MicroRNAs are digested, not absorbed

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Milk contains microRNA moleules. They are digested in the astrointestinal tract of suckling mice (symbol image). Credit: Colourbox

There has been a lot of controversy in recent years over the issue of whether exogenous microRNA molecules can be absorbed from food and even have a physiological effect. A new study by ETH professor Markus Stoffel using mouse models settles the question by demonstrating that the posited dietary uptake does not take place. This questions the potentially promising concept of creating functional foods based on microRNAs.

The scientific world was astonished when, in 2011, Chinese researchers claimed to have found evidence suggesting that minute fragments of plant genetic material - so-called microRNA molecules - of rice ingested from food could play a role in regulating physiological processes in the human body. If this is indeed true, it might even be possible to deliberately modify human physiological functions via this route, for instance by incorporating microRNAs into novel functional foods. As a strategy, this holds considerable potential. For example, certain endogenous microRNA molecules have been shown to suppress cancer cell growth, and others are known to be involved in the development of diseases such as obesity and diabetes.

The idea of using microRNAs as a functional food ingredient was supported by American researchers who, in a study published last year, concluded that microRNAs ingested from cow's milk is absorbed and can pass into the human bloodstream. Mammalian milk generally contains large quantities of microRNAs. For many years, scientists have therefore been investigating the possibility that these molecules may naturally modify the metabolism, especially the immune system of infants.

Controversial studies

Nonetheless, the studies of microRNA transfer from rice and cow's milk stirred up much controversy within the scientific community. Some supporting data in both of these studies remained ambiguous. These reservations have now been reinforced by a new study led by Markus Stoffel, a professor in the Department of Biology at ETH Zurich. His experiments using mouse models show that the dietary uptake of microRNAs is barely significant, and certainly insufficient to affect physiological functions. Moreover, the microRNA molecules are broken down in the small intestine. This effectively dampens the enthusiasm for functional foods based on microRNAs.

The ETH biologists used two families of mice to conduct their study. One descended from a standard race of laboratory mice (the so-called wild type), while the other consisted of mice in which a specific microRNA molecule had been knocked out. The molecule in question goes by the name of miR-375 and is normally produced in the pancreas, the intestine and the mammary glands. It is one of the microRNA molecules found in high concentrations in maternal milk.

Experiment using foster mothers

The scientists allowed the two mouse families to reproduce, but exchanged their offspring immediately after birth. In this way, the researchers were able to conduct their experiments on juvenile mice that did not express miR-375 but were suckled by a female whose milk contained miR-375.

When the researchers examined the stomach milk content of the juvenile mice raised in this way, they found high concentrations of miR-375. "MicroRNA molecules are relatively resistant to gastric acids," explains Stoffel. On the other hand, they only found minute traces of miR-375 in other parts of the body. The concentrations they measured were at least a thousand times lower than the level needed to regulate gene expression and thereby modify physiological and metabolic processes. In particular, the researchers detected nothing more than the slightest concentrations of miR-375 in the cellular lining of the small intestine. This is relevant because all digested food has to pass through this barrier before entering the bloodstream. Furthermore, analysis of the blood and the liver provided no evidence of the presence of miR-375.

Breakdown of microRNAs

"We can only assume that the microRNAs are broken down into smaller

components by the enzymes in the gastrointestinal tract," says Stoffel. In a laboratory experiment in which milk containing miRNAs is mixed with digestive juices present in the small intestine the researchers proved that this is indeed the case.

But if microRNAs in maternal milk are broken down before they enter the bloodstream of the suckling infant, why did Mother Nature go to such pains to ensure that maternal milk contains large quantities of microRNAs? For Stoffel, the answer may be simple: Babies grow rapidly and to do so they need RNA building blocks in addition to the many other nutrients that promote cell growth. These components are produced in the small intestine by the digestive processes that break down microRNAs from the mother's milk. "It is reasonable to conclude that these components are quite simply there to nourish the infant," says Stoffel.

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