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Integrating early pregnancy markers and placental biomarkers to predict gestational diabetes severity and outcomes.

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Introduction

- Gestational diabetes mellitus (GDM) affects 15–20% of pregnancies and is linked to placental dysfunction, yet current screening can not identify early which women will progress to severe, medication-requiring disease.
- The Clinical Problem
 - Significant heterogeneity in severity
 - Some women progress rapidly → medication + adverse outcomes
 - Current pathways do not differentiate risk early
- **Aim:** We integrated clinical, biochemical, and placental molecular data from the Placental Health Study cohort to improve early prediction of GDM severity and understand the biology driving it.

Methods

This study was conducted within the Placental Health Study (PHS), a prospective pregnancy cohort at Gold Coast University Hospital, Australia. Maternal demographics, first-trimester screening markers (free β -hCG, PAPP-A) and oral glucose tolerance test (OGTT) patterns were combined with detailed placental molecular analyses, including an 84-gene cellular stress panel, total antioxidant capacity, and profiling of ~800 circulating microRNAs. Associations with GDM onset, requirement for pharmacological treatment, and adverse pregnancy outcomes were then assessed across the cohort.

Study Cohort: 543 pregnancies from the PHS.

Results

Maternal biomarkers predict GDM progression and severity.

Clinical predictors: Maternal age, BMI, and ethnicity independently predicted GDM onset (AUC = 0.76), while OGTT glucose pattern and earlier diagnosis strongly predicted requirement for pharmacological treatment (AUC = 0.98) (Table 1). Elevated first-trimester free β -hCG independently predicted adverse neonatal outcomes.

Placental molecular findings: Cellular stress responses were impaired, and antioxidant capacity reduced in severe GDM (sex-specific) (Figure 1); 23 stress-response genes were differentially expressed, with antioxidant and metabolic pathways downregulated.

MicroRNA findings: Circulating miRNA profiles differed between diet- and medication-treated GDM, with four miRNAs (miR-210, miR-504, miR-373, miR-675) emerging as regulatory hubs linked to placental dysfunction (Figure 2).

Conclusion

- Combining routine clinical markers (fasting glucose, timing of diagnosis, first-trimester screening) with molecular findings could improve early identification of women at risk of severe GDM and adverse outcomes.
- Impaired placental stress adaptation and oxidative imbalance appear to drive more severe disease, pointing to future biomarker-guided management.
- Validation in larger cohorts is needed before clinical translation.

Variable	GDM Prediction	Medication requirement prediction
	aOR (95% CI)	aOR (95% CI)
Maternal age (per year)	1.12 (1.06, 1.17)	-
BMI (per kg/m ²)	1.15 (1.1, 1.2)	-
Ethnicity (vs White)		
Asian	3.06 (1.55, 6.1)	-
OGTT AUC (per unit)	-	4.60 (2.68, 7.92)
OGTT GA (per day)	-	0.92 (0.89, 0.95)
AUC (95% CI)	0.76 (0.71, 0.80)	0.98 (0.97,0.99)

Table 1. Multivariable logistic regression models for GDM prediction and medication requirement.

