

Sievert and colleagues hypothesize that early SNM may preserve nerve plasticity, such that C fibers remain silent, detrusor overactivity is avoided, and sympathetic preganglionic neuron activation in the thoracolumbar cord is suppressed. Further studies, however, are required to elucidate the exact mechanism of action. In addition, it would be of great interest to investigate whether noninvasive neuromodulation provides similar results as the invasive and quite costly SNM.

Nevertheless, if the benefits of early SNM in patients with complete SCI are reproduced in randomized trials and if these findings are conveyed to patients with other neurologic diseases or injuries, the management of neurogenic LUTD will be completely revolutionized. We are breaking new ground in neuro-urology. What a promising future!

Conflicts of interest: The author has acted as a consultant for Medtronic and Allergan.

Re: MicroRNA Regulation of Oncolytic Herpes Simplex Virus-1 for Selective Killing of Prostate Cancer Cells

Lee CYF, Rennie PS, Jia WWG

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Experts' summary:

The authors developed a novel strategy for the treatment of prostate cancer combining three aspects: the oncolytic destruction of cells infected with a herpesvirus, the regulatory role of microRNAs (miRNAs) in protein synthesis, and the downregulation of certain miRNAs in cancer cells. miRNAs are endogenous RNAs of about 22 nucleotides that decisively control the translation from messenger RNA to protein. To date, some 700 human miRNAs have been identified and about 1000 are predicted.

By genetic manipulation, the authors created a special type of virus, the replication of which was inhibited by miRNAs found to be downregulated in prostate cancer. Injections of the modified viruses into subcutaneous tumors with human prostate cancer cells in mice reduced the tumor volume dramatically without substantial toxicity to other normal tissues. Since prostate cancer cells do not contain these inhibitory miRNAs, viral replication could occur without restraint, inducing strong oncolytic effects. In contrast, animals treated with unmodified viruses died of herpetic viral complications. The authors concluded that this principle of miRNA-based regulation of viral replication could be a useful tool to target cancer cells selectively and prevent normal tissues from viral damage.

Experts' comments:

This study shows for the first time how data from the exciting miRNA research could be applied to develop novel treatments for prostate cancer. miRNAs are key molecules with either oncogenic or tumor suppressive activities in the regulation of all hallmarks of cancer [1]. The identification of their regulatory role may not only help better understanding of prostate cancer carcinogenesis but also, in addition to their use as diagnostic

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and prognostic biomarkers, may lead to novel therapeutic strategies [2].

Current miRNA-based strategies in cancer treatment focus mainly on approaches to inhibit oncogenic miRNAs, to replace tumor-suppressive miRNAs, or to modulate the expression of regulatory miRNAs. In contrast to these direct interactions with miRNA regulatory networks, the present study is based on an intelligent combination of different biologic aspects with the regulatory role of miRNAs as a key element. Furthermore, this therapy concept offers the opportunity to optimize the oncolytic effect regarding the selectivity and efficiency against cancer cells by using further specifications of viral replication [3].

The principle of intratumoral/intraprostatic injection of the miRNA-regulated virus as used in the present study can be assumed to be a feasible approach to focal therapy of image-guided ablation of prostate cancer [4].

In conclusion, this study presents a promising novel treatment strategy for prostate cancer and generally exemplifies the manifold potential of miRNAs for clinical practice in future.

Conflicts of interest: The authors have nothing to disclose.

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