

Oncolytic Viruses: Can be Applicable Tools for Cancer Therapy?

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Despite the remarkable developments in medical science, cancer treatment still remains a serious challenge. Oncolytic viruses destroy the cancer cells directly or induce immunogenic cell death without harming normal healthy cells [1]. The concept of viral therapy has started several decades ago, when some tumor patients were recovered after naturally receiving viral infections. In 1949, serum containing hepatitis B virus could treat 22 patients with Hodgkin's lymphoma. Since the 1950, oncolytic viruses have been considered as new tools for treatment of cancers, and clinical trials were performed to evaluate the effect of wild type or naturally attenuated viruses on tumors. During two decades, researchers introduced a wide variety of viruses that killed naturally tumor cells. Wild-types of vaccinia virus, vesicular stomatitis virus, poliovirus, reovirus, seneca virus and semliki forest virus had oncolytic behavior. The using naturally oncolytic

viruses for the cancer therapy was abandoned from 1970 because of the lack the known methods to control viral virulence in subjects under viral therapy [2].

With development of genetic engineering and recombinant DNA technology in 1990, the viral therapy started again. Today, some viruses are engineered to gain the ideal anti-tumor activity. Novel mechanisms for modification in the viral genome have improved oncolytic activity or them selective replication. Directed evolution method is used to generate a combination of adenovirus serotype 11 and 3 that has higher potency and tumor selectivity compared to any of these types alone [3]. In attenuation approach, the deletion of a part of the viral genome generated a virus that replicated in tumor cells, but not in normal cells. In addition, transductional and non-transductional targeting strategies have used for generating

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tumor-selective viruses [4]. MiRNA-targeting technology is the newest method for controlling virus replication in normal and tumor cells. In this method, specific microRNA binding sequences are introduced into the viral genome to regulate the viral replication by levels of cellular miRNA [1, 5].

In the recent years, a number of oncolytic viruses introduced to the market. A recombinant human adenovirus type 5 was the first commercial oncolytic virus which was produced by Shanghai Sunway Biotech Co., Ltd and approved by the China food and drug administration in 2005 for treatment of nasopharynx cancer in combination with chemotherapy. Clinical trials showed that the response rate of the group under combination therapy was about 40% more than the response rate of the group under chemotherapy alone. In 2015, the food and drug administration (FDA) for the first time approved a live herpes simplex virus (HSV) armed with the granulocyte-macrophage colony-stimulating factor (GM-CSF) gene (T-VEC: Imlygic) for treatment of patients with melanoma. When Imlygic injected to 436 patients with metastatic melanoma, skin and lymph node lesions regressed in 16.3% of subjects. In 2015, the FDA granted an oncolytic reovirus (REOLYSIN) for treatment of glioma tumor. REOLYSIN is evaluating in several clinical trials in variety of tumors, including prostate, lung, colorectal, breast, bladder, head and neck, ovarian and pancreatic cancers. RIGVIR is a nongenetically engineered enteric cytopathic human orphan type 7 virus (echovirus) that was approved by the State Agency of Medicines of the Republic of Latvia in 2004 for melanoma therapy (2). This oncolytic virus could not obtain FDA approval, and some clinical trials in 2017 are not shown an adequate anticancer therapeutic effect for RIGVIR.

Finally, an overview of the progress of viral therapy researches in recent years suggests that oncolytic viruses can be applicable tools for cancer therapy. Of course, it should be noted that there is still a long way to reach this goal. Despite the recent advances in design and evaluation of oncolytic viruses, future studies are required to perform an ideal viral therapy. Cancer treatment using viruses is an interesting field in medicine. More research and

publishing of findings in scientific journals can help to other researchers to fix weaknesses of viral therapy.

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