New studies refocus attention on the genotoxicity of AAV vectors in gene therapy

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A growing number of preclinical studies in mice suggests that therapeutic gene delivery using recombinant adeno-associated viral vectors (rAAVs) can cause insertional mutagenesis and increase the risk of hepatocellular carcinoma. Despite the apparent safety of rAAV-mediated gene therapy in human clinical applications, the data emerging from some mouse studies emphasize the need to carefully reconsider the potential risk of genotoxicity, according to the authors of a provocative article published in *Human Gene Therapy*.

Randy Chandler and Charles Venditti, National Human Genome Research Institute, National Institutes of Health (Bethesda, MD) and Mark Sands, Washington University School of Medicine (St. Louis, MO), present a comprehensive overview of the published studies assessing rAAV gene delivery and hepatocellular carcinoma formation. In the article in *Human Gene Therapy* entitled "Recombinant Adeno-Associated Viral Integration and Genotoxicity: Insights from Animal Models," the authors review the published data that suggest a potential increased risk for genotoxicity related to rAAV. They discuss the need for additional studies to characterize rAAV integration and other proposed directions for future research.

"AAV is clearly the most promising vector for *Human Gene Therapy* applications, yet concerns remain regarding whether or not using it incurs some risk of causing cancer," says Editor-in-Chief Terence R. Flotte, MD, Celia and Isaac Haidak Professor of Medical Education and Dean, Provost, and Executive Deputy Chancellor, University of Massachusetts Medical School, Worcester, MA. "There is strong data on both sides of this issue and further research on this issue is essential."

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