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# In Cancer, One Cure Does Not Fit All



One characteristic of cancer is its pathological diversity, which is why more than one treatment strategy exists. Rather than deciding on a treatment path based on the name of the disease alone, it is necessary to develop a plan individually tailored to the patient's condition. According to Katsuaki Uno M.D., Ph.D. of TOKYO MIT CLINIC, "The true start of cancer treatment is when cancer progresses to a highly advanced stage."

Dr. Katsuaki Uno began his career as a specialist in digestive-system surgery and emergency medical care. In 2012, he opened TOKYO MIT CLINIC in Yaesu, Tokyo, offering neoantigen combined immunotherapy based on a new technology only to patients with highly advanced cancer.



Why this particular treatment? Dr. Uno says that, surprisingly, once cancer progresses beyond a certain point, there are unexpectedly few treatment options available under the Japanese public health care system. The health care system defines patients diagnosed with cancer as being provided with surgical operations, chemotherapy or radiotherapy under the defined

standards of care. New medical procedures are also introduced. Of course, there are no problems if follow-up confirms the cancer has been completely cured.

Approximately 40% of cancer patients eventually face relapse or metastasis, leading to the terminal stage. If there is the possibility of a permanent cure, the case will be classified as needing acute medical care including treatment. If it is inoperable, however, or a patient begins to weaken because the cancer recurs or metastasizes, the patient will be given terminal palliative care. If the patient's condition is between these categories, the patient is often in an unclear medical situation. This is because the treatment of patients in a condition far from the terminal stage of their disease has not been clearly defined, and in many cases patients' satisfaction with their current treatment is low. In these instances, medical practitioners tend to lump such patients into the same category as terminal-stage patients and can give up on them very quickly.

### **Creating an alternative**

Dr. Uno questioned this situation. He was engaged in medical care in tumor immunology/aging control medicine while working as a surgeon at a university hospital. In particular, he spent many years researching the special molecular structure of the major histocompatibility complex (MHC).

One day, a professor who was an authority on transplantation studies, said to him: "Organ transplantation requires that the recipient and donor have compatible MHC, because the donor needs an organ similar to their own cells. However, immunotherapy requires the opposite in cancer treatment. It has to eliminate cancer cells by using MHC that is different from normal cells as a marker." The professor continued, "Do you know a technique for luring MHC to the surface of cancer cells? If not, I will supervise you." So in a twist of good fortune, Dr. Uno learned this technique.

MHC is a complex of peptide molecules that appears on the surface of cells, a chain of amino acids. It is used as an identification marker showing the internal state of cells. Specifically, the expression of the MHC-Class I complex on the surface of cancer cells is necessary to identify the cancer for immunotherapy. Dr. Uno introduced this technique into cancer immunotherapy to sequentially reflect the cancer identification information provided by MHC in the immune response system.

Building on the technique he learned, Dr. Uno incorporated new research findings, transforming neoantigen immunotherapy into a unique immunotherapy approach, which he is now leveraging to benefit patients with advanced-stage cancer.

### **The limits of testing**

According to the rules of Japan's social insurance system, blood testing is generally limited to several types of tumor markers (cancer antigens) and genetic testing for cancer risk.

A characteristic of cancer, however, is its diverse pathological conditions. The approved tests were ineffective in investigating the cancer

pathology, cancer activity arising from each patient's DNA mutations or their immune response to cancer. Consequently, Dr. Uno began to develop Risk Checker, a new blood-testing system for better understanding the pathological conditions of cancer.



Risk Checker assesses the overall pathological condition of a patient's cancer by examining 21 items related to cancer-associated antigens and seven items of cancer-related immune tests. The testing system investigates the aging-related changes and immune exhaustion of cells, which serve as indicators of the "neo-aging" cycle in human cells, by assessing the presence or absence of a cytokine storm that suggests a runaway reaction of immune-physiologically active substances. This concept was separately introduced by Dr. Uno's research group. This added a concurrent therapy option: neoantigen combined immunotherapy.

Eight years have passed since U.S. President Barack Obama launched the Precision Medicine Initiative, an approach taking into account individual differences in genes, environment and lifestyle. In Japan, meanwhile, there are still only a few medical doctors providing cancer patients with such treatments. "As an oncologist," says Dr. Uno, "it has real meaning for me when my patients are happy. I believe my mission is creating an environment that allows us to satisfy patients' unmet needs."

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