Preventing disease before it starts

With a history of promoting healthy eating, Kewpie is researching **THE EFFECT OF DIET ON MICRO-RNA COUNTS** with a view to preventing disease.

Could a healthy diet help to revert a pre-disease state to a healthy one?

Kurataka Otsuka measuring microRNA levels of samples.

Many natural compounds may have the ability to modulate microRNA levels.

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It might seem strange that a Japanese food company best known for its mayonnaises is pursuing medical research, but there is a connection. Since its establishment about a century ago, Kewpie has been promoting the consumption of European-style salads in Japan, a country where eating raw green vegetables is a relatively recent concept. Kewpie's research into preventing cancer and other diseases is a natural extension of that drive to promote health through diet.

PREVENTING DISEASE BEFORE IT STRIKES WILL REDUCE HEALTHCARE COSTS AND IMPROVE QUALITY OF LIFE

CATCHING DISEASE BEFORE IT HAPPENS

A major focus of modern medicine is treating existing conditions, but a promising approach is to try to detect elevated susceptibility to a condition before it becomes a diagnosable disease. "The pre-disease state, where someone has increased susceptibility to developing diseases, such as cancer, is widely considered the best period for intervening," explains Yoshinori Kono, project leader at Kewpie. "Treating disease is important, but preventing disease before it strikes will reduce healthcare costs and improve quality of life."

In the search for reliable ways to detect the pre-disease state, short snippets of non-coding RNA, known as microRNAs (miRNAs), have great potential. First discovered in 1993 in nematodes, miRNAs help to regulate gene expression.

Many human diseases, including cancer, exhibit imbalances in miRNA expression. In particular, by controlling the expression of oncogenic and tumour-suppressor proteins, miRNAs are thought to play an important role in the development of cancers by aiding tumour cell proliferation, growth-suppressor evasion and cell-death resistance. They may also promote metastasis by circulating through the bloodstream. Thus, miRNAs in the bloodstream are promising biomarkers for the pre-disease state.

In a national project commissioned by Japan's New Energy and Industrial Technology Development Organization (NEDO), Kewpie, together with researchers at various Japanese universities, is striving to develop a system that harnesses artificial intelligence (AI) to help detect the pre-disease state and to establish links between miRNA levels and risks of specific diseases. The company's goal is to develop 'explainable AI' that doesn't just give correlations between miRNA levels and the pre-disease states of certain diseases, but can also provide clues about why levels of certain miRNAs are related to higher risks of developing specific diseases.

REVERSING THE DAMAGE THROUGH DIET

Just identifying the pre-disease state isn't very helpful if nothing can be done to restore a person to a healthy state. So the second, and more difficult, challenge that Kewpie researchers are tackling is discovering how diet and other lifestyle factors could revert the pre-disease state to a healthy one.

Dietary factors have been estimated to explain about 30% of cancers in Westerners. But if a poor diet is a factor that can lead to disease, then that raises the intriguing possibility that a well-balanced diet that includes the intake of vegetables and fruits may drive the pre-disease state in the opposite direction — towards a healthy state.

It won't be easy to determine which specific diets could restore health from the pre-disease state, but it's an approach that could reap results. Kurataka Otsuka, corporate scientist at Kewpie, is already making connections. In a recent review paper, he examined evidence that naturally occurring compounds can make a positive impact on tumour-related miRNAs. This points to the possibility of using compounds derived from foods to modulate miRNA levels. For example, some evidence indicates that curcumin, a compound derived from the spice turmeric, may promote apoptosis or inhibit growth of cancer cells in various cancers by modulating certain miRNAs. Similar effects have been found for epigallocatechin-3-gallate (EGCG) and resveratrol. This may be just the beginning — many food compounds may have yet unknown functions, and monitoring miRNA levels could help uncover them.

"Research on prevention takes time and is extremely difficult, and it's not an issue that can be tackled by a single laboratory or a single company," Otsuka says.

While Kewpie researchers are aware that many other factors, such as regular exercise and reducing stress levels, are likely to contribute to steering the pre-disease state back to a healthy state, they will initially focus on diet using indicators including miRNAs. "It's important to create an index that will allow us to understand the state of pre-disease," says Kono. "This will help us compare the effects of food components on miRNA expression and its impact on health. The relationship between food, miRNAs and health status is very interesting."

By proposing diets based on the miRNA results, Kewpie hopes to develop a healthcare service that can prevent cancer and other diseases by improving eating habits. The focus will be on a well-balanced diet, rather than individual components or supplements. With cancer the second leading cause of death in the world, the potential benefits are vast. ■

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