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Juntendo University Corporate Communications

Juntendo University research: Potential immunotherapy approach to cervical cancer

(Tokyo, 27 October) Researchers at Juntendo University report in the journal *Molecular Therapy* that specially prepared 'T cells' can be used to suppress cervical cancer. The approach is based on immunotherapy, with the prepared T cells being toxic to tumors caused by the human papilloma virus.

Human papilloma virus (HPV) is known to cause different kinds of cancer, including cervical cancer. Current treatments either imply a risk of premature delivery (in the case of cancer tissue removal) or fertility loss (in the case of womb removal), or have a very poor prognosis (chemotherapy). New approaches to finding a cure for cervical cancer are much needed. Miki Ando from Juntendo University and colleagues have now made an important step forward: they show that introducing specially prepared cells into the cervical cancerous system results in a tumor-suppressive effect.

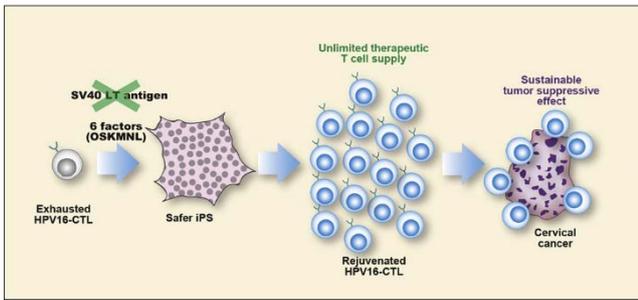
The approach of Ando and colleagues is based on adoptive T cell therapy, in which particular types of cells (called cytotoxic T cells) are introduced to a cancer patient. The T cells can then recognize and kill tumor cells. For cervical cancer, the scientists identified two proteins, known as E6 and E7, as targets for adoptive T cell therapy — these oncoproteins are only expressed by cervical cancer cells, and not found in healthy tissue.

Adoptive T cell therapy is not feasible as such for treating cervical cancer, though. T cells often get exhausted during continuous exposure to their targets, and solid cancers often show reduced susceptibility to T-cell-triggered destruction. The researchers therefore included induced pluripotent stem cell (iPSC) technology in their approach: rather than using 'normal' T cells, they worked with virus-specific cytotoxic T cells that were generated from iPSCs, in turn derived from T cells. Such iPSC-derived T cells are 'rejuvenated': they retain their destructive function much longer, in some cases up to 6 months.

The scientists investigated whether virus-specific rejuvenated T cells (HPV-rejT cells) targeting the E6 and E7 oncoproteins can be used for treating cervical cancer. Promisingly, they found that such specially prepared cells exhibit robust and sustained tumor-destructive power.

Importantly, experiments were made with mice, showing that the rejuvenated T cells robustly suppressed cervical cancer and enhanced chances of survival *in vivo*. Also, the researchers checked and confirmed that no chromosomal abnormalities arose in the process — such side effects need to be ruled out as they could actually lead to tumorigenesis.

In summary, in the words of Ando and colleagues: "HPV-rejT therapy against refractory cervical cancer utilizing iPSC technology offers us access to stable and abundant cell resources that permit establishment of "off-the-shelf" T cell therapy."



(Molecular Therapy,2020)

Using rejuvenated T Cells derived from iPSCs leads to a sustained tumor-suppressive effect in cervical cancer.

Background

Induced pluripotent stem cells (iPSCs) and regenerative medicine

Stem cells are cells that have the ability to differentiate — that is, become cells of a specialized type. An important attribute of a stem cell is its potency, indicating into what types of cells the stem cell can differentiate. So-called pluripotent stem cells (PSCs) can develop into organisms, because they can differentiate into cells of any of the three different germ layers characteristic of organisms.

An induced pluripotent stem cell (iPSC) is a PSC artificially generated from a non-PSC. The procedure for creating iPSCs was discovered in 2006 by Shinya Yamanaka (for which he received the 2012 Nobel Prize in Physiology or Medicine). Nowadays, iPSC generation is a promising technique in the field of regenerative medicine: damaged or badly functioning human cells can be replaced by cells regenerated using the iPSC technique. Miko Ando from Juntendo University and colleagues have now used iPSCs, derived from T cells that are virus-specific for the human papilloma virus, to show that a treatment for cervical cancer based on such cells might be possible.

Cervical cancer

Cervical cancer arises due to the abnormal growth of cells in the cervix, with these cells capable of invading or spreading to other parts of the body. More than 90% of cervical cancer cases are caused by infection with the human papilloma virus (HPV). Common treatments include surgery, chemotherapy, and radiation therapy. Prognosis associated with these treatments, or combinations thereof, are generally poor, however.

Ando and colleagues have now explored a possible immunotherapy for cervical cancer, by developing specially prepared cells, toxic to cancer cells, derived from iPSCs. Their results show that such cells display promising sustainable tumor-suppressive capabilities in vivo.

Reference

Tadahiro Honda, Miki Ando, Jun Ando, Midori Ishii, Yumi Sakiyama, Kazuo Ohara, Tokuko Toyota, Manami Ohtaka, Ayako Masuda, Yasuhisa Terao, Mahito Nakanishi, Hiromitsu Nakauchi & Norio Komatsu. Sustainable Tumor-Suppressive Effect of iPSC-Derived Rejuvenated T Cells Targeting Cervical Cancers. *Molecular Therapy* **28**, No 11 November, 2020

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Further information about Juntendo University

Mission Statement

The mission of Juntendo University is to strive for advances in society through education, research, and healthcare, guided by the motto “Jin – I exist as you exist” and the principle of “Fudan Zenshin - Continuously Moving Forward”. The spirit of “Jin”, which is the ideal of all those who gather at Juntendo University, entails being kind and considerate of others. The principle of “Fudan Zenshin” conveys the belief of the founders that education and research activities will only flourish in an environment of free competition. Our academic environment enables us to educate outstanding students to become healthcare professionals patients can believe in, scientists capable of innovative discoveries and inventions, and global citizens ready to serve society.

History of Juntendo University

Juntendo was originally founded in 1838 as a Dutch School of Medicine at a time when Western medical education was not yet embedded as a normal part of Japanese society. With the creation of Juntendo, the founders hoped to create a place where people could come together with the shared goal of helping society through the powers of medical education and practices. Their aspirations led to the establishment of Juntendo Hospital, the first private hospital in Japan. Through the years the institution's experience and perspective as an institution of higher education and a place of clinical practice has enabled Juntendo University to play an integral role in the shaping of Japanese medical education and practices. Along the way the focus of the institution has also expanded, now consisting of six undergraduate programs and three graduate programs, the university specializes in the fields of health science, health and sports science, nursing health care and sciences, and international liberal arts, as well as medicine. Today, Juntendo University continues to pursue innovative approaches to international level education and research with the goal of applying the results to society.