Oncolytic Viruses for Cancer Immunotherapy

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Introduction

In preclinical and clinical research, oncolytic virotherapy has yielded promise but limited results. Induction of tumor-specific immunity is an important therapeutic mechanism of oncolytic virotherapy, in addition to direct oncolytic activity. As a result, the insertion of immune stimulator genes and sensible combinatorial therapy with other immunotherapies can boost the efficacy of oncolytic viruses. (1)

Methods

There are currently 57 different adenovirus serotypes that have been identified and categorized into seven subgroups: A through G. While adenoviruses are known for causing frequent flu illnesses, they are also one of the most adaptable platforms for cancer treatment. The most widely utilized backbone for oncolytic viral design is serotype 5 (group C). Its structure consists of an icosahedral shaped capsid (made primarily of hexon, penton, and fiber proteins) around a non-enveloped double-stranded DNA. Adenoviruses can infect cells regardless of whether or not they are dividing. (1,2)

Discussion

Mechanism of Cancer Immunity

The tumor microenvironment of advanced cancers is “cold” due to the lack of immunological activity. Oncolytic virus therapy restores the immunological activity of immune tumor infiltrates. a Danger signal release and DC maturation. Oncolytic adenoviruses infect tumor cells and cause oncolysis, releasing new virus progeny but also DAMPS and PAMPS, which will activate nearby dendritic cells and foster their maturation by upregulating co-stimulatory markers, such as CD80, CD83, and CD86. b Mature dendritic cells will process tumor debris and present tumor-associated and virus antigens to local and distant T cells. Concurrently, the ongoing virus infection attracts T cells to the tumor site. c The activation of B cells by CD4+ T cells or BCR-virus interaction causes the release of neutralizing antibodies, which mark infected tumor cells for ADCC by NK cells, or phagocytosis by M1 macrophages. d CD8+ T cells and NK cells destroy infected and non-infected tumor cells through INFg/GranzB and GranzB/Perforins, respectively. The oncolytic adenovirus infection also upregulates class I HLA in tumor cells, allowing for increased exposure to CD8+ T cells. Overall, the components of this modulation allow the tumor microenvironment to become “hot” with increased immunological activity.(1,2,3)

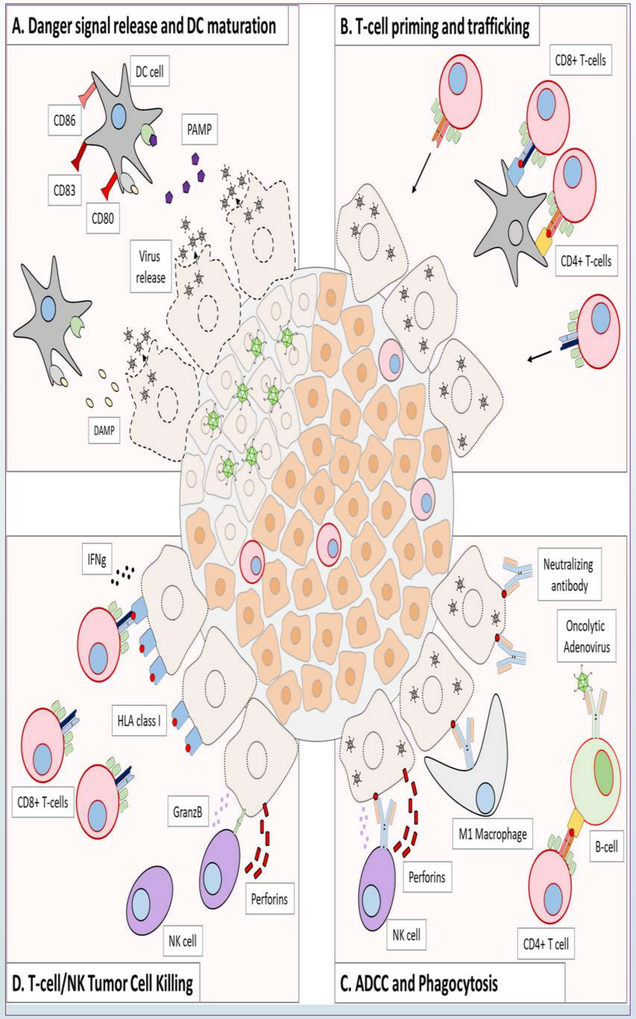

Figure (1) Oncolytic Virus in Cancer Immunotherapy (1)

Conclusion

While preclinical research for oncolytic adenoviruses is promising, and clinical data has demonstrated efficacy, more powerful treatment techniques are required to establish long-term tumor control in patients. As a result, it's only natural that a variety of ways are being used to improve the potency of oncolytic viruses.

References

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