →

Increasing metabolites:
- TCA intermediates
- β-hydroxybutyrate
- Phospholipids
- Threonine

Decreasing metabolites:
- BCAA
- Free carnitine, acyl-carn
- Lyso-Phospholipids

[1] Sivan, Diabetes, 1999
[2] Lindsay, PLoS One, 2016

PREOBE – STUDY DESIGN

Aim

- To better understand the intrauterine effects of GDM and obesity, separately

Study design

- Pregnant women were recruited at the University of Granada
- 3 Groups (Median BMI):
  - 31 Healthy controls (22.5 kg/m2)
  - 29 Obese (31.6 kg/m2)
  - 32 GDM (23.3 kg/m2)
- GDM were treated with nutrition counselling, antidiabetics or insulin

	CTR		GDM			Obese		
	M (IQR)	n	M (IQR)	n	p-value	M (IQR)	n	p-value
Maternal age [y]	31 (6)	31	32 (5)	15	0.306	29 (4)	17	0.087
Prepregnancy BMI [kg/m^2]	22.5 (2.5)	31	23.3 (2.7)	15	0.439	31.6 (3.3)	17	>0.001
Weight gain (week 34) [kg]	13.3 (3.5)	31	11 (6.6)	15	0.069	6.1 (5.8)	17	>0.001
Placenta weight [g]	480 (100)	29	500 (175)	15	0.179	555 (148)	16	0.018

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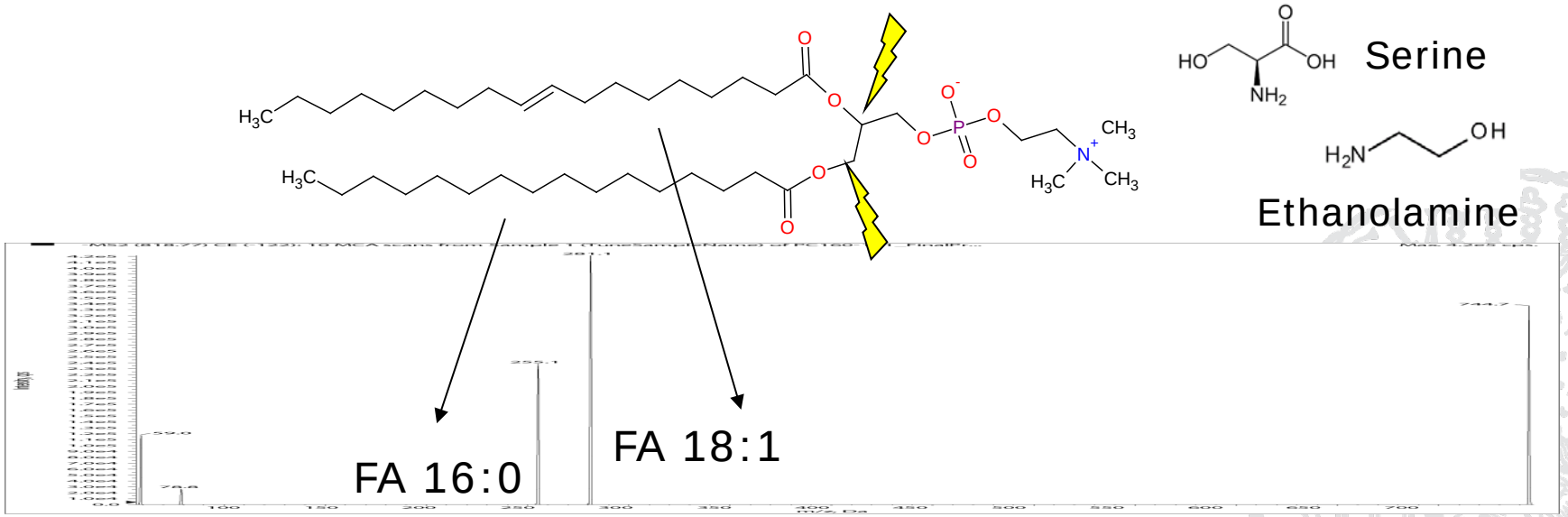
PREOBE - METHODS

