



The Food-Borne Micro RNA and its Controversy on Human Health



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Editorial

A micro-RNA (mi-RNA) is a small non-coding RNA molecule containing about 21-25 nucleotides. Micro-RNAs are partially complementary to one or more messenger RNA (mRNA) molecules, and their main function is to down regulate the gene expression in a variety of manners, including translational repression, mRNA cleavage, and deadenylation. This mechanism relies on the seed region of nucleotide sequence of mi-RNAs that bind to target mRNA [1]. Imperfect pairing of sequences in the seed region in mi-RNA to mRNA impairs gene down-regulation at the protein or RNA level [2]. The mRNA degradation occurs if the mi-RNA nucleotide sequence has a high degree of complementarities to the mRNA sequence [3,4]. Most of the circulating mi-RNAs exist in packaged exosomes [5,6]. Exosomes are the extracellular vesicles containing variety of compounds, lipids, proteins including mRNAs, micro-RNAs (mi-RNAs), and other non-coding RNAs (ncRNAs) [7,8]. Exosomes are not only play essential roles in cell-to-cell communication but also in the role of protection against enzymatic and non-enzymatic degradation of cargos.

In the past, endogenous-mi-RNA has been considered as a regulator of the expression of genes within the host. Evidence suggests that the endogenous synthesis of mi-RNAs can be altered by the dietary bioactive components. Polyphenolic compounds from food sources like fruits and beverages such as tea, coffee, and wine can modulate the expression of mi-RNAs that regulate mRNA which are involved in various biological functions, such as apoptosis, inflammation, lipid metabolism, and cell migration [9].

Interestingly, mature exogenous mi-RNAs may also be obtained from dietary sources [10]. Recently it has been claimed that the mi-RNA from the food-borne especially plants and animals-origin mi-RNAs are bio available and can affect gene expression. For instance, Zhang et al. [11] reported that orally administered exogenous plant mi-RNAs through food intake are present in the sera and tissues of various animals and finally can regulate the expression of target genes in mammals. They reported that *osa*-MIR-168a (found in rice) decreased low-density lipoprotein receptor adapter protein 1 mRNA in the mouse liver. The plant-origin mi-RNAs were also

identified by the Lukasik & Zielenkiewicz [12] reported that some plant mi-RNA molecules are abundant in human and porcine breast milk exosomes. However, studies regarding on the bioavailability of plant-origin mi-RNAs are also controversial. Snow et al. [13] concluded that "Horizontal delivery of micro-RNAs via typical dietary ingestion is neither a robust nor a frequent mechanism to maintain steady-state micro-RNA levels in a variety of model animal organisms, thus defining the biological limits of these molecules in vivo". Dickinson et al. [14] did not detect the oral bioavailability of plant micro-RNAs after feeding in mice.

Animal-origin mi-RNAs are bio available and can affect gene expression in mice and human [15]. The main discovery of the Zemleni group on dietary mi-RNA concluded that

- A. humans absorb biologically meaningful amounts of mi-RNAs from nutritionally relevant doses of cow's milk,
- B. Milk mi-RNAs are delivered to peripheral human tissues,
- C. physiological concentrations of milk mi-RNAs affect human gene expression in vivo and in cell cultures, and
- D. Endogenous synthesis of mi-RNAs does not compensate for dietary mi-RNAs deficiency in mice" [16].

In their plant-origin mi-RNAs study, they did not detect the Brassica-specific mi-RNAs in a broccoli sprout-feeding study.

There are some evidences that mi-RNAs (endogenous as well as exogenous) are contained in exosomes, providing protection against degradation from acidic environment of intestine and adequately stable to pass through the gastrointestinal (GI) tract and enter into circulation without losing its functionality. This intestinal uptake of micro-RNAs contained exosomes is mediated by endocytosis where the protein/protein recognition plays an important role in the intestinal uptake in humans and rats [17]. The glycosylated proteins are important to the endocytosis of food-borne exosomes. The more compatibility of glycoprotein's with the receptors on the apical surface of mammalian cells the more bioavailability of mi-RNAs. When compared to animal-origin mi-RNAs, bioavailability

of plant-origin mi-RNAs is quite low, that could be due to the poor compatibility of plant vesicles [17].

To explore more on the exogenous mi-RNAs and its effect on peripheral gene expression on human, one should understand the information of mi-RNA molecules through the computational analytical approaches; more experiments in characterization of intestinal mi-RNA transport mechanisms and alter the gene expression through binding to mRNA in hosts; and molecular interaction of the glycoprotein's involved in the endocytosis of dietary micro-RNAs.

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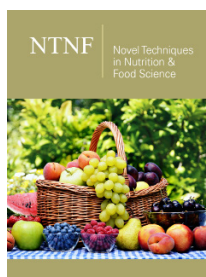
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