MedicalXpress

Study shows promise for new cancer-stopping therapy

June 11 2009

Researchers at Nationwide Children's Hospital and Johns Hopkins University have discovered that delivering a small molecule that is highly expressed in normal tissues but lost in diseased cells can result in tumor suppression.

MicroRNAs (miRNA) are a class of small RNA molecules that are highly expressed in normal tissues and are critical in gene expression and in maintaining normal cell development and cell balance. Dysfunction of miRNAs has been linked to multiple human diseases including schizophrenia, autism and cancer.

"The pattern of expression of miRNAs has emerged as critically useful information for understanding cancer development and could be used to establish prognosis and treatment responses," said Janaiah Kota, PhD, a postdoctoral scientist from Nationwide Children's.

In a study reported in *Cell*, the team of researchers employed a novel strategy to treat an important form of cancer. Studies targeted hepatocellular (liver) cancer (HCC), the third leading cause of cancer-related deaths. HCC is commonly associated with underlying liver abnormalities, such as hepatitis B and C infections and cirrhosis. HCC is difficult to treat since it is often diagnosed at an advanced stage and because its biologic composition makes the tumor highly resistant to current drug therapies. However, the research reported in *Cell* suggests that miRNA gene delivery may be a clinically viable therapy when delivered by a recombinant adeno-associated virus (AAV).

HCC expresses a reduced number of miRNAs, including miR-26a. By combining miRNA technology developed at Johns Hopkins University with the gene delivery expertise of Nationwide Children's Hospital, scientists were able to successfully deliver AAV carrying miR-26a to a mouse with established HCC. This gene therapy strategy inhibited growth of cancer cells and led to tumor reduction and cell death, without causing toxic side effects to the remainder of the liver. This demonstrates for the first time that therapeutic delivery of a miRNA in an animal can result in tumor suppression, without the need for specifically targeting the cancer causing oncogene.

"We are eagerly looking forward to applying this methodology to other tumor types in the laboratory and potentially bringing this approach forward for clinical testing in patients," said Jerry Mendell, MD, director, Center for Gene Therapy in The Research Institute at Nationwide Children's Hospital and a faculty member of The Ohio State University College of Medicine. "While there remains significant work to be done both in identifying such miRNAs and optimizing their delivery, our findings highlight the therapeutic promise of this approach."

The findings of therapeutic miRNA gene replacement in HCC has potential for applicability to other types of cancers, as well. The delivery and restoration of miRNA expression via AAV mediated gene transfer of the miRNA may be beneficial to a large number of cancer subtypes.

"This concept of replacing microRNAs that are expressed in high levels in normal tissues but lost in diseases hasn't been explored before," said Josh Mendell, M.D., Ph.D., an associate professor in the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine. "Our work raises the possibility of a more general therapeutic approach that is based on restoring microRNAs to diseased tissues."

Source: Nationwide Children's Hospital (news : web)