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PROSTATE CANCER

cDNA vaccination using a viral vector can cure prostate tumors

Intravenous injection of a virus-borne, human-derived cDNA library can induce regression of established prostate tumors in mice, according to a study published in *Nature Medicine*.

Immunotherapy for cancers has great potential. Realizing this potential has been hampered by the need to identify specific tumor-associated antigens, and to directly target the tumor. Now, a team comprised of researchers from the USA and the UK has overcome these hurdles.

Using normal human prostate tissue, Richard Vile and colleagues created an 'altered self-antigen and epitope cDNA library' (ASEL), which they cloned into the highly immunogenic vesicular stomatitis virus (VSV).

Three intravenous injections of ASEL–VSV prolonged the life of mice harboring TC2 tumors, an effect not induced by intratumoral administration. The therapeutic impact of ASEL–VSV increased with the dose—nine intravenous injections cured over 80% of tumors. Importantly, intravenous administration induced none of the adverse autoimmune effects associated with intraprostatic injection.

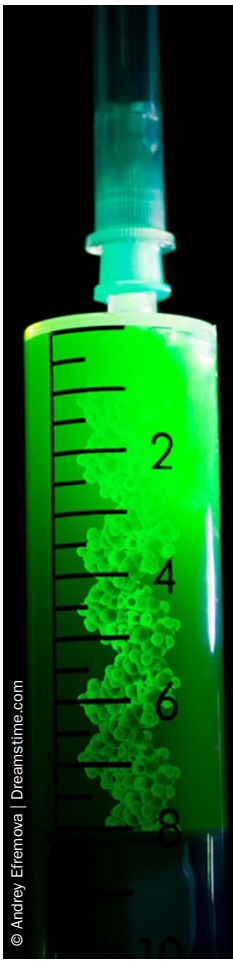
Despite the survival benefit, the three-injection regimen was inevitably associated with recurrence of more-aggressive and histologically distinct tumors. This clinically important 'escape' phenomenon was successfully countered by vaccination with a virally expressed 'immune-escape epitope library' (IEEL) derived from recurrence tumors. Preloading of IEEL–VSV onto $CD8^+$ T cells prevented neutralization by anti-VSV antibodies. IEEL–VSV-treated mice developed recurrence far more slowly, and in some cases, not at all.

"Our manuscript shows that it may be possible to educate the immune system of patients to react against their own prostate cancers," comments Vile. "This was done in mice by displaying a wide variety of proteins associated with cancer cells by expressing them from a very immunogenic virus, VSV. By linking these diverse cancer-associated antigens with the immunogenic virus, the immune systems of prostate cancer-bearing mice reacted as though the cancer proteins were pathogenic and, therefore, dangerous."

Immunotherapy that targets unidentified tumor-associated antigens without needing to be personalized to a specific patient's tumor could provide an 'off the shelf' treatment for prostate cancer. By targeting a wide range of antigens, virus-borne cDNA libraries might limit the emergence of treatment-resistant disease. Clinical trials remain some years away, but are keenly awaited.

Annette Fenner

Original article Kottke, T. *et al.* Broad antigenic coverage induced by vaccination with virus-based cDNA libraries cures established tumors. *Nat. Med.* **17**, 854–859 (2011)



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