Nanoparticle-delivered RNA interference drug stops head and neck cancer growth

April 6 2012

(Phys.org) -- A nanoparticle drug delivery vehicle for small interfering RNA molecules (siRNA), that is already being tested in human clinical trials, now shows promise for the treatment of head and neck cancer. Dong Shin, of Emory University, and Mark E. Davis, of the Nanosystems Biology Cancer Center at the California Institute of Technology, led this study. The results were published in the *Journal of Controlled Release*.

Drugs based on siRNA technology are designed to turn off the production of specific proteins that are critically involved in a disease such as cancer. While a significant body of evidence has shown this approach to targeting critical disease pathways can be highly effective, siRNA molecules themselves do not survive in the blood stream. Dr. Davis and his colleagues have long been leaders in the effort to use tumor-targeted nanoparticles to protect siRNAs from degradation and deliver them to where they are needed in the body.

In this study Dr. Davis's group, which had previously developed a nanoparticle that encapsulates a siRNA agent aimed at a protein known as RRM2, has teamed up with Dr. Shin's group to evaluate the effectiveness of these particles in head and neck cancer. RRM2, when over expressed in these tumor types, plays an active role in tumor progression and in the development of drug resistance. Initial tests on head and neck tumor cells growing in culture showed that this construct was taken up by the tumor cells, and as a result growth of the cells was inhibited substantially. The investigators obtained similar results when

they tested the drug on cultured non-small cell lung cancer cells.

Based on these findings, the researchers tested the siRNA-loaded nanoparticle in a mouse model of human head and neck cancer. One intravenous injection of the drug shut down production of RRM2 for at least 10 days, with the nanoparticle being present in the tumor for three days. Four injections given over 10 days triggered a substantial amount of tumor cell death and significantly reduced tumor progression. The researchers note that they did not observe any adverse effects or changes in body weight during the course of therapy. They also showed that the drug had no effect on RRM2 production in the liver.

This work, which is detailed in a paper titled, "Systemic delivery of siRNA nanoparticles targeting RRM2 suppresses head and neck tumor growth," was supported in part by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer.

More information: View abstract here.

Provided by National Cancer Institute