

NEW ADENOVIRUS
INDUCES RESPONSE

The antitumor efficacy of oncolytic viruses can be influenced by the immune system. Adenoviruses are among the most advanced cancer gene therapy approaches; however, despite evidence of activity of these agents in clinical trials, single-agent efficacy has been disappointing. Researchers from Helsinki generated an oncolytic adenovirus that coded for granulocyte macrophage colony-stimulating factor (GM-CSF), which is a potent activator of innate and adaptive immunity, to generate Ad5-D24-GM-CSF. This oncolytic virus was tested in 20 patients with advanced and refractory solid tumors. "This is the first time that an oncolytic adenovirus has been shown to be capable of inducing antitumor immunity in humans" explains Akseli Hemminki, senior investigator of the study.

Most patients had mild flu-like symptoms, injection-site pain and fatigue but overall the treatment was well tolerated. Of the 16 radiologically evaluable patients, two had complete responses, one had a minor response, and five had disease stabilization. The investigators were interested to characterize the adenovirus response and tumor-specific T-cell responses. They showed that both tumor-specific and virus-specific responses were induced by Ad5-D24-GM-CSF, as assessed by ELISPOT and pentamer assays. A striking T-cell response was induced by the adenovirus and since it replicates in a tumor-specific manner, this finding indicates that the tumor microenvironment may mount an immune-response against the tumor epitopes.

"We believe that Ad5-D24-GM-CSF is highly useful for inducing antitumor immunity in cancer patients. Most importantly, it will be key to confirm these findings in a larger amount of patients, optimally in a randomized setting" concludes Hemminki.

Lisa Hutchinson

Original article Cerullo, V. *et al.* Oncolytic adenovirus coding for granulocyte macrophage colony-stimulating factor induces antitumoral immunity in cancer patients. *Cancer Res.* **70**, 4297–4309 (2010)