

Development of oncolytic adenovirus agents composed of human adenovirus type 35

Principal Investigator

Graduate School of Pharmaceutical Sciences, The University of Osaka

Professor Hiroyuki MIZUGUCHI

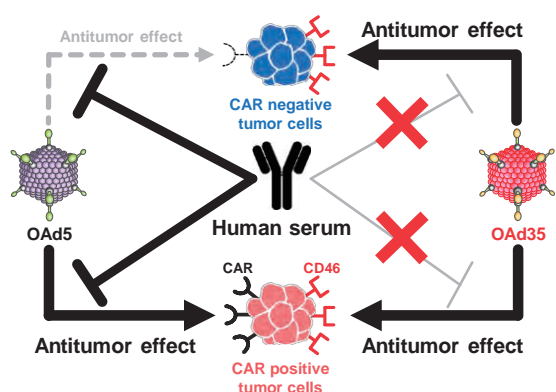
Project Outline

[Abstract]

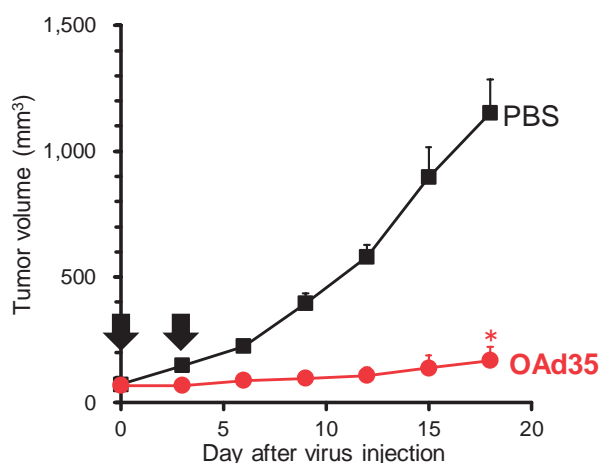
Oncolytic viruses, which can specifically replicate in and kill tumor cells without apparent toxicity to normal cells, are attracting much attention as a novel cancer therapeutic agent. Among various types of oncolytic viruses, the oncolytic adenoviruses (OAd5) are one of the most promising. Almost all OAd5 are composed of human adenovirus (Ad) serotype 5 (Ad5), which belongs to species C. However, the OAd5 composed of Ad5 (OAd5) has two major drawbacks. OAd5 recognizes coxsackievirus-adenovirus receptor (CAR) as an infection receptor. CAR expression is often reduced on malignant tumor cells, leading to inefficient infection with OAd5. In addition, more than 80% of adults have neutralizing antibodies against Ad5 due to natural infection with Ad5 during childhood. In order to overcome these drawbacks, we developed a novel OAd fully composed of human Ad serotype 35 (Ad35) (OAd35), which belongs to species B2. Ad35 recognizes human CD46 as an infection receptor. CD46, which is a complement regulatory protein, is ubiquitously expressed on all human cells except erythrocytes. Moreover, CD46 is often upregulated on malignant tumor cells. In addition, 20% or fewer adults have neutralizing antibodies against Ad35. OAd35 efficiently killed not only CAR-positive but also CAR-negative tumor cells. Anti-Ad5 serum did not inhibit the OAd35-mediated tumor cell killing. Intratumoral administration of OAd35 resulted in significant growth suppression of the subcutaneous CAR-positive and CAR-negative tumors.

[Significance of the research and Future perspective]

OAd35 become a promising alternative oncolytic virus, especially for tumors resistant to a conventional oncolytic Ad.



Characteristics of OAd35



Intratumoral administration of OAd35 significantly suppressed tumor growth

Target disease. : Cancer

Patent information : Patent No. JP7508109, Application No. JP2023-138116, PCT/JP2024/28319, Application No. JP2025-027505

Reference papers : Mol. Ther. Oncolytics. 2021, 20, 399-409. doi: 10.1016/j.omto.2021.01.015
J. ImmunoTher. Cancer, 2025, 13, e006558. doi: 10.1136/jitc-2022-006558.
<https://doi.org/10.1101/2022.12.09.519732>.

Subject for development : Preclinical studies in clinically relevant models (currently in progress)

Details of desired corporate collaboration : General research support for clinical application