# Antioxidant and microRNAs: An Applied Overview

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The balance of antioxidants defenses which sustain also the balance of inflammation response is of significant importance to prevent several chronic diseases. Epigenetic regulators such as microRNAs (miRs) are emerging in this field and are now recognized to play a central role in the regulation of several arrays of biological processes. MiRs are the trait *d'union* of genetic, biochemical, and structural studies in the understanding of diseases in which cellular redox with the generation of reactive oxygen species (ROS), that when not in balance, plays a critical role.

MiRs are able to "fine-tune" the regulation of processes including those directly interacting with the Nrf2 pathway and the generation of ROS. Therefore, redox-sensitive miRs or "redoximiRs" add an important regulatory mechanism for redox signaling out there of the well-characterized actions of Nrf2. The potential exists for miR-based therapies. Several chronic diseases, where diminished antioxidant defenses and dysregulated redox signaling can lead to metabolic and cardiovascular diseases, cancers, neurodegeneration, and fostering the aging process.

Although mechanics explanations are important in the aetiology of the pathogenesis. To keep health status, we should consider the human body a whole biological system, in which each component works in harmony with all others. The overview of the human body let us to demonstrate how the ketogenic diet (KD) regimen, acts on the circulating miRs expression profile identifying 11 miRs crucial for this epigenetic change [1]. The 11 miRs are able to control the metabolic network identified so far in subjects on KD were almost normalized and closer to lean subjects. Besides that, new miRs targeting identified genes linked to the homeostasis of oxidant–antioxidant pathways were identified [2]. These latter molecules act as epigenetic regulators and have the peculiarity of regulating gene expression targeting the 3′UTR mRNA region and play a role also in insulin secretion often impaired in obesity and prediabetic condition [3].

Predicted and validated target genes were assessed by us, using DIANA Tools. The hsa-miR-let7e-5p has a role in pathogen recognition [4]. A low level of hsa-miR-520h was found in the alteration of the placenta, mediated by oxidative stress [5], and hsa-miR-548d-3p was found to be involved in the control of the homeostasis of oxidative stress damage, the metabolic network and survival pathways [6]. We found an in silico interaction of that miR with glutathione peroxidase 7 (GPX7), tet methylcytosine dioxygenase 3 (TET3) and superoxide dismutase 2 (SOD2). GPX7 is a glutathione peroxidase homolog for which the exact biochemistry is not fully understood [7]. TET3, which is aberrantly expressed in acute myeloid leukemia, promotes DNA oxidation [8,9]. The mitochondria-localized manganese superoxide, SOD2, has a dichotomous role and aids in the regulation of several types of cancers [10]. All those proteins directly or indirectly exhibit a physical interaction with catalase (CAT). This latter protein was monitored through Western blot analysis and decreased after KD regime. The hsa-miR-30a-5p was found to target the 3′UTR regions of CAT. It is worth noting that the family of hsa-miR-30, to which hsa-miR-30a-5p belongs, is a promising regulator in both development and disease [11]. In the interplay of oxidative stress, pro-oxidants, and antioxidants, this is already known [12]. In particular, the regulation of antioxidant genes such as SOD, CAT, and GPX was studied in mice models kept in KD. The short time-frame of KD did not affect the SOD expression protein while it significantly decreased both GPX and CAT [13].

It is worth to note that the administration of KD for a relatively long period is safe and can be considerate a nutritional therapy for weight reduction in obese patients [14]. Besides that, to keep KD beneficial, lifestyle change is mandatory and is the harder part of nutritional intervention during KD, with documented improvement of the endurance exercise capacity, better recovery from fatigue and exercise-induced muscle and organ damage prevention in obese subjects. Besides that, the anti-inflammatory action of physical activity was also recently reviewed [15]. Nutraceuticals with antioxidant properties were proposed to help in the treatment of obesity, but they are not enough when taken alone [16,17]. Several scientific approaches to date have tried to describe this disorder by way of genetic or environmental factors [18] and the role of epigenetics in human diseases has been well described relatively recently. Obesity and epigenetics is a consolidated union [19,20], and bariatric surgery induces epigenetic change in obese subjects [21] pointing out a balance of epigenetic mechanisms in the loss of weight.

An aberration in this balance modulates host immunity that affects normal cellular signaling pathways resulting in uncontrolled proliferation of cells leading to neocarcinogenesis [22] but for decades, there have been scientific debates on the use of antioxidants for the treatment of human cancers. What remains to be fully elucidated is how miRs can coordinate cellular redox homeostasis, which in turn plays a central role in a large number of physiological and pathophysiological processes. The redox-sensitive transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) serves as a "master regulator" of cell survival through the coordinated induction of phase II and antioxidant defense enzymes to counteract oxidative stress and modulate redox signaling events

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