Perspective

MicroRNA Opens up a New World for Nutrition Research

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Several landmark discoveries have deepened our understanding of living organisms, for example the structure of the cell, the role of organelles, and the mechanisms of protein synthesis. Recent food and health metabolomic research has gone one step beyond classical nutrient-based concepts of nutrition, approaching the essence of biology. So far, we have delved into the cause of diseases at the genome and epigenome level. A further step is the discovery of microRNAs (miRNA), and their importance in controlling health and diseases [1-4]. We are thus closer to understanding the mysteries of life.

"Small-interfering RNA" were discovered in nematodes in 1993 [1]. Small RNA molecules are made of single-stranded mRNA, and their sequences are complementary to specific mRNA, to which they bind for silencing gene expression. On the other hand, miRNA have partially complementary sequences. They bind to a number of mRNA sequences, and suppress the expression of various genes by physically inhibiting the translation of their mRNA [2-4]. The initial description of miRNA appeared in a paper published in Science in 2001, and research has been progressing rapidly since then. New types of miRNA are being discovered every year. It appears that miRNAs exist in various types of plants and animals, regardless of species [5-8]. So far, in humans, 2656 miRNAs have been identified with a precise length of 22 bases.

When a gene is activated, the DNA- is transcribed into messenger RNA (mRNA), which moves to ribosomes outside of the nucleus. During the transit of the mRNA to the cytoplasm, miRNAs are considered to be the most important regulator of post-transcriptional regulation by binding to mRNA. Multiple miRNAs interact to suppress the expression of specific mRNAs. In this way, miRNA and mRNA form a complex gene expression control network, with-miRNA maintaining the balance of regulatory functions and the ho-

meostasis of the organism. The miRNAs are perhaps the most important regulators of post-transcriptional stability of mRNA [9-11].

In the serum, miRNA are wrapped in areas of the endoplasmic reticulum called exosomes. On average, 500 to 600 miRNA molecules can be found in one exosome. A specific pattern of expression is seen in certain cancer, with a stage-specific distribution.

Leading multi-center research by more than 100 institutes, Dr. Takahiro Ochiya has been the principal investigator of diagnostic methods using miRNA to diagnose cancer. The National Cancer Research Center developed laboratory tests to diagnose thirteen different kinds of cancer simply from a drop of blood. Pancreatic cancer and ovarian cancer are typically difficult to detect, but they can now be diagnosed through the detection of miRNA patterns. There are two types of miRNAs involved in cancer: those that promote cancer progression and those that suppress cancer growth. Thus therapeutic applications are also on the horizon. In relation to cancer immunity, miRNA enhances NK activity fourfold after treatment with low-molecular fucoidan. In animal experiments, it has been established that excess miRNA could be reduced by chemotherapy, while decreased miRNA stores are replenished and restored by appropriate foods elements in various diseases [12-14].

Tochucha (Chinese tea), resveratrol, red wine, blueberries, etc. can increase miRNA level in the body. White rice miRNA has been found to lower liver cholesterol levels.

Traces of miRNA are also found in Escherichia coli and yeast, and together 100 trillion intestinal bacteria seem to produce a lot of miRNA. This brings up the idea that the fungus flora is involved in miRNA regulation in the body.

It has been found that microinflammation of the fat tissue in obese people causes insulin resistance and leads to diabetes. The next candidate to cause minute inflammation would be the intestine. Aging and frailty can be reduced by focusing on healthy eating. In the same way as miRNAs patterns are sensitive to inflammation, the relationship between changes of miRNA and food intake is likely to be clarified in the future.

Eating meal is not simply about taking nutrients, but it also involves complex system biological mechanisms of life as a whole. Returning to the old idea of food regimen, that is created by nature, would be reminded.

Individual responses to the effect of nutrition are not attributable to any cause and could well be explained by individual differences in miRNA composition.

These results show that miRNA functions as a new biomarker and prognostic indicator [15].

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