- Immediately after delivery, placentas were frozen at -80°C
- Frozen placentas were divided into small pieces
- Placenta samples were defrosted and washed with saline solution to remove blood
- Lipids were extracted with chloroform/ methanol
- Phospholipids were analysed by liquid chromatography coupled to triple quadrupole mass spectrometry [1]



[1] Uhl, J Chrom B, 2011

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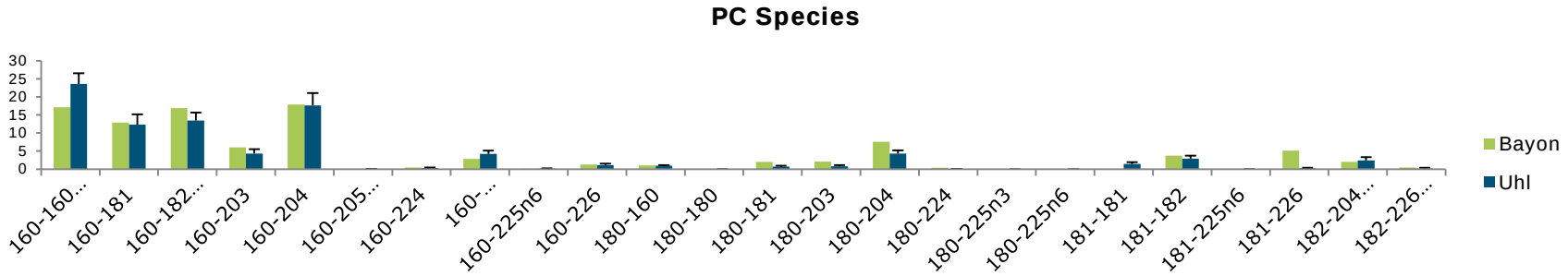
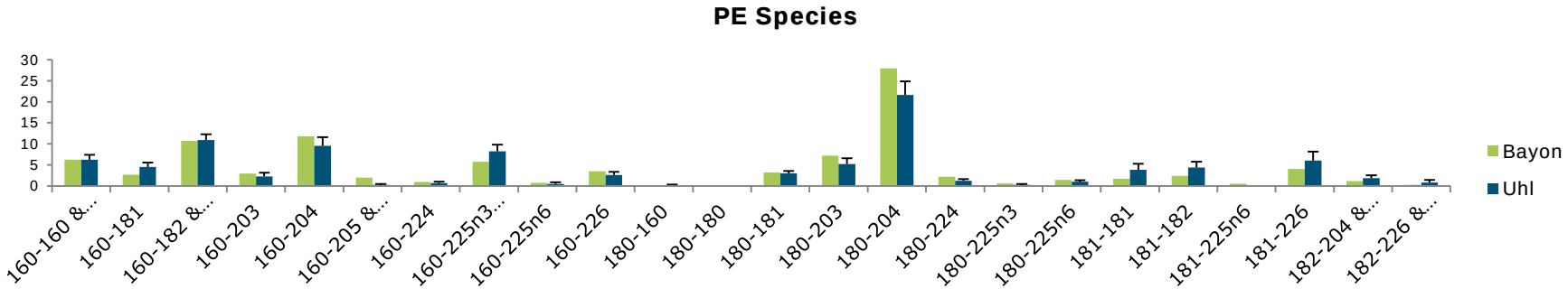
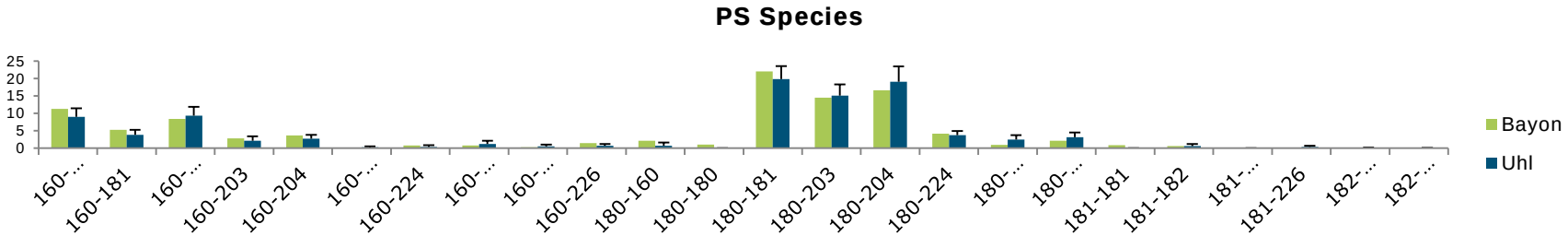
BAYON, LIPIDS, 1993



