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Intranasal and intraperitoneal adeno-associated virus based formulations for cancer gene therapy applications

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Introduction: Melanoma is a cutaneous cancer characterized by the highest mortality rates and a malignancy with the highest potential of dissemination. The prognosis of patients with metastatic melanoma is poor. Treatment proposed so far has not produced beneficial effects. Therefore, one of the current therapeutic approaches to melanoma is gene therapy with the use of recombinant adeno-associated viruses (rAAV) as gene vectors. The rAAV vectors are the principal candidates for virus-based gene therapy because of their small size, broad tissue tropism, safety profile and low immunogenicity. The purpose of this study involved a targeted delivery of rAAV 2/2 and 2/6 formulations to melanoma cells metastasized into murine lungs. Methodology: In our experiments, we used intranasal (in) and intraperitoneal rAAV (ip) formulations of serotype 2/2 and 2/6 encoding *Gfp* reporter under the control of cmv promoter. The experiments were performed in vivo on B16-F10 melanoma tumor-bearing C57BL/6 mice. The mice were injected with B16-F10 tumor cells *via* the tail vein. After 14 days the rAAV vectors were administered to the mice by *in* or *ip* injection, and 7 days later the mice were euthanized, and the infected tissues collected for further tests. The infection efficiency of melanoma cells metastasized into murine lungs was assessed with qPCR method. At the same time, we performed the analysis of the bio-distribution of rAAV vectors to different organs in mice. Conclusion: The study demonstrated the usefulness of rAAV formulations in introducing genes into metastatic melanoma cells. The highest infection efficiency was observed for serotype 2 after intraperitoneal injection. Gene therapy with the use of rAAV formulations may be a promising therapeutic strategy for melanoma and lung cancer in the future. This work was supported by a grant from NCBiR (Strategmed1/233264/4/NCBR/2014, MentorEYE).

Recent Publications

1.Santry LA, Ingrao JC, Yu DL, de Jong JG, van Lieshout LP, Wood GA, Wootton SK (2017) AAV vector distribution in the mouse respiratory tract following four different methods of administration. BMC Biotechnology 17:43-54.

2.Kurosaki F1, Uchibori R1, Mato N, Sehara Y, Saga Y1, Urabe M, Mizukami H, Sugiyama Y, Kume A (2017) Optimization of adeno-associated virus vector-mediated gene transfer to the respiratory tract. Gene Ther. 24: 290-297.

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Biography

Maciej Malecki, PhD, Prof, is working at the Department of Applied Pharmacy in the Medical University of Warsaw, Poland. He is the author of about 100 publications in the field of medical biology and pharmacy. He is interested in cancer gene therapy and rAAV vectorology.

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