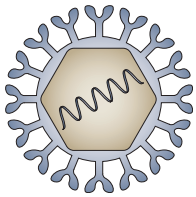
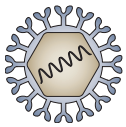
PROSTATE CANCER

Tumor cells driven to suicide by inactivated virus



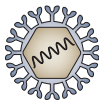
A modified form of the Sendai paramyxovirus can selectively destroy hormone-resistant prostate cancer cells and completely eradicate tumors, according to new research from Yasafumi Kanaeda and his team at Osaka University in Japan. This discovery highlights the inactivated viral particles as a promising novel therapy for hormone-refractory prostate cancer, which is notoriously hard to treat. Affected patients suffer multiple metastases, respond poorly to conventional therapy, and often die from the disease.



Kanaeda and colleagues have previously demonstrated that inactivated Sendai virus (also known as hemagglutinating virus of Japan envelope, or HVJ-E) stimulates anti-tumor immunity in renal and colon cancer by activating natural killer cells and generating cytotoxic T lymphocytes. The investigators have now turned their attention to prostate cancer. HVJ-E has clear potential as an immunotherapeutic drug that could prove beneficial in treating the metastatic aspect of hormone-resistant prostate cancer. The researchers propose that local injection of HVJ-E to residual tumors and lymph nodes could activate a systemic immune response to eliminate metastases.

Kanaeda and colleagues' latest experiments, published in the *International Journal of Cancer*, reveal that HVJ-E can trigger suicide directly in prostate cancer cells. Furthermore, cell death is confined to androgen-resistant cells, with no consequence on hormone-sensitive or normal prostate epithelium. The direct injection of HVJ-E completely destroyed hormone-resistant tumors in 85% of mice ($n = 13$).

The viral particles exert their effect by specifically binding and fusing to hormone-resistant cells, stimulating type 1 interferon production and triggering apoptosis. Further analysis revealed that the capability of HVJ-E to specifically target hormone-resistant cells is due to the exclusive and abundant expression of its membrane receptors, which are barely detectable in the other cell lines. The authors propose that upregulation of HVJ-E receptor expression occurs when prostate cancer progresses into the hormone-refractory phase, and hypothesize that when injected into prostate tissue, the inactivated viral particles would selectively kill cancer cells with limited damage to normal epithelium.



It seems then, that inactivated Sendai virus particles perform a two-pronged attack on hormone-resistant prostate cancer, inducing both cell suicide and anti-tumor immunity. Kanaeda and his team are now starting clinical trials, hoping that the combination of these modalities will result in a potent drug for the treatment of hormone-refractory prostate cancer.

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Original article Kawaguchi, Y. *et al.* Efficient eradication of hormone-resistant human prostate cancers by inactivated Sendai virus particle. *Int. J. Cancer* **124**, 2478–2487 (2009).