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Evaluation of the Reproductive Safety of Adenovirus Vectors in Mouse

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An important aspect of characterizing gene therapy vectors is their tissue biodistribution. This is particularly important if vector distributes to gonads, raising the possibility of inadvertent germ-line transmission. To evaluate the reproductive toxicity of in vivo adenovirus mediated gene transfer, we studied the biodistribution and potential germ-line transmission of p53 and LacZ-expressing adenoviral vectors(Ad-CMV-p53, Ad-CMV-LacZ). Both male and female Balb/c mice were injected Ad-CMV-Lp53 or Ad-CMV-LacZ by ip injection. The PCR analysis showed detection of the transgene and vector sequences from most tissues. Real-time PCR result confirmed a significant decrease of adenovirus in most tissues after day 15. Male and female mice injected directly into testis and ovary were mated and then their offspring were investigated. We have also developed for the cell specific localization of viral DNA in gonad tissues by using in-situ PCR. No positive signal were detected in embryos and germ cell related cells. These data provide strong evidence that the risk of the inadvertent germ-line transmission of vector sequences following direct injection into genito-urinary system of adenovirus is extremely low, although vector distributed gonadal tissues.

Keyword : Adenovirus, reproductive toxicity, Germ-line transmission