

A longitudinal study on miRNAs circulating levels in a cohort of SGA and AGA subjects, evaluated during childhood and young adulthood

E. Inzaghi^{1,2}, A. Kistner³, A. Deodati^{1,2}, D. Germani², L. Legnevall⁴, M. Vanpee⁴, K. Berinder⁵, S. Cianfarani^{1,2,4}

¹ D.P.U.O. "Bambino Gesù" Children's Hospital, "Tor vergata" University, Rome, Italy; ² Endocrinology and Diabetology Unit "Bambino Gesù" Children's Hospital, Rome, Italy; ³ Department of Molecular Medicine and Surgery, Karolinska Institutet and Department of Radiology, Karolinska University Hospital, Stockholm, Sweden; ⁴ Women's and Children's Health, Karolinska Institutet, and Neonatology Department, Astrid Lindgren Children's Hospital, Stockholm, Sweden; ⁵ Department of Endocrinology, Metabolism and Diabetes, Departments of Medicine and Molecular Medicine and Surgery, Karolinska Institutet at Karolinska University Hospital, Stockholm, Sweden.

Background

A low birth weight has been associated with an increased cardiometabolic risk in adult age. MiRNA serum levels have been associated with metabolic parameters and diseases.

Objective: The aim of the current study was to investigate the circulating levels of mir-122, mir-16, mir-126, and mir-486 in a cohort of SGA and AGA subjects, evaluated longitudinally in childhood and early adulthood

Methods

Anthropometric and biochemical-metabolic evaluation at the age of 9 and 21 years has been performed on 23 SGA (13 F/10 M) and 28 AGA (17 F/11M) subjects. IGF-I and IGF-II levels have been studied. Serum levels of mir-122, mir-16, mir-126, and mir-486 have been analyzed by qPCR.

Results

SGA subjects are shorter than AGA ones, both at 9 years ($0.08 \text{ sds} \pm 1.06$ vs $0.76 \text{ sds} \pm 1.2$, $p=0.04$) and at 21 years ($-0.21 \text{ sds} \pm 0.76$ vs $0.65 \text{ sds} \pm 1.32$, $p=0.03$) whereas metabolic profile and IGFs are not different. MiRNAs expression is not different between females and males. In all subjects, mir-122 and mir-486 expression is not influenced by the age, while mir-16 and mir-126 levels are higher at 9 years than at 21 years. Mir-122, mir-16, mir-126, and mir-486 expression is not different between SGA and AGA subjects, either at 9 and 21 years. In SGA subjects, mir-122 expression at 9 years is inversely related to Adiponectin levels at 21 years ($r=-0.48$, $p=0.05$) and mir-486 expression at 9 years is inversely related to WBISI (whole-body insulin sensitivity) at 9 years ($r=-0.52$, $p=0.034$) and directly related to Hb1Ac at 21 years ($r=0.52$, $p=0.032$). In AGA subjects, mir-122 expression at 9 years is directly related with BMI sds ($r=0.5$, $p=0.04$) and LDL-cholesterol levels ($r=0.5$, $p=0.03$) at 21 years and mir-486 expression at 9 years is directly related to leptin at 9 years ($r=0.5$, $p=0.02$) and mir-486 expression at 21 years is inversely related to Adiponectin levels at 21 years ($r=0.5$, $p=0.02$).