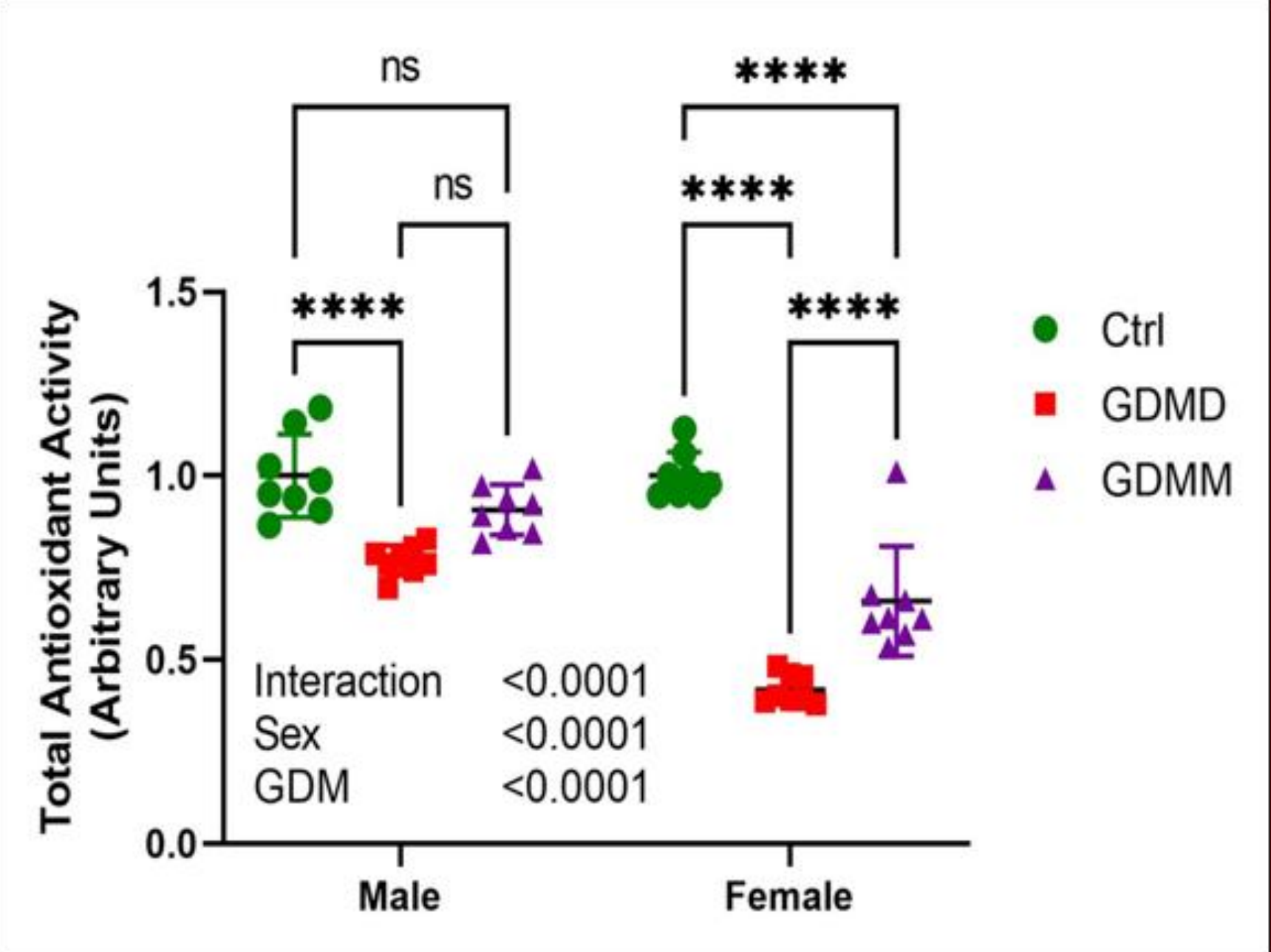


Figure 1. Total antioxidant capacity (TAC) in placental tissue. ****p<0.0001; **p<0.01; ns, not significant.

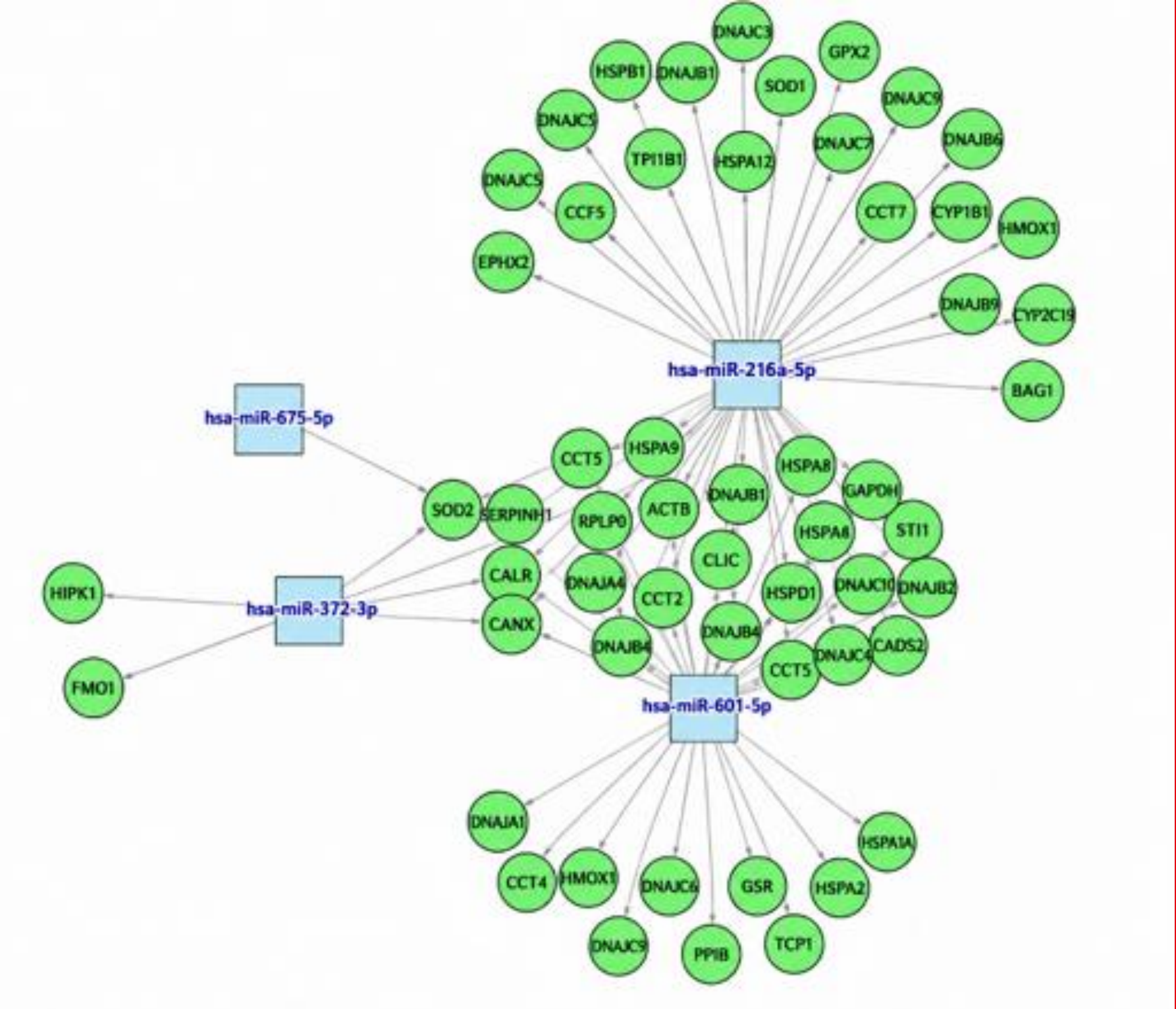


Figure 2. MicroRNA-gene interaction network in severe versus mild GDM placental tissue.