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Circulating micro-RNAs in obese and diabetic patients: What meaning?

MicroRNAs (miRNAs) are short noncoding RNA sequences synthesized in the cell nucleus, through a complex multi-step biosynthetic process starting from RNA polymerase II; it is estimated that the human genome contains more than 2500 mature miRNAs.miRNAs regulate a wide range of biological processes as cell differentiation, proliferation and development, cell-to-cell communication, cell metabolism and apoptosis. miRNAs seem also regulate insulin signaling, immune-mediated inflammation, adipokine expression, adipogenesis, lipid metabolism, and food intake. There is evidence that miRNAs may have a role in molecular mechanisms linked to cellular pathways of some diseases, as viral infections, cancer, diabetes, obesity and cardiovascular disease. The recent discovery of circulating miRNAs easily detectable and measurable in plasma and other body fluids, led to the hypothesis of their potential role as disease indicators.Altered circulating levels of several miRNAs were found to be linked to type 1 and type 2 diabetes, both at onset and in advanced disease. At least 12 circulating miRNAs were found consistently dysregulated in type 1 diabetes mellitus and, more or less, 40 circulating miRNAs in type 2 diabetic patients. miR-126 seems to be miRNA most linked to pathways and development of type 1 and type 2 diabetes and their complications.

Dysregulation of several miRNAs involves different aspects of diabetic disease: glycemic control, residual beta cell function, insulin secretion and sensitivity, micro- and macro-vascular complications, particularly endothelial dysfunction, renal disease and retinopathy. Altered expression and dysregulation of circulating miRNAs are confirmed to correlate to obesity and its related diseases; a broad panel of circulating miRNAs is involved as miR-17-5p, -132, -140-5p, -142-3p, -222, -532-5p, -125b, -130b, -221, -15a, -423-5p, -520c-3p. Although different levels of several circulating miRNA were found significantly associated with weight gain, most of the data concern comorbidities and complications of obesity as insulin resistance, pre-diabetes, diabetes (miR-15b, -138, -376a and -503 particularly), lipid metabolism alterations, adipogenesis dysregulation (miR-143 and -221) and inflammatory processes. Moreover, several evidences were obtained in obese children (miR-122 and -199a) and some data in newborns and maternal pre-gestational and gestational obesity (miR-122, -324-3p, -375, -652 and -625); the expression of some miRNAs differs in infants born to obese women compared with infants born to lean women then changes in miRNA expression might participate in epigenetic fetal programming of metabolic disorders in children born to obese women.

In obese children, miR-486, -146b and -15b might be useful in predicting future risk of type 2 diabetes. Circulating early-mid-pregnancy miRNAs are associated with gestational diabetes, particularly in women who are overweight pre-pregnancy. At last, significant down-regulation of several and different miRNAs was observed in overweight/obese subjects after low or high glycemic index diet and after low-fat diet; moreover, circulating miRNAs might be potential novel biomarkers for the benefits of bariatric surgery and the effects of mild exercise, in predicting improvements in

cardiometabolic risk. There are scientific evidences suggesting a potential role of circulating miRNAs detection as useful source of diagnostic, prognostic and therapeutic biomarkers in obese and diabetic patients. Major limits: number, duration and sample size of clinical studies are small; source of circulating miRNAs, extraction procedures, quantities of blood samples and methods of analysis, as well as promiscuous nature of miRNAs targets, difficulties of obtaining tissue specificity and, in particular, high costs required for miRNAs detection may contribute to the uncertainty observed in the literature, highlighting the need for reproducible and well standardized methods. Moreover, low-cost and wide availability assays to detect circulating miRNAs with high sensitivity/specificity should be developed.Large, long-term and randomized controlled clinical studies are need to determine whether circulating miRNAs could play a role as biomarkers for obesity and diabetes in daily clinical practice.

Biography

Angelo Michele Carella, after graduating in Medicine, obtained specialization in Internal Medicine, attended postgraduate courses on Diabetes and Obesity and obtained university Master in Healthcare Management.Currently, he operates at the Internal Medicine Department of "T. Masselli - Mascia" Hospital in San Severo (Foggia), Italy. He teaches at Medical Faculty of Foggia University, degree course in Health Professions. He took part as researcher/co-researcher in some clinical studies, published in international journals, as DAVID Study, ESPORT Study, ATA-AF Study and DIAMOND Study. He is Editorial Board member and Reviewer of a lot of scientific journals and Author of several scientific publications (h-index 5, according to Google Scholar citation search; ORCID iD: 0000-0003-4825-9620). He took part, as speaker, in scientific congresses and meetings and he is member of scientific societies as "Italian Association of Diabetes specialists" (affiliated with IDF), "Italian Association of Dietetics and clinical nutrition", "Italian Federation of Hospital Internists Associations"; moreover he is member of "Diabetes and Cardiovascular Disease Study Group", official study group of EASD. He is registered in Google Scholar and Research Gate. Research areas and field of expertise: Internal medicine, Diabetology, obesity and metabolism, cardiovascular diseases, oncology.

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