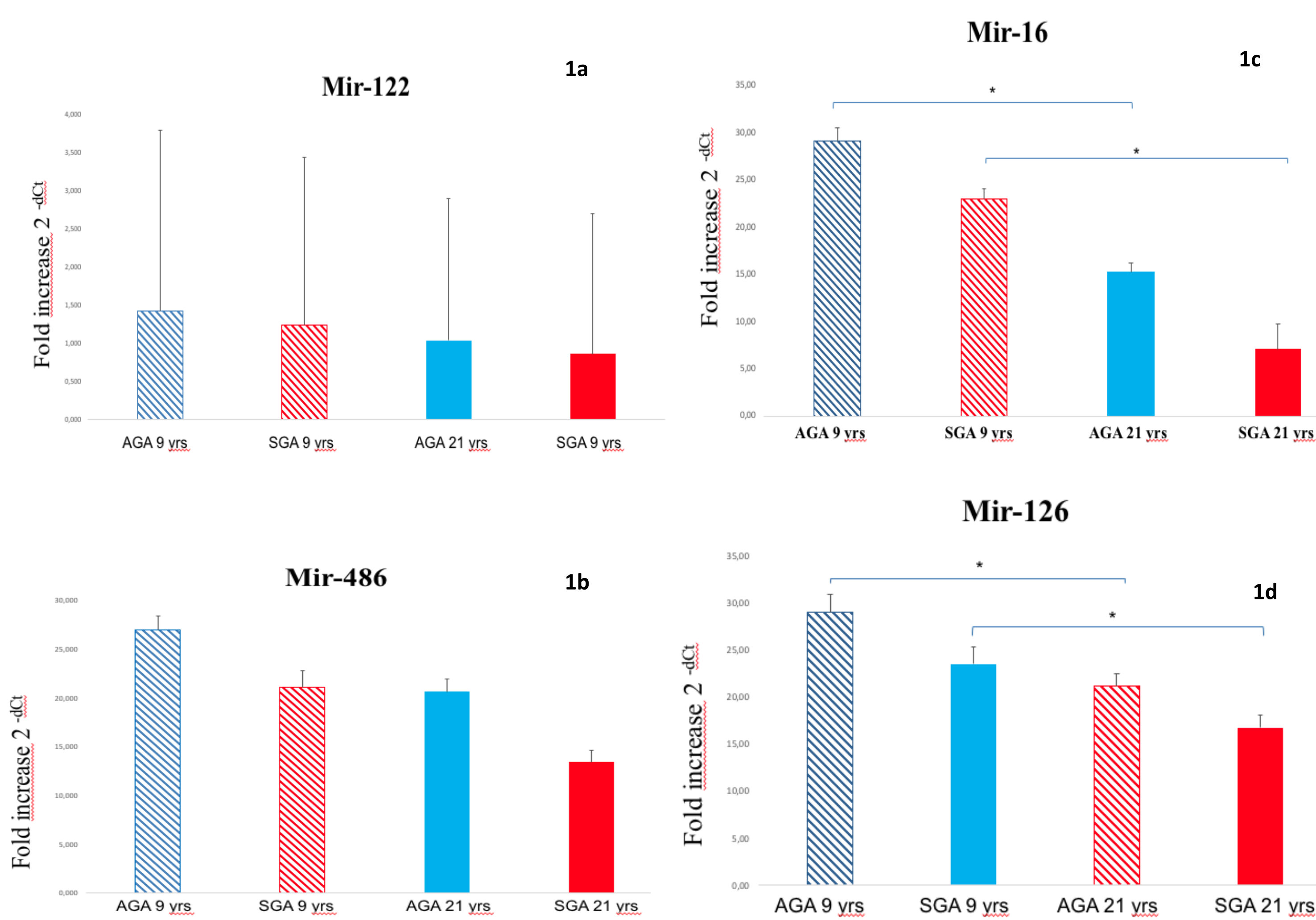


Fig 1a. Mir-122 expression in AGA and SGA subjects at 9 and 21 years. Fig 1b. Mir-486 expression in AGA and SGA subjects at 9 and 21 years. Fig 1c. Mir-16 expression in AGA and SGA subjects at 9 and 21 years. Fig 1d. Mir-126 expression in AGA and SGA subjects at 9 and 21 years.

