S19-2 Development of recombinant adenovirus carrying microRNA-regulated gene expression system

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Target cell-specific delivery and transcription of foreign genes are desirable for safe and effective gene therapy. Two approaches for this purpose, “targeting delivery” and “transcriptional targeting”, have been reported, however another approach is necessary to fully achieve this purpose. Then, we utilized microRNA (miRNA)-regulated gene expression system for target cell-specific gene expression. Ad vectors originally have liver tropism, therefore, Ad vectors locally injected into organs are leaked from the injected points and accumulated in liver, leading to efficient transduction in liver. To reduce the hepatic expression, complementary sequences of liver–specific miRNA, miR-122a, were inserted into the 3’ untranslated region of transgene expression cassette. Intratumor injection of this Ad vector resulted in approximately 100-fold lower hepatic expression, without reducing gene expression in the tumor. miRNA-regulated transgene expression system mediates “post-transcriptional de-targeting”, in which translation of transgene is suppressed in an organ-specific manner, however, organ-specific transgene expression can be achieved by miRNA-regulated gene expression system, after taking tropism of gene delivery vehicles into consideration. We will also present data of oncolyitc Ad carrying miRNA-regulated gene expression system.