

CPB 69700 RESEARCH SEMINAR

DEPARTMENT OF COMPARATIVE PATHOBIOLOGY

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“Biodistribution, persistence, transgene expression and potential toxicity of adenoviral vectors in a breast cancer mouse model.”

Thurs., November 5, 2009
VPTH 112
3:30 pm

Abstract: To circumvent the pre-existing immunity against human adenovirus serotype 5 (HAd5), bovine adenovirus serotype 3 (BAd3) has been developed as an alternate gene delivery vector. The BAd3 vector persisted for a longer duration and efficiently transduced the heart, kidney, lung, liver and spleen following intravenous inoculation in mice. In order to explore the usefulness of the BAd3 vector for breast cancer gene therapy, an immunocompetant (FVB/n) mouse model of breast cancer was used to evaluate the biodistribution, persistence, transgene expression and potential toxicity of BAd3 and HAd5 vectors following intra-tumoral (i.t.) inoculation. Mice were sacrificed at various time points (0.25, 0.5, 1, 2, 4, 8 and 16 days) post-inoculation and the tumor tissue, liver, spleen, lung, heart and kidney were collected for various analyses. The vector biodistribution, persistence and transgene expression in tumors and other organs was determined by real-time quantitative PCR analysis, while protein expression was determined by immunohistochemistry. BAd3 vectors efficiently transduced tumors, spleen, liver, kidney, lung, and heart, and persisted comparable to HAd5 vectors. An altered biodistribution pattern of BAd3 vectors with higher persistence in the kidney and heart was evident. BAd3 and HAd5 vectors incorporating the green fluorescent protein (GFP) transgene efficiently expressed the GFP transcript within the tumor tissue and other organs. In addition, BAd vectors induced a transient rise of hepatic enzymes (AST and ALT) and mildly modulated the innate immune responses. Overall, the results support the further development and use of BAd vectors as an alternate to HAd5 vectors for breast cancer therapy.