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Adenovirus Library for Novel Transductional Targeting

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Adenovirus (Ad) vector and oncolytic adenovirus has been engineered as therapeutics taking advantage of high in vivo transduction efficiency. However, targeting by selective infection (transductional targeting) and its incorporation to virus-coding sequence has been a nightmare in many vectors including Ad vectors. A lot of targeting peptide-coding sequences have been placed into capsid coding regions but extremely limited number of the targeting moiety successfully worked in Ad capsid, presumably due to structural limitation of the virus structure. Thus, it is natural to screen the peptide presented on adenovirus capsid format from the beginning. However, to date, the library size achievable in Ad system has been low. Conventional system makes few plaques from 1ug viral DNA. The most advanced system with Cre-loxP system yields 10^6 order diversity. Recently, we have developed a novel hyper-efficient Ad vector generation system by overcoming three major bottle necks for Ad vector production by performing the process in fiber complementing producer cell with newly designed shuttle plasmid and rescue virus. We applied this technology for Ad targeting ligand library generation and achieved 10^10 diversity. High throughput screening of the library identified novel targeting motifs which selectively bindto cell surface protein highly expressed in several major cancers including pancreatic cancer. The oncolytic virus with one of these targeting motifs showed selective and potent antitumor effect in vitro and in vivo in the receptor positive cells. In summary, we have developed a new way to identify the adenovirus transductional targeting ligand. Such vectors with preferential distribution and the system to generate them are expected to be beneficial for the development of systemically injectable cancer targeted vector system.

Biography

Dr. Yamamoto, Masato obtained his M.D & Ph.D from Osaka University School of Medicine, Osaka, Japan. He is board-certified gastroenterologist in Japan. He has been working for cancer gene therapy with adenovirus vectors. His lab has developed a series of replication competent adenovirus vectors and is considered to be one of the leading labs for replication competent adenovirus vectors. His group has been a leading lab for the application of oncolytic virus in the field of GI cancers including pancreatic and esophageal cancers. He has rich experience of experiments with clinical materials and evaluation of the oncolytic viruses. He was awarded *John R. Durant Award for Excellence in Cancer research 2001-Junior Faculty Category University of Alabama at Birmingham Comprehensive Cancer Center. The MCMRC Excellence Award at the 14th Intl. Conference on Gene Therapy of Cancer in 2005.*