We are not only eating 'materials', we are also eating 'information'

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In a new study, Chen-Yu Zhang's group at Nanjing university present a rather striking finding that plant miRNAs could make into the host blood and tissues via the route of food-intake. Moreover, once inside the host, they can elicit functions by regulating host "target" genes and thus regulate host physiology.

MicroRNAs are a class of 19-24 nucleotide non-coding RNAs that do not code for proteins. MicroRNAs bind to target messenger RNAs to inhibit protein translation. In previous studies, the same group has demonstrated that stable microRNAs (miRNAs) in mammalian serum and plasma are actively secreted from tissues and cells and can serve as a novel class of biomarkers for disease and act as signaling molecules in intercellular communication.

Here, they report the surprising finding that exogenous plant miRNAs are present in the sera and tissues of various animals and that these exogenous plant miRNAs are primarily acquired orally, through food intake. MIR168a is abundant in rice and is one of the most highly enriched exogenous plant miRNAs in the sera of Chinese subjects. Functional studies in vitro and in vivo demonstrated that MIR168a could bind to the human/mouse low density lipoprotein receptor adapter protein 1 (LDLRAP1) mRNA, inhibit LDLRAP1 expression in liver, and consequently decrease LDL removal from mouse plasma. These findings demonstrate that exogenous plant miRNAs in food can regulate the expression of target genes in and thus physiology of mammals.

The finding is obviously very thought-provoking; for instance, it would indicate that in addition to eating "materials" (in the form of carbohydrates, proteins, etc), you are also eating "information" (as different miRNAs from distinct food sources could well bear different consequences on the regulation of host physiology once taken by the host due to potential regulation of different target genes as determined by the "information" contained within the miRNA sequence), thus providing a whole new dimension to "You are what you eat". Furthermore, the potential significances of this finding would be:

1. has significantly expanded the functions of miRNAs;
2. is an extremely intriguing and novel idea that has far-ranging implications for human health and metabolism;
3. shed new light on our understanding of cross-domain (such as animal-plant) interactions, or perhaps even the 'co-evolution', and to open new ways of thinking about regulation of miRNAs, and about the potential roles of exogenous miRNAs such as those from food, plants and insects in prey-predator interactions;
4. provides evidence that plant miRNAs maybe the seventh "nutrient" in the food (the six others are: H2O, protein, FFA, carbohydrate, vitamins and real elements);
5. provides a novel mechanism of development of metabolic disorder.
6. provides evidence that plant miRNAs may represent essential functional molecules in Chinese traditional herb medicine,

Importantly, these results have far-reaching implications, including the establishment of a powerful experimental methodology to deliver small RNAs to animals for in vivo gene silencing and miRNA gain-of-function studies. These findings also have major implications for the genetic engineering of plants using RNAi technologies and for the development of therapeutics that rely on small RNA delivery, since those interested in

therapeutic applications of small RNAs inject doses of formulated or non-formulated RNAs that are up to 100mg/kg body weight - unimaginably higher - and have difficulty seeing an effect.

More information: Zhang et al.: " Exogenous plant MIR168a specifically targets mammalian LDLRAP1: an evidence of cross-kingdom regulation by microRNA " Publishing on *Cell Research*, September 20, 2011.

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