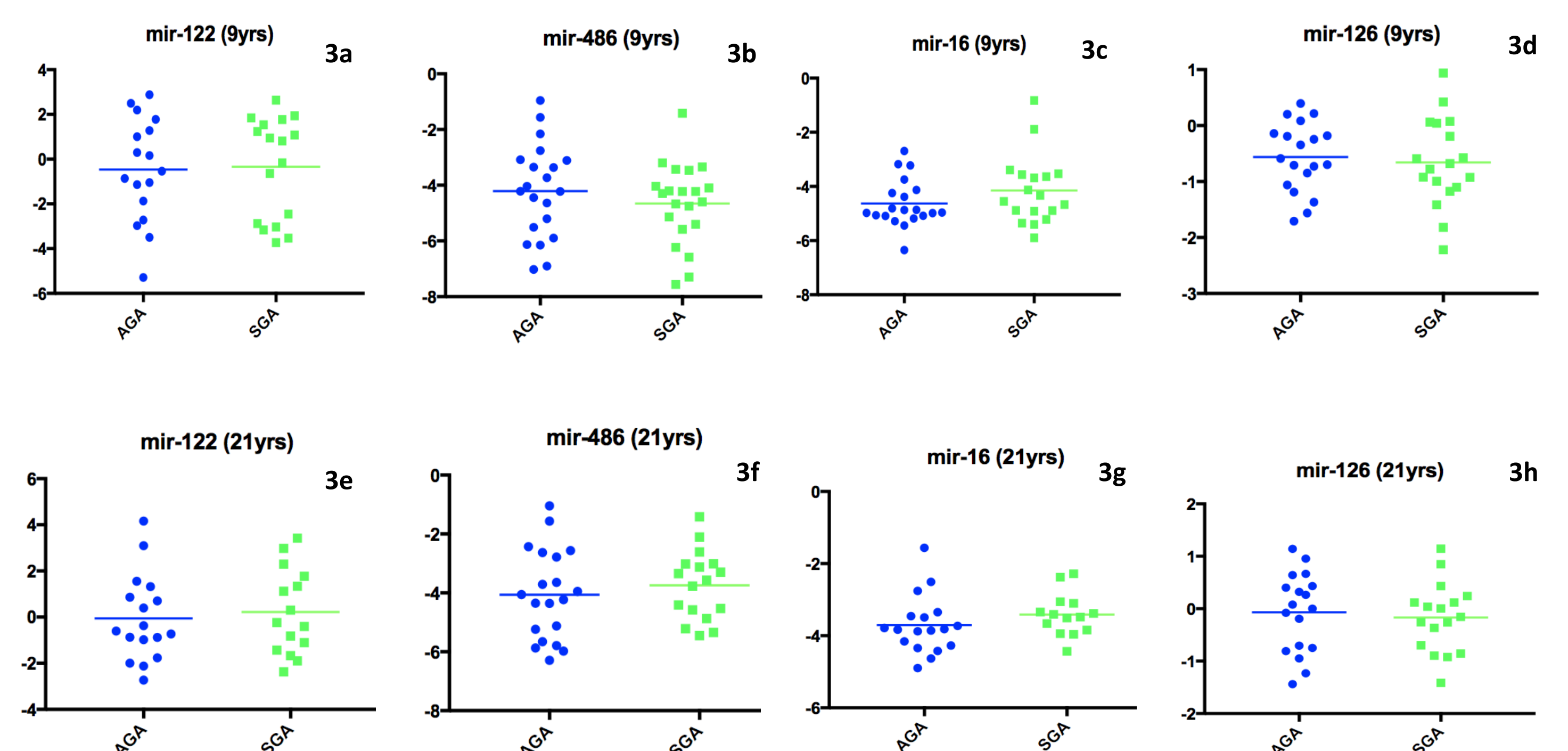


Figure 3 a-h. Comparison of microRNA expression between SGA and AGA subjects at 9 and 21 years.

