

Thus, during this study the authors found that subcutaneous xenografts can be efficiently infected with the oncolytic virus with the intravenous doses of the virus starting at 10^5 pfu. Therefore, it can be concluded that in the mouse model the intravenous administration can deliver infectious viral particles to tumor sites to initiate the process of infection of susceptible tumor cells. The destruction of the tumor under the influence of the virus is accompanied by the release of the infectious virus into the blood, which ensures a permanent presence of viral particles at a level that is sufficient for the reinfection of the remaining tumor cells. Certainly, the persistence of the virus in the mouse depends on the presence of tumor-susceptible tumor cells, since even a high virus dose introduced to non-tumor-bearing mice does not ensure the virus presence in the blood 5 days after the injection, while it was found at high titers in the blood of the tumor bearing mice. Only after the tumors completely disappear, the virus can no longer be detected in the blood.

The authors found that xenografts of human glioma cells in athymic mice are an effective and sensitive system for studying viral delivery to tumor sites. This model could be found suitable for testing other modes of administration, such as the use of cell-based carriers infected with the virus *in vitro* and then introduced into the blood stream. Such mode of virus administration would reduce the initial load of the virus and might increase the penetration efficiency into the tumor.

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REFERENCES

- Hanahan, D., Weinberg, R.A. 2000. The hallmarks of cancer. *Cell*. **100**, 57-70.
- Zheltukhin, A.O., Chumakov, P.M. 2010. Constitutive and induced functions of the p53 gene. *Biochemistry (Mosc)*. **75**, 1692-1721.
- Chumakov, P.M. 2007. Versatile functions of p53 protein in multicellular organisms. *Biochemistry (Mosc)*. **72**, 1399-1421.
- Stojdl, D.F., Lichty, B., Knowles, S., Marius, R., Atkins, H., Sonenberg, N., Bell, J.C. 2000. Exploiting tumor-specific defects in the interferon pathway with a previously unknown oncolytic virus. *Nat Med*. **6**, 821-825.
- Bell J.C., Garson K.A., Lichty B.D., Stojdl D.F. 2002. Oncolytic viruses: programmable tumour hunters. *Curr Gene Ther*. **2**, 243-254.
- Russell S.J. 2002. RNA viruses as virotherapy agents. *Cancer Gene Ther*. **9**, 961-966.
- Bell J.C., Lichty B., Stojdl D. 2003. Getting oncolytic virus therapies off the ground. *Cancer cell*. **4**, 7-11.
- Bell J. 2005. Replicating oncolytic virus therapeutics - Third International Meeting. *IDrugs*. **8**, 360-363.
- Parato K.A., Senger D., Forsyth P.A., Bell J.C. 2005. Recent progress in the battle between oncolytic viruses and tumours. *Nat Rev Cancer*. **5**, 965-976.
- Pikor L.A., Bell J.C., Diallo J.-S. 2015. Oncolytic viruses: exploiting cancer's deal with the Devil. *Trends in Cancer*. **1**, 266-277.
- Parker B.S., Rautela J., Hertzog P.J. 2016. Antitumour actions of interferons: implications for cancer therapy. *Nat Rev Cancer*. **16**, 131-144.
- Aitken A., Roy D., Bourgeois-Daigneault M.-C. 2017. Taking a Stab at Cancer; Oncolytic Virus-Mediated Anti-Cancer Vaccination Strategies. *Biomedicines*. **5**, 3.
- Platanias L.C. 2005. Mechanisms of type-I- and type-II-interferon-mediated signalling. *Nat Rev Immunol*. **5**, 375-386.
- Naik S., Russell S.J. 2009. Engineering oncolytic viruses to exploit tumor specific defects in innate immune signaling pathways. *Expert Opin Biol Ther*. **9**, 1163-1176.
- Li Q., Tainsky M.A. 2011. Epigenetic silencing of IRF7 and/or IRF5 in lung cancer cells leads to increased sensitivity to oncolytic viruses. *PLoS One*. **6**, e28683.
- Heiber J.F., Barber G.N. 2012. Evaluation of innate immune signaling pathways in transformed cells. *Methods Mol Biol*. **797**, 217-238.
- Stark G.R., Darnell J.E., Jr. 2012. The JAK-STAT pathway at twenty. *Immunity*. **36**, 503-514.
- Ivashkiv L.B., Donlin L.T. 2014. Regulation of type I interferon responses. *Nat Rev Immunol*. **14**, 36-49.
- Zitvogel L., Galluzzi L., Kepp O., Smyth M.J., Kroemer G. 2015. Type I interferons in anticancer immunity. *Nat Rev Immunol*. **15**, 405-414.
- Suryawanshi Y.R., Zhang T., Essani K. 2017. Oncolytic viruses: emerging options for the treatment of breast cancer. *Med Oncol*. **34**, 43.
- Fukuhara H., Ino Y., Todo T. 2016. Oncolytic virus therapy: A new era of cancer treatment at dawn. *Cancer Sci*. **107**, 1373-1379.
- Shen W., Patnaik M.M., Ruiz A., Russell S.J., Peng K.W. 2016. Immunovirotherapy with vesicular stomatitis virus and PD-L1 blockade enhances therapeutic outcome in murine acute myeloid leukemia. *Blood*. **127**, 1449-1458.
- Papaioannou N.E., Beniata O.V., Vitsos P., Tsitsilonis O., Samara P. 2016. Harnessing the immune system to improve cancer therapy. *Annals of translational medicine*. **4**, 261.
- Miao D., Van Allen E.M. 2016. Genomic determinants of cancer immunotherapy. *Curr Opin Immunol*. **41**, 32-38.
- Keller B.A., Bell J.C. 2016. Oncolytic viruses-immunotherapeutics on the rise. *J Mol Med (Berl)*. **94**, 979-991.
- Liston A., Farr A.G., Chen Z., Benoist C., Mathis D., Manley N.R., Rudensky A.Y. 2007. Lack of Foxp3 function and expression in the thymic epithelium. *J Exp Med*. **204**, 475-480.
- Bastida E., Ordinas A., Escolar G., Jamieson G.A. 1984. Tissue factor in microvesicles shed from U87MG human glioblastoma cells induces coagulation, platelet aggregation, and thrombogenesis. *Blood*. **64**, 177-184.