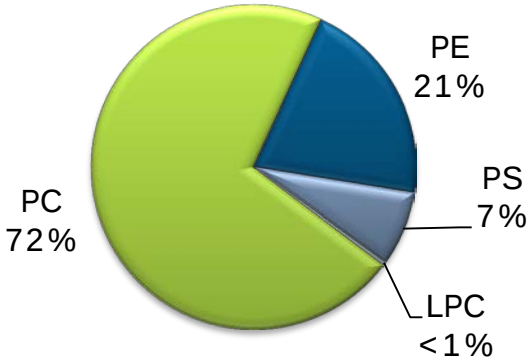




PREOBE - RESULTS

- Unique PL pattern: highest LC-PUFA concentration of all kinds of tissues
- DHA was counted to 67.3% in PE
- AA was counted 66.7% in PC
- Highest species: PC(16:0/16:0), PC(16:0/20:4), PC(16:0/18:2), PC(16:0/18:1)
- PC sn-1: 75% palmitic acid (16:0)
- PS sn-1: 100% oleic acid (18:0)

Phospholipid classes



Species	Comp. [%]	Species	Comp. [%]
LPC(16:0)	0.32	PE(16:0/18:1)	1.03
PC(16:0/14:0)	1.19	PE(16:0/18:2)	0.88
PC(16:0/16:0)	15.69	PE(16:0/20:3)	0.55
PC(16:0/16:1)	1.72	PE(16:0/20:4)	2.03
PC(16:0/18:1)	8.88	PE(16:0/22:6)	0.54
PC(16:0/18:2)	8.90	PE(18:0/18:1)	0.66
PC(16:0/20:3)	3.29	PE(18:0/18:2)	1.28
PC(16:0/20:4)	12.47	PE(18:0/20:3)	1.22
PC(16:0/22:6)	0.86	PE(18:0/20:4)	4.73
PC(18:0/16:0)	0.68	PE(18:0/22:6)	1.20
PC(18:0/18:1)	0.54	PE(18:1/18:1)	0.96
PC(18:0/18:2)	1.93	PE(18:1/18:2)	1.04
PC(18:0/20:3)	0.73	PE(18:1/20:3)	0.57
PC(18:0/20:4)	3.13	PE(18:1/20:4)	1.90
PC(18:1/18:1)	1.03	PE(18:1/22:6)	1.41
PC(18:1/18:2)	2.26	PS(18:0/18:1)	2.07
PC(18:1/20:3)	0.83	PS(18:0/18:2)	1.02
PC(18:1/20:4)	3.07	PS(18:0/20:3)	1.64
PC(18:2/18:2)	1.27	PS(18:0/20:4)	2.13
PC(18:2/20:4)	1.98	PS(18:0/22:6)	0.71

