CyTIX, Inc.
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# Fusion cancer vaccine targets combination therapy trials

**With its innovative fusion cancer vaccine that greatly enhances the target specificity of T cells, Tokyo-based CyTIX is poised to take advantage of the biopharma industry's increasing interest in next-generation cancer vaccines.**

Cancer immunotherapy is designed to harness or boost the body's own immune system to fight cancer. For example, the human immune system contains built-in brakes (or 'checkpoints') designed to shut down some immune responses so as to prevent the body from attacking itself. Many cancers, however, corrupt these checkpoints to avoid immune detection. Recently, researchers have shown that interfering with these brakes via checkpoint inhibitors increases the activity of the immune system.

Although checkpoint inhibitors can stop cancer from hijacking the immune system, it is the cytotoxic T lymphocytes (CTLs), a subset of T cells, that actually destroy the cancer. So another immune-stimulant approach is to prime a patient's CTLs to specifically target and attack a tumor by 'educating' them about specific tumor antigens, the abnormal proteins on the surface of tumor cells that identify them as malignant; over the past two decades there have been big efforts to define these cancer antigens.

However, this antigen-specific approach does not account for the fact that cancer cells can skillfully evade the immune system by mutating and by hiding target antigens inside of themselves, said CyTIX CEO Koichi Okubo. As CTLs are able to 'see' antigens only on the surface of cancer cells, they miss those antigens that are altered or hidden inside the cells, potentially leaving cancer unchecked. For CTLs to destroy cancer, they must also target these other, more challenging antigens, which are not yet defined—so-called neoantigens. "For successful immune cell therapy, CTLs must recognize *all* of the cancer antigens, including neoantigens," said Okubo.

## Dendritic cell–tumor cell fusion vaccine

Enter CyTIX, a biotech company boasting a main researcher, Tsuneya Ohno, who has been working in the immuno-oncology area for over 40 years. CyTIX has created a vaccine in which dendritic cells (also known as antigen-presenting cells) are able to 'show' *all* of the cancer antigens—including neoantigens—to the immune system, activating CTLs to target all of them. "Our fusion vaccine induces as many different kinds of CTLs as is possible," explained Okubo.

To achieve this, cancer cells and dendritic cells from a patient's blood are fused together using a relatively simple technique of culturing in polyethylene glycol (**Fig. 1**). This causes the cancer cells and dendritic cells to merge and produce a fused dendritic–tumor cell containing *all* the cancer antigens, including neoantigens.

When injected back into the patient, the fused dendritic–tumor cells present the antigens to the immune system, resulting in the creation of CTLs that target them all, including neoantigens. "Past cancer vaccine strategies have failed due to a poor understanding of the role of dendritic cells in immunization," said Okubo. "By creating dendritic cells capable of presenting neoantigens to the immune system, our innovative fusion cancer vaccine technology is a simple but effective way to greatly enhance CTL specificity."

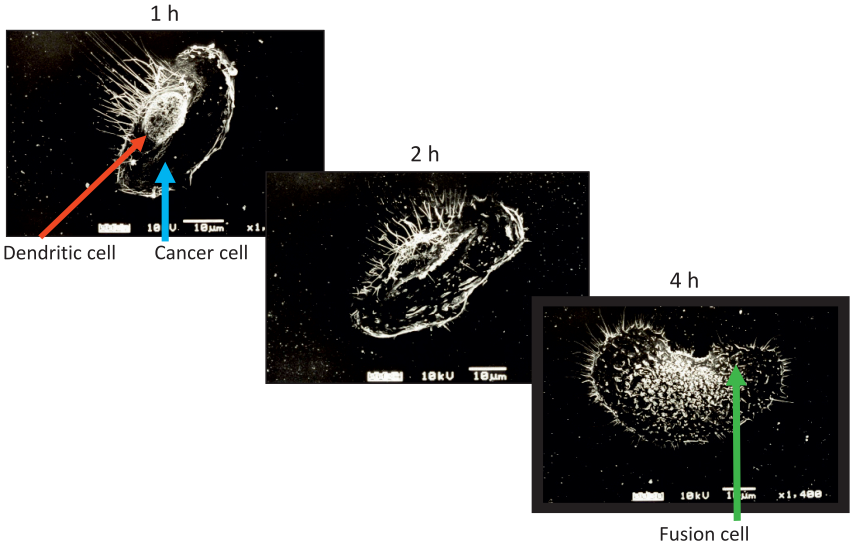


**Figure 1: Generation of dendritic cell–tumor fusion hybrid.** Polyethylene glycol (PEG), a polymer of ethylene oxide, was used for cell fusion.

To further boost the effectiveness of its personalized vaccine, CyTIX concurrently injects patients with interleukin-12 (IL-12), a glycoprotein naturally produced by dendritic cells. "IL-12 is involved in promoting the development and differentiation of T cells. Adding it to our vaccine enhances stimulation of CTLs and is a vital component in optimizing our dendritic cell–tumor fusion-based immunotherapy," explained Okubo.

Clinical results to date are promising. In a phase 1 study of 15 glioma patients for whom standard treatment had failed, 46% showed some kind of response (4 partial remissions and 3 patients showing no change) to the fusion vaccine combined with IL-12—data CyTIX has used in its application for orphan drug designation to the US Food and Drug Administration and European Medicines Agency. "We feel very strongly that the platform can be applied to any kind of solid tumor and some blood cancers," said Okubo.

The technology has also been used to privately treat some 400 patients in Japan—where the government allows treatment with an experimental vaccine— in phase 1 studies, which have demonstrated a satisfactory safety profile. The vaccine prolongs life in many cases, according to Okubo, who said he is grateful to the Japanese Ministry of Health, Labor and Welfare and Ministry of Economy, Trade and Industry for revisions in the regenerative-medicine law allowing the use of CyTIX's technology.

## Partnering for combinations and licensing

The innovative platform combining fusion vaccine technology and IL-12 is well suited to combination therapy, most likely in conjunction with checkpoint inhibitors, chemotherapies or radiation treatments. It is available for licensing from CyTIX, which is also interested in finding collaborative partners to co-develop its programs, as well as research funding to expand clinical studies.

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