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Okayama University research: Attacking tumors from the inside

(Okayama, 26 January) **A specially-created group of immune cells that can infiltrate cancer cells can successfully deliver viral vectors into tumors and destroy them from the inside.**

The targeted delivery of drugs directly into cancer cells is becoming an increasingly common method of ensuring more accurate, safer cancer treatments. Scientists are now exploring the concept of using specially-created groups of immune cells to carry biologics – drugs derived from natural sources such as viruses - to target and kill cancerous tumors.

'Cell-in-cell' phenomena, wherein one cell infiltrates and occupies another cell, naturally occur in the human body. For example, the process whereby foreign, harmful substances are consumed by phagocytes, or when tumor cells invade immune cells, killing them in order to flourish themselves.

Now, Toshiyoshi Fujiwara and co-workers at Okayama University and scientists across Japan have utilized cell-in-cell behavior to their advantage, developing a tumor-targeting system using a novel human T-cell line called HOZOT that naturally targets and infiltrates human cancer cells. Their results could inspire many applications in the fight against different cancers.

HOZOT cell lines are established by co-cultivating human umbilical cord blood cells with mouse stromal cells. Crucially, the HOZOT cells are toxic only to cancer cells, and do not target normal healthy tissues. The HOZOT cells infiltrate tumor cells whole, and attack them from the inside. Fujiwara's team hypothesized that these cells could be used as carriers for biologics. In this case, the researchers developed an adenovirus (OBP-401/F35) that would spread rapidly inside the tumor, killing it from the inside.

The virus-loaded HOZOT cells behaved in the same way as virus-free HOZOT lines, and so the team proceeded with trials against various human cancer cells, including colon cancer. The HOZOT carriers significantly reduced the viability of human cancer cells and suppressed the formation of tumor spheres. Additional trials on tumor-bearing mice showed increased survival rates in those treated by the HOZOT method. Also, the HOZOT carriers appear to prevent attack on the carried virus by the host's immune system, which would recognize the virus if it was sent into the body without HOZOT cell protection.

As Fujiwara's team state in their paper in *Scientific Reports* (2016); "The unique cell-in-cell property of virus-loaded HOZOT cells provides a platform for selective delivery of biologics into human cancer cells, an outcome that has important implications for the treatment of human cancers."

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Background

Cell-based cancer treatments

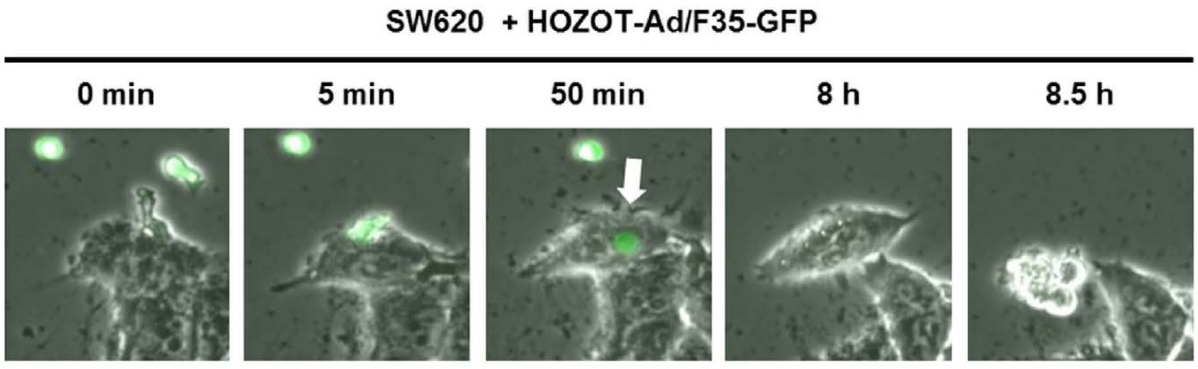
The idea of enhancing the body's own immune system defences against cancers is providing scientists with the inspiration to investigate novel, targeted drug delivery methods using immune cells. The discovery that the novel HOZOT T-cell line, derived from human umbilical cord blood, is capable of specifically targeting cancer cells by infiltrating and ending up fully inside them, motivated Fujiwara's team to trial the HOZOT line as a biologic drug carrier.