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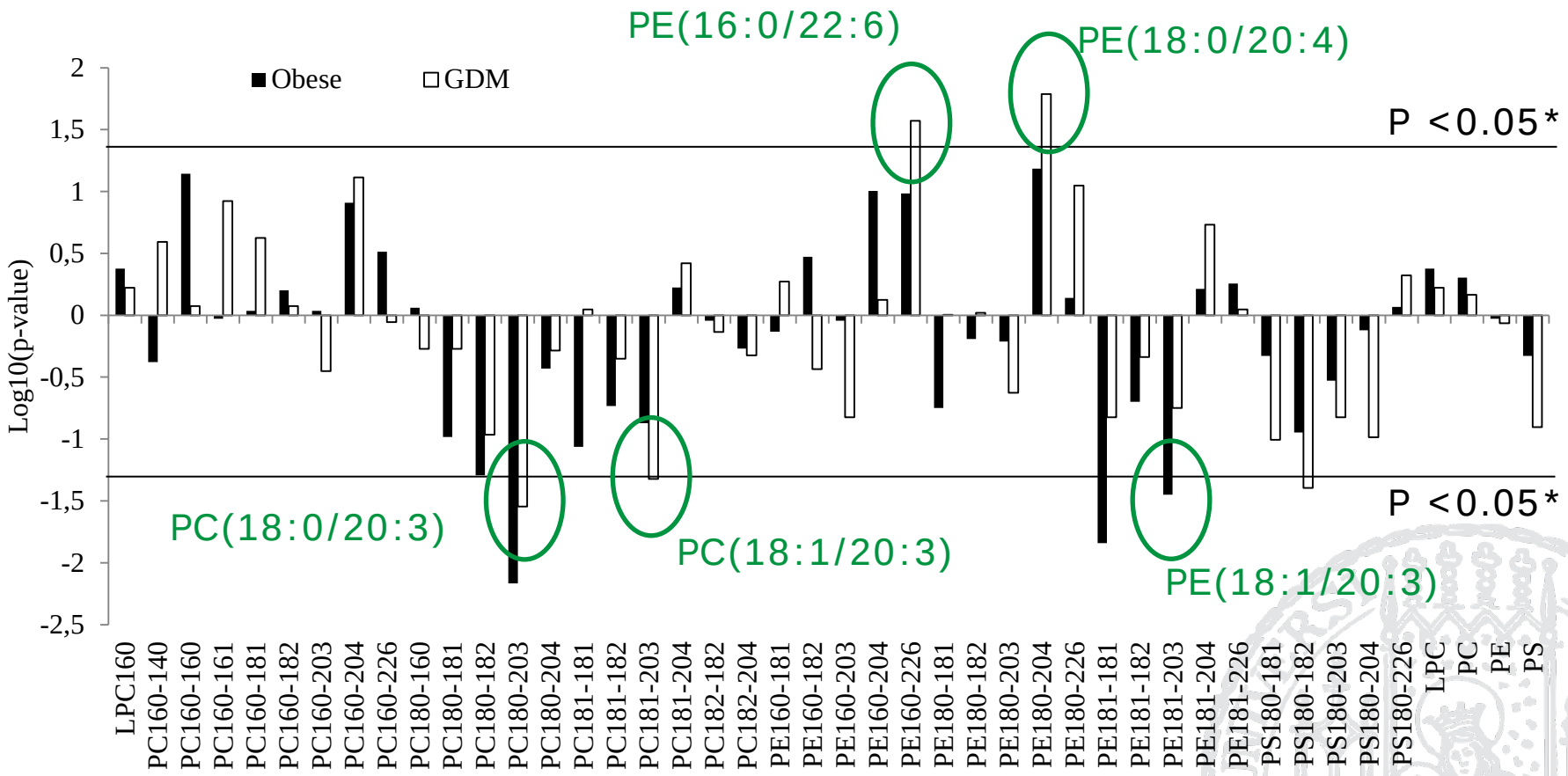
GPL PATTERN OF GDM AND OBESE IN COMPARISON TO CONTROLS



