GESTATIONAL DIABETES IS ASSOCIATED WITH CHANGES IN PLACENTAL MICROBIOTA AND MICROBIOME

Judit Bassols[1], Matteo Serino [2], Gemma Carreras-Badosa[1], Rémy Burcelin[2], Vincent Blasco-Baque[2], Anna Prats-Puig[3], Francis de Zegher [4], Lourdes Ibáñez[5], Jose-Manuel Fernandez-Real[1], Abel López Bermejo[1]

[1]Girona Biomedical Research Institute (IDIBGI), Dr. Trueta University Hospital, Girona, Spain [2]Institut National de la Santé et de la Recherche Médicale (INSERM), Toulouse, France, [3]EUSES University School, University of Girona, Girona, Spain, [4]University of Leuven, Belgium, 5Hospital Sant Joan de Déu, Barcelona, Spain

Authors have nothing to declare.

Background:

The human microbiota has emerged as an unexpected modulator of the immune system. The placenta, long thought to be sterile, harbors a unique microbiome and variations in their composition could be related to prevent pregnancy disorders.

Objective and hypotheses:

To profile the placental microbiota (microorganisms) and microbiome (group of microbial genomes in an environment) in women with gestational diabetes (GDM) and study their relation to maternal metabolism and placental expression of anti-inflammatory cytokines.

Methods:

Placental microbiota and microbiome and expression of anti-inflammatory cytokines (IL10, TIMP3, ITGAX and MRC1MR) were analysed in placentas from women with GDM (n=11) and from control women (n=11; all samples were obtained under sterile conditions). Fasting insulin, pre- and post-load glucose, lipids and white blood cell counts were assessed at 2nd and 3rd trimester of pregnancy.

Results:

Bacteria belonging to the *Acinetobacter* genus and *Pseudomonadales* order showed lower relative abundance in women with GDM compared to control ($p<0.05$). In GDM women, lower abundance of placental *Acinetobacter* was associated with a more adverse metabolic (higher post-load glucose) and inflammatory phenotype (lower blood eosinophil count and lower placental expression of *IL10* and *TIMP3*) ($p<0.05$ to $p=0.001$). In GDM women, placental microbiome showed increased expression of genes involved in calcium signalling (PC1, PC2 and PC3).

Table 1. Clinical characteristics of pregnant women enrolled in the study

	Control (n=11)	GDM (n=11)	P value
Age (yrs)	32 ± 1	31 ± 1	Ns
Pregestational weight (kg)	61 ± 3	60 ± 3	Ns
Pregestacional BMI (kg/m^2)	23 ± 1	22 ± 1	Ns
2nd trimester			
Weight (kg)	69.5 ± 4.2	69.3 ± 3.4	Ns
BMI (kg/m^2)	26.3 ± 1.2	26.0 ± 1.2	Ns
Fasting glucose (mg/dL)	74.1 ± 1.6	80.0 ± 1.2	0.011
O'Sullivan glucose (mg/dL)	98.4 ± 5.1	154.7 ± 17.0	0.005
$HbA1_C$ (%)	4.8 ± 0.1	4.4 ± 0.5	Ns
TG (mg/dL)	125.4 ± 14.0	131.6 ± 17.9	Ns
HDL-c (mg/dL)	94.7 ± 5.2	70.82 ± 8.2	0.024
Blood eosinophil count (%)	2.0 ± 0.5	1.3 ± 0.2	Ns
Blood neutrophil count (%)	69.2 ± 1.8	71.6 ± 2.1	Ns
3r trimester			
Weight (kg)	74.2 ± 4.9	72.1 ± 4.4	Ns
BMI (kg/m^2)	28.2 ± 1.4	27.0 ± 1.6	Ns
Fasting glucose (mg/dL)	54.9 ± 10.9	55.4 ± 11.0	Ns
$HbA1_C$ (%)	3.4 ± 0.8	3.2 ± 0.9	Ns
TG (mg/dL)	142.1 ± 32.2	128.8 ± 34.7	Ns
HDL-c (mg/dL)	62.5 ± 12.9	47.9 ± 11.2	Ns
Blood eosinophil count (%)	1.8 ± 0.6	1.3 ± 0.3	Ns
Blood neutrophil count (%)	69.9 ± 1.2	72.0 ± 3.1	Ns

