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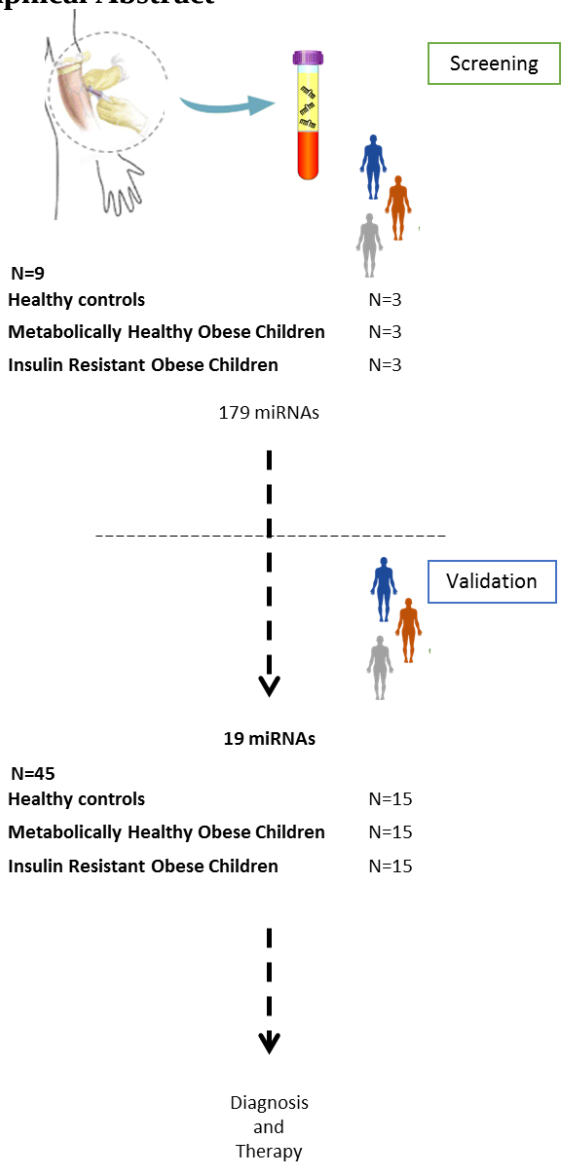
Circulating microRNA profile in Insulin Resistant Childhood Obesity.

Thalía Belmonte García [1], Álvaro González Domínguez [1]*, Jorge Carlos Morales Camino [2], Jesús Domínguez Riscart [1,3], Celia Morales Pérez [1,3], Francisco Manuel Visiedo García [1], Rosa María Mateos [1,4], Alfonso María Lechuga Sancho [1,5]

1. Biomedical Research and Innovation Institute of Cádiz (INIBICA). Research Unit, Puerta del Mar University Hospital, 11009, Cádiz, Spain.
2. Clinical Analysis Department, Puerta del Mar University Hospital, 11009, Cádiz, Spain.
3. Pediatrics Department, Puerta del Mar University Hospital, 11009, Cádiz, Spain.
4. Biomedicine, Biothecnology and Public Health Department. Biochemistry and Molecular Biology Area. University of Cádiz (UCA), 11001 Cádiz, Spain.
5. Mother and Child Health and Radiology Department. University of Cádiz (UCA), 11002, Cádiz, Spain.

Graphical Abstract



Abstract.

Objective: *Circulating microRNAs (miRNAs) have been proposed as emerging biomarkers for obesity and metabolic comorbidities. Our aim was to characterize miRNA signatures and assess their utility to discriminate between insulin resistance (IR) phenotypes in paediatric obesity and evaluate their role in diverse metabolic pathways.*

Methods: *Observational, case-control study, including prepubertal children between 6 and 10 years, divided in three study groups: a) healthy control (n=3), b) metabolically healthy obese children (n=3) and c) IR obese children (n=3). Obese patients were defined by a body mass index > 2 SD for age and sex. IR patients fulfilled at least one of the ADA's insulin resistance criteria (Basal Insulin>15 U/mL; Insulin along the OGTT>150 U/mL; Insulin>75U/mL at 120' on the OGTT; and/or, iHOMA>3,5). We first screened 179 miRNAs to identify differentially expressed miRNAs between groups. Total RNA was extracted from plasma using the miRNeasy Serum/Plasma Advanced Kit (Qiagen). Correlations between miRNA levels and clinical parameters were investigated.*

Results: *The established criteria for miRNA candidate's selection were high expression levels (Max. Cq<39 and detected in at least 95% of all samples) and statistical*

significance ($p<0.05$). We found 19 miRNAs highly expressed and differentially detected between a) metabolically healthy obese vs. IR obese children and b) healthy subjects vs. obese children, including miRNAs with previously reported roles in iron and glucose metabolism, oxidative stress, inflammation and erythrocyte integrity.

Conclusion: *The miRNA profile identified new candidates related to pediatric obesity, and enables to differentiate between IR phenotype and metabolically healthy obese children.*

Key words: *Insulin Resistance; Iron Metabolism; Childhood obesity; miRNAs; Oxidative Stress.*