* Mann-Whitney-U test, Significance was accepted at p <0.05

Uhl, Diab Res Clin Prac, 2015

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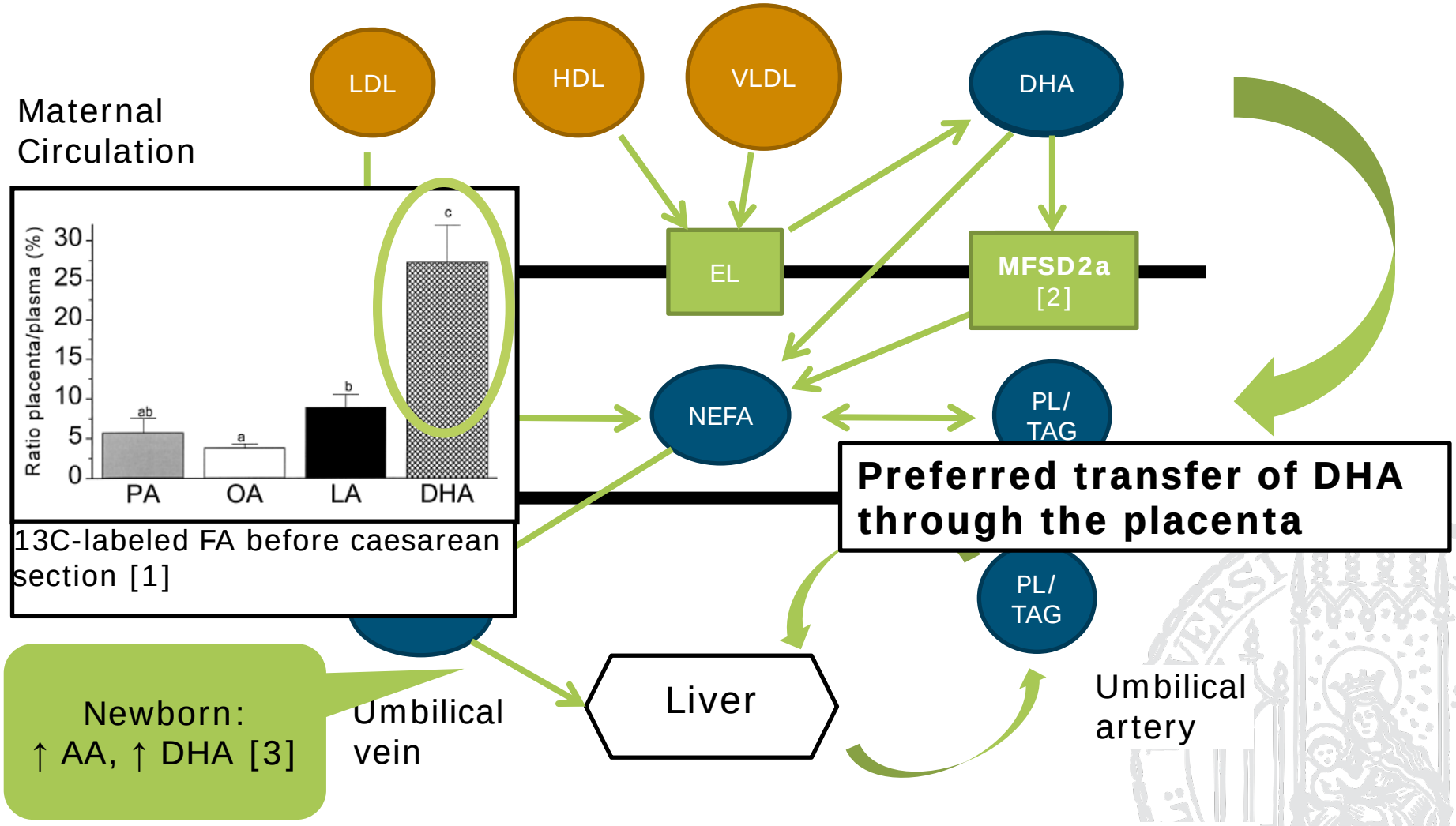
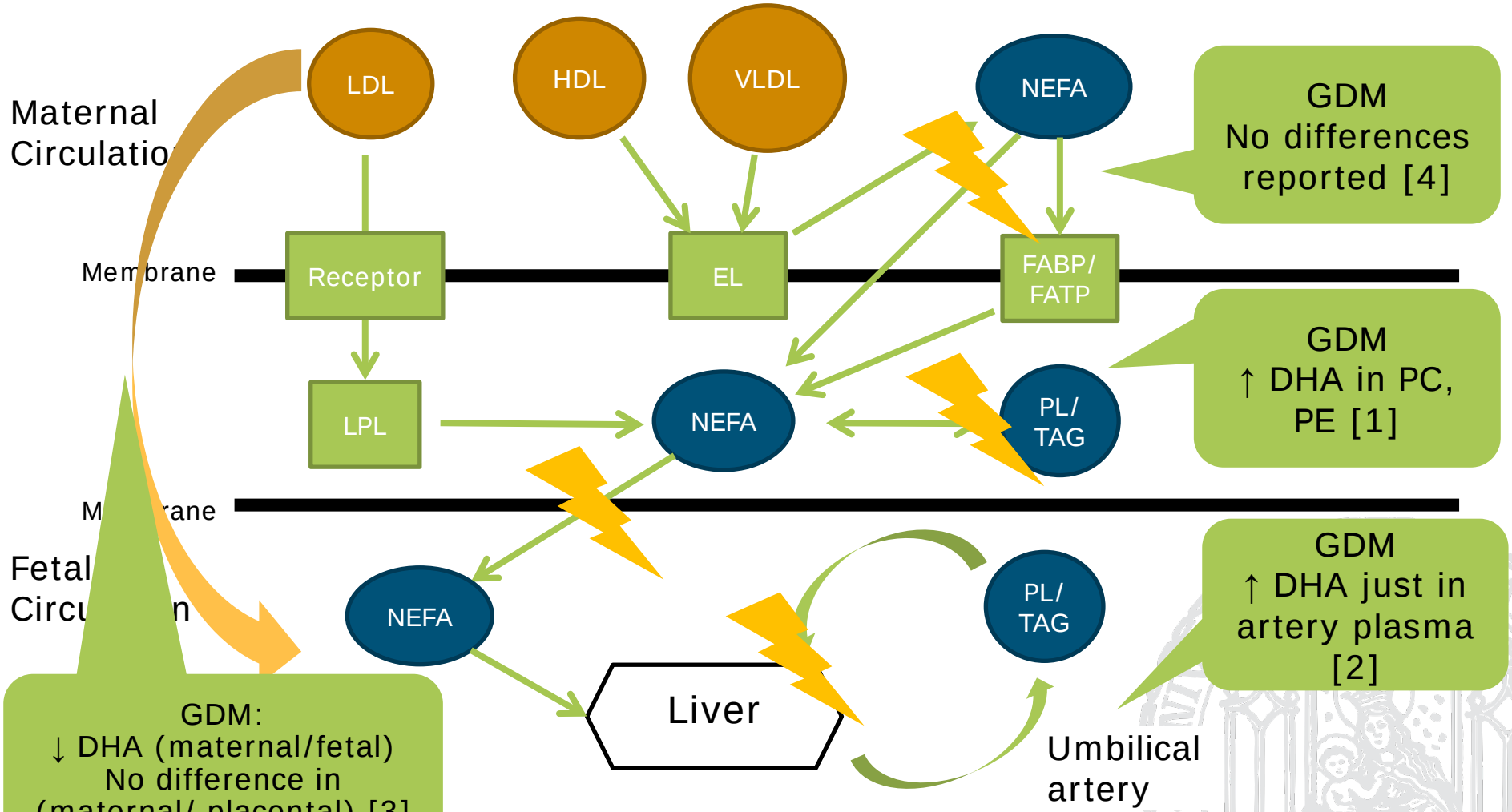
DHA TRANSFER



