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Oncolytic viral therapy: a review and promising future directions

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Abstract

Oncolytic viral therapy is quickly emerging as a promising subset of immunotherapy, which theoretically can target tumor cells while sparing surrounding healthy cells by harnessing the replication machinery of viruses with tropism for tumor cells, resulting in direct oncolysis, and by transforming immunologically "cold" tumor into areas that elicit the host's immune response. This review provides an overview of oncolytic viral therapy until the present day, starting with the original concept in 1912. The general mechanism of oncolytic viruses (OVs) depends on selectively integrating them into tumor cells based on genetic engineering of viral genomic material, inducing oncolysis and eliciting the host's innate immune response. Moreover, a major component of oncolytic viral therapy has been herpes simplex virus, with talimogene laherparepvec being the only FDA-approved oncolytic viral therapy for the treatment of melanomas. This review explores the characteristics, advantages, disadvantages, and therapeutic uses of several DNA and RNA viral families. A snapshot of the oncolytic viral treatments used in the most recent and advanced clinical trials is also provided. Lastly, the challenges of implementing oncolytic viral therapy are explored, both at a molecular and clinical level, with a highlight of promising future directions. In particular, the lack of an optimal delivery method based on tumor type for oncolytic viral therapy poses a significant obstacle, even in clinical studies. Intrathecal continuous delivery of OVs is a promising prospect, potentially by adapting the novel continuous irrigation and drainage IRRAflow catheter. Further exploration and testing of the IRRAflow catheter should be undertaken.

Keywords: HSV; glioblastoma; herpes simplex virus; intrathecal delivery; oncology; oncolytic viral therapy.