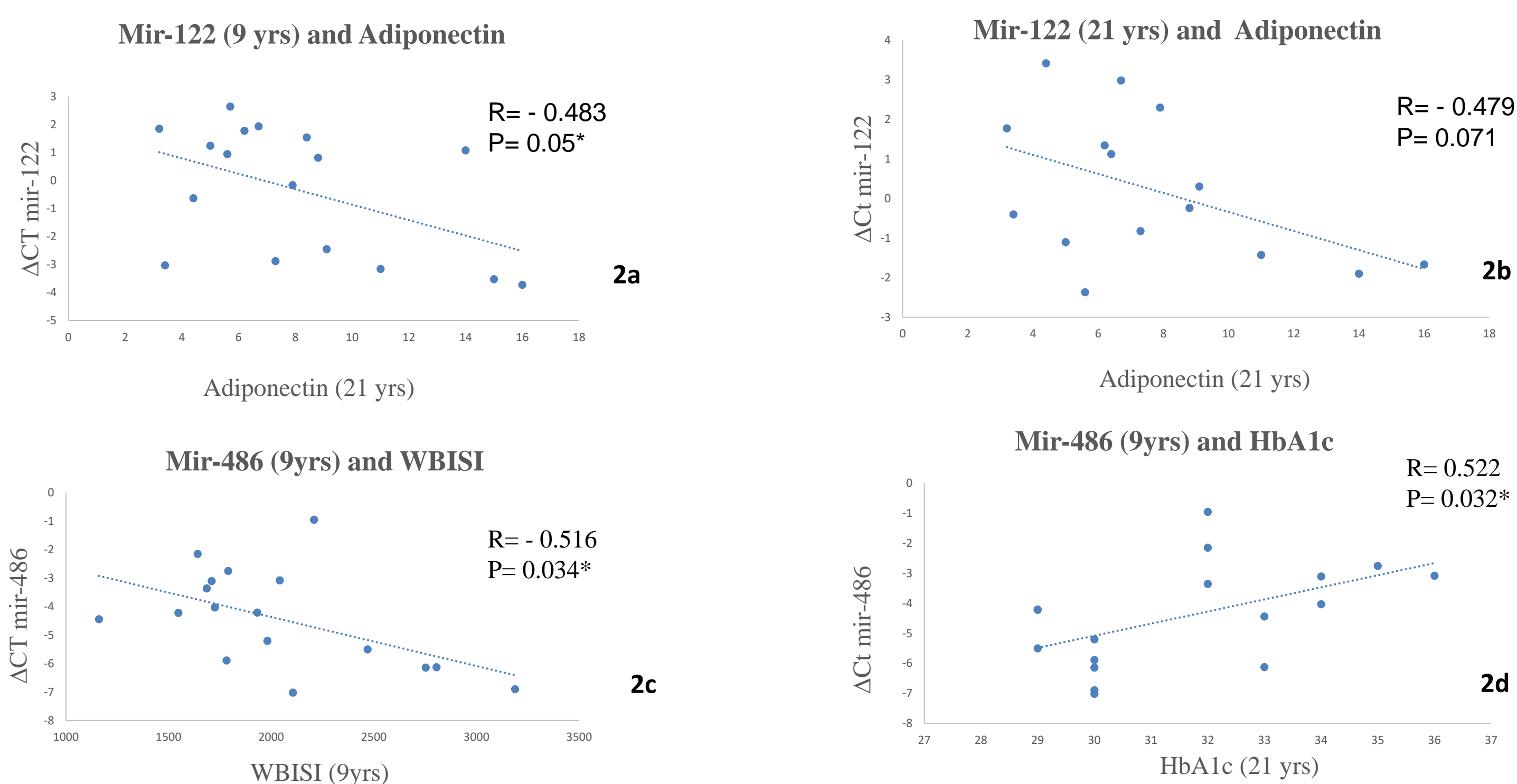


Fig 2a. Correlation between mir-122 expression at 9 years and Adiponectin levels at 21 years. Fig 2b. Correlation between mir-122 expression at 21 years and Adiponectin levels at 21 years. Fig 2c. Correlation between mir-486 expression at 9 years and WBISI at 9 years. Fig 2d. Correlation between mir-486 expression at 9 years and HbA1c levels at 21 years.

Conclusions

SGA and AGA subjects do not show significant differences in biochemical and endocrine markers of metabolic risk and in miRNAs circulating levels. The relationship between miRNA levels and metabolic parameters in SGA and AGA subjects requires further studies aiming at evaluating the possible use of miRNAs as markers of increased cardiometabolic risk.