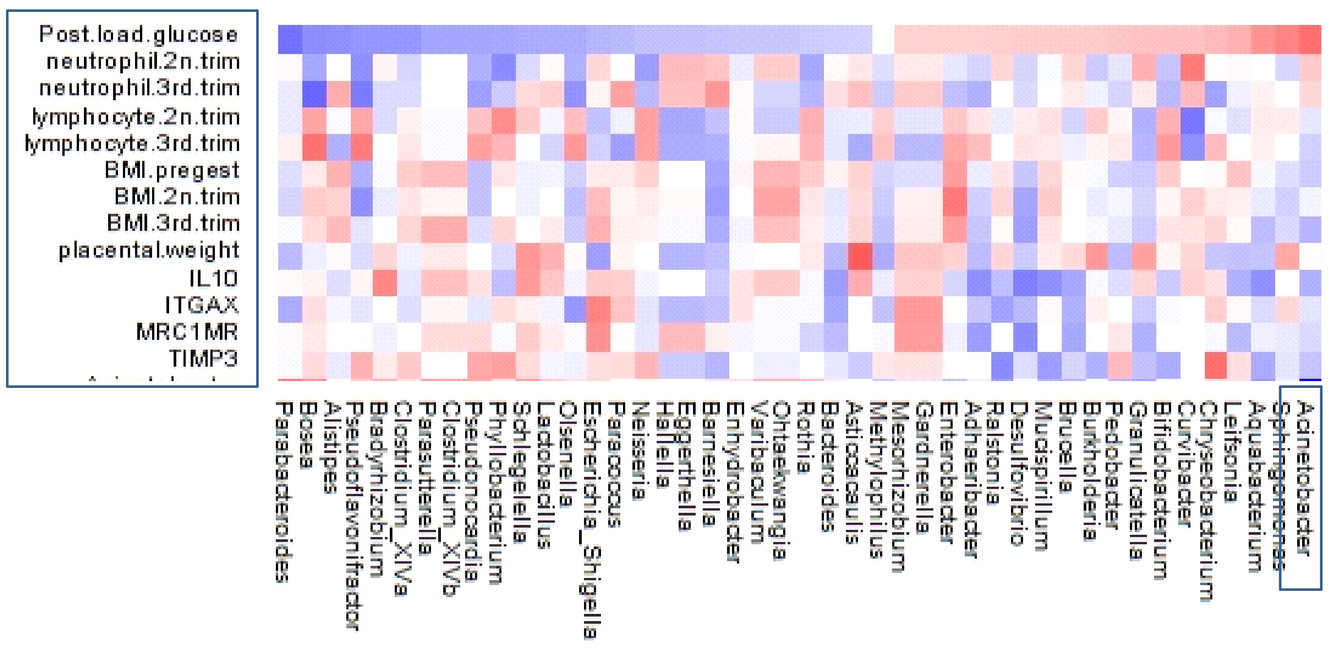

Figure 1. Heat-maps of placental microbiota at the "Genus" level and selected metabolic and anti-inflammatory parameters.

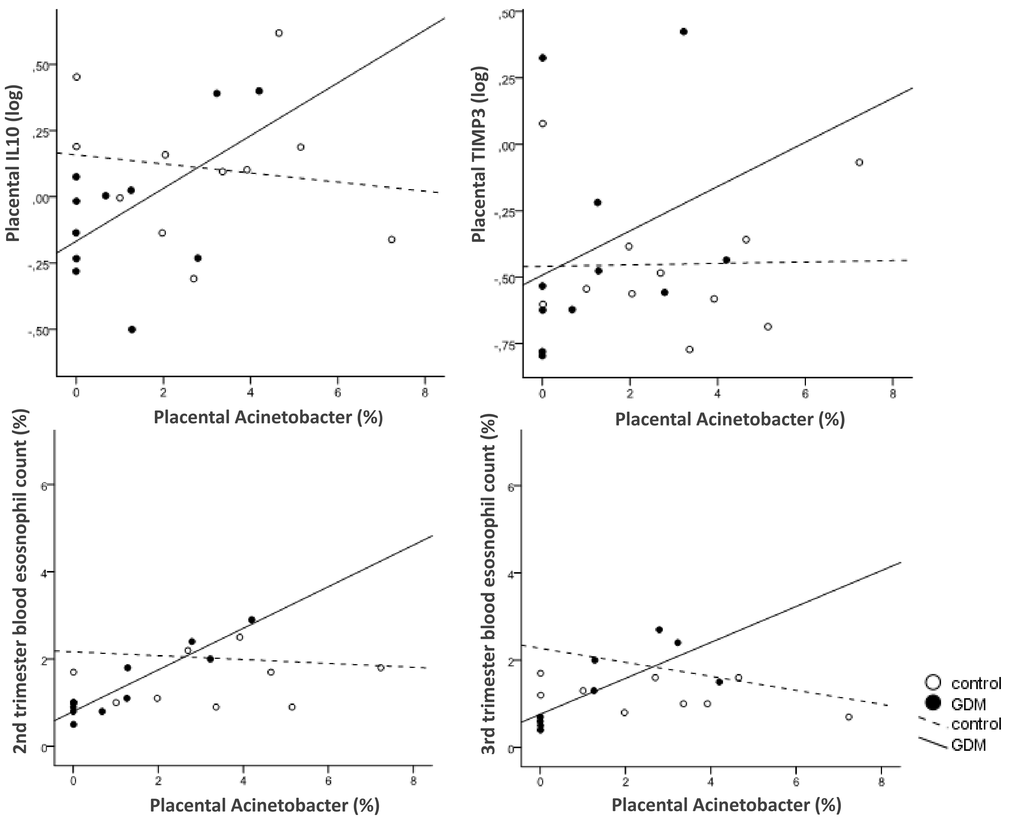

Figure 2. Correlation graphs between relative abundance of placental Acinetobacter and inflammatory parameters

Conclusion:

Placental microbiota and placental gene expression profiles were different in pregnant women with GDM compared to controls. Pregnant women with GDM showed lower abundance of *Acinetobacter* and decreased expression of IL-10. GDM could constitute a state of placental microbiota-driven altered immunologic tolerance, making placental microbiota a new target for therapy in GDM.

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