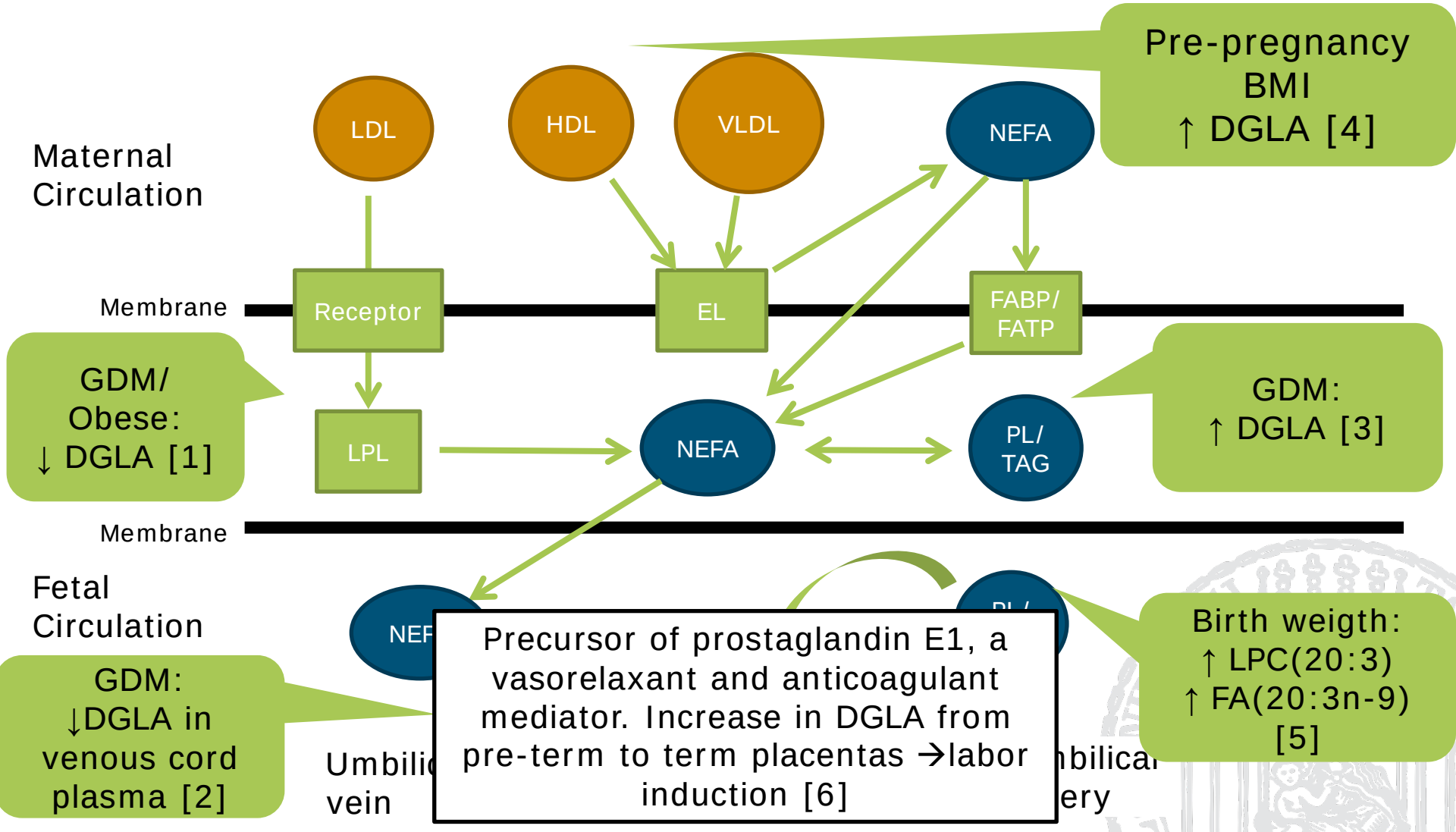
[1] Larque, Journal of lipid research, 2003
[2] Prieto-Sánchez, Clin Nutr, 2016
[3] Uhl, PLoS One, 2016

DHA TRANSFER IN GDM PREGNANCIES



[1] Bitsanis, Lipids, 2006
[2] Ortega, Diabetes Care, 2009
[3] Pagan, Am J Physiol Endocrinol Metab, 2013
[4] Thomas, Eur J Clin Nutr, 2004

DGLA TRANSFER IN GDM PREGNANCIES



[1] Uhl, Diab Res Clin Prac, 2015
[2] Thomas, PLEFA, 2005
[3] Bitsanis, Lipids, 2006
[4] Hellmuth, Int J Obesity, accepted
[5] Hellmuth, Obes Facts, submitted
[6] Bitsanis, J Nutr, 2005

PLACENTAL STRUCTURE

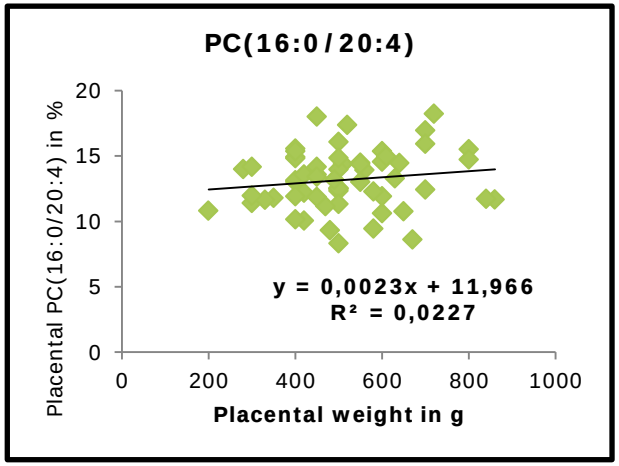
- Complex structure with different cells with different function
- GDM leads to histological changes in the syncytiotrophoblast [1]
- Lipid Droplets [2]:
  - Intracellular structures
  - Surrounded by phospholipids and proteins
  - Contain triacylglycerols and cholesterol ester
  - Role in placenta?

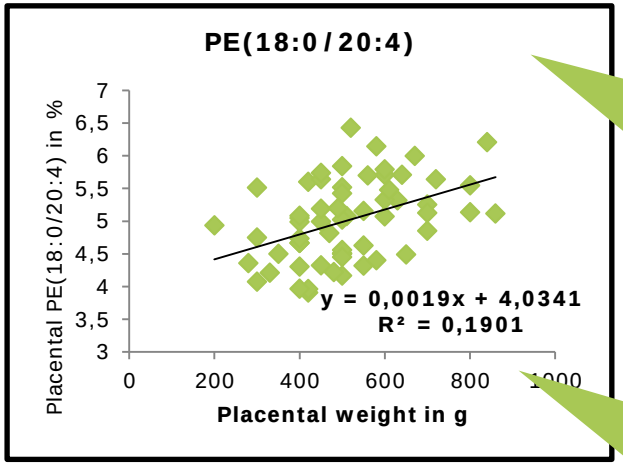
→Poster I-4
Antonio Gázquez

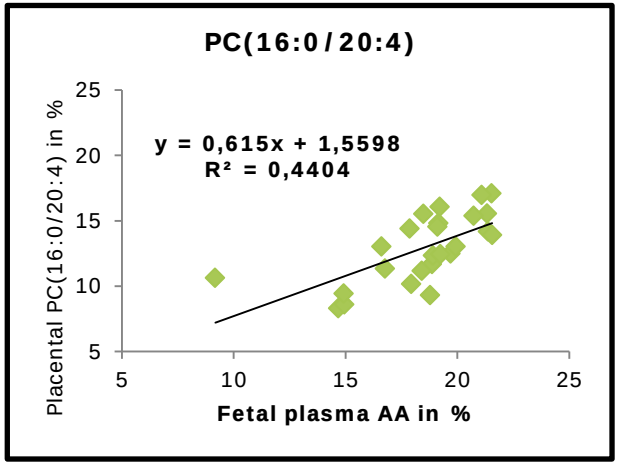
„Placental Lipid Droplet Composition is Associated with Maternal Clinical Parameters and Cord Blood Metabolites“

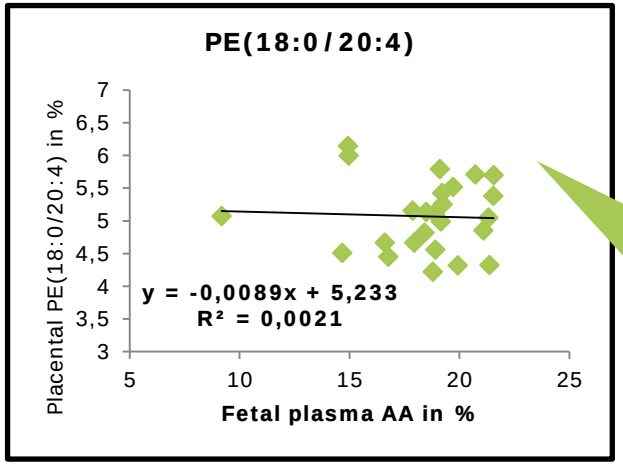
[1] Al-Okail, Endocrine Journal, 1994
[2] Hernandez-Albaladejo, ACTA Obst Gyn, 2014

PREOBE - RESULTS









AA: ↑ cell and tissue growth [1]

PE(AA) ~ birth weight [2]

Plasma TAG(AA) ~ body weight [3]

[1] Sellmayer, Lipids, 1999
[2] Crawford, Am J Clin Nutr, 2000
[3] Koletzko, Ann Nutr Metab, 1991

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SUMMARY

Results

- Elevated levels of AA and DHA in GDM placentas
- Lower levels of DGLA in GDM
- Comparable disarrangement of GPL species pattern between obese and GDM
- PC(AA) → Fetal supply
- PE(AA) → Placental development

Limitations

- Dietary bias of GDM patients
- Complex structure of placental tissue
- No correction for multiple testing

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THANKS FOR YOUR ATTENTION

EARLYNUTRITION
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