Various strategies have been trialled for using cells to transfer drugs into cancerous tumors. Stem cell technologies provide one such method, but the stem cells lack the unique 'cell-in-cell' activity of the novel HOZOT cells described here. Instead, stem cell-based techniques deliver drugs to the surrounding stromal tissue in tumors, rather than right inside the cancer cells, rendering the treatment less effective.

Because many cancer treatments have already been developed using adenoviruses – viral-based drugs that attack and kill harmful tissues – many cancer patients have built up a degree of immunity to viral vectors. This is another reason why using HOZOT cells as carriers has proven successful, because the virus is protected by the cell inside the body, and the host's immune response of releasing neutralising antibodies to target the virus is not triggered.

Future work

Fujiwara's team believe their strategy may prove useful in combination with immunotherapy in cancer patients. The researchers will continue exploring the potential for immune cells to aid in drug delivery for the treatment of human cancers.



Caption

Researchers at Okayama University have demonstrated a novel method using HOZOT cells (immune cells derived from human umbilical cord blood, in green here) to carry biologics to cancerous tumors. The HOZOT cells infiltrate cancer cells whole before releasing their drug-load directly into the center of the cancer cell, killing it from the inside.

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Reference

Teppei Onishi, Hiroshi Tazawa, Yuuri Hashimoto, Makoto Takeuchi, Takeshi Otani, Shuji Nakamura, Fuminori Sakurai, Hiroyuki Mizuguchi, Hiroyuki Kishimoto, Yuzo Umeda, Yasuhiro Shirakawa, Yasuo Urata, Shunsuke Kagawa, and Toshiyoshi Fujiwara. Tumor-specific delivery of biologics by a novel T-cell line HOZOT. *Scientific Reports*, 6:38060, 2016.
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Reference (OU-MRU) : Professor Fujiwara's team

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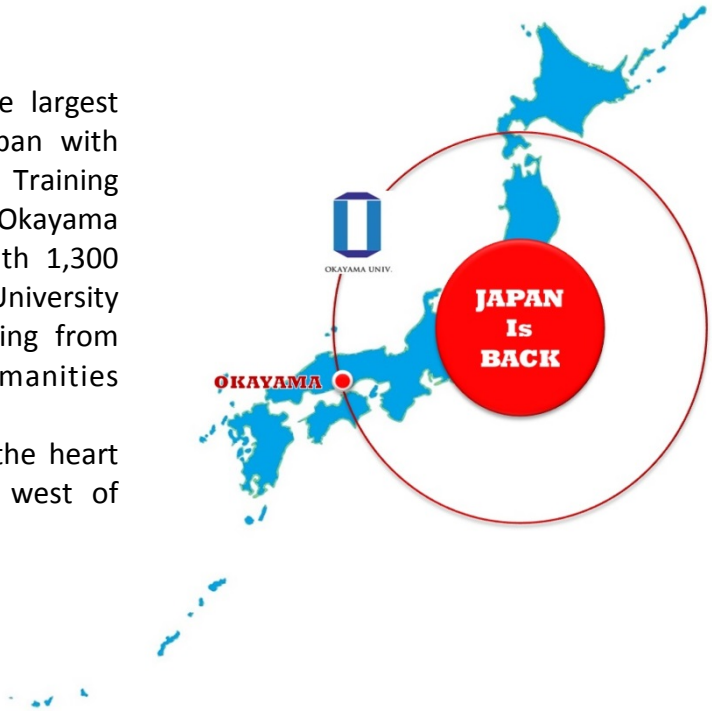
About Okayama University

Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 14,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.
Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.



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