National Cancer Center (NCC) Japan, NCC Seed Acceleration Program（NCC SAP）

Development and Commercialization of Next-Generation Oncolytic Virus for Cancer Virotherapy

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Vision

- We aim to develop next-generation oncolytic vaccinia virus for refractory cancers that are resistant to current standard treatments.
- Virotherapy using live viruses can attack tumors via various modes of action compared to standard chemotherapy and radiation therapy.
- Oncolytic virus infects and replicates within tumor cells and directly lyse them, followed by induction of antitumor immunity. However, the clinical benefits and target cancers are limited due to complexity of tumor microenvironment and intratumoral injection of virus.
- To address these issues, we have developed next-generation oncolytic vaccinia virus (FUVAC121), and planned to get clinical POC by intratumoral administration of FUVAC121 while we promote R&D for intravenous administration of FUVAC121.

Marketability

- The societal impact is significant since approved drugs will be replaced with virotherapy that is more effective and lower side effects.
- Intratumoral injection is suitable for locally advanced head and neck cancer on the body surface, and bladder and pancreatic cancer with catheter or under image guidance. Each is estimated to target 0.5 to 1.5 million patients worldwide, with a market size of $2 to $5 billion.
- Intravenous administration targets metastatic tumors. The market size worldwide is estimated at $30 billion with CAGR of 8% in the future.
- Only two competing products are approved in US and Japan, and there is not yet vaccinia virus-based approval oncolytic agent.

Innovation

Intellectual property (IP) for tumor-specific viral replication has been obtained globally (PCT/JP2014/081484). IPs for enhanced tumor lysis by cell fusion (PCT/JP2020/018976) and antitumor immunity by expressions of IL12 and CCL21 (PCT/JP2021/041825) are being transferred to Japan, US, Europe and other countries. The combination makes FUVAC121 highly novel and superior to competing products. Furthermore, we would realize intravenous administration by taking advantage of vaccinia-specific infectious particles which is resistant to neutralize in the blood (JP7274138).

Partnering

【 Expected partners 】

Pharmaceuticals・ Chemical/Fibers ・ Medical institute ・
IT, Electronics/Digital ・ Biotech/Drug Discovery Service・Machinery/Device ・
CMO/CDMO/CRO/SMO ・ Food/Beverages ・Medical/Diagnosis/Research Devices ・
Venture capitals

【 Expectation 】

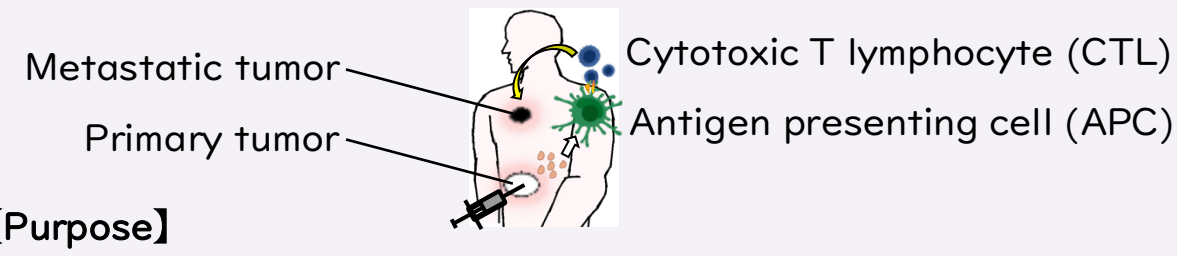
Investigational New Drug Manufacturing, Clinical trials, Startup support

Research Outline

Key Words: #Virotherapy, #Oncolytic virus, #Immune response, #Project Management

【Issues of current cancer virotherapy】

×Clinical benefits are limited by complexity of tumor microenvironment.
×Target cancers are limited by intratumoral administration of virus.



【Purpose】

As the 1st pipeline, we will conduct FIH trials for IT injection of FUVAC121. As the 2nd pipeline, we will promote R&D for IV injection of FUVAC121.

【Research and Development】

1st pipeline （Intratumoral administration of FUVAC121）

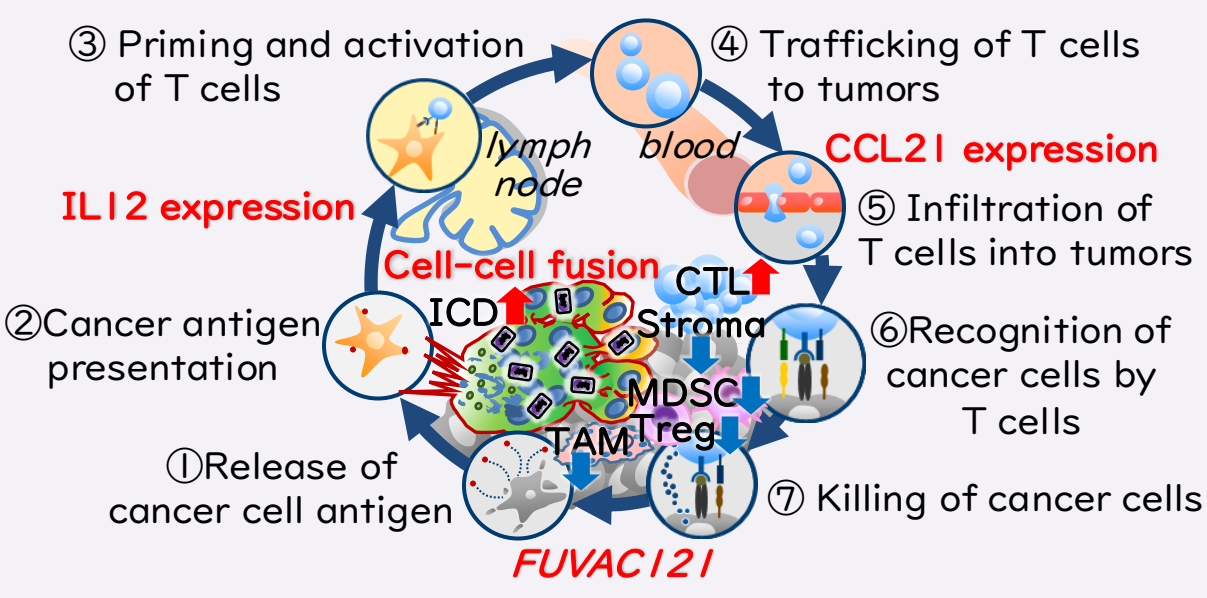
- ☐ Evaluation of antitumor effects and biodistribution in preclinical models
- ☐ Determination of target cancer, viral dose and frequency for FIH study
- ☐ Manufacturing and testing of engineering product of FUVAC121

2nd pipeline （Intravenous administration of FUVAC121 ）

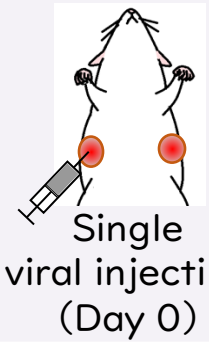
- ☐ Availability of intravenous injection in murine tumor models
- ☐ Optimization of manufacturing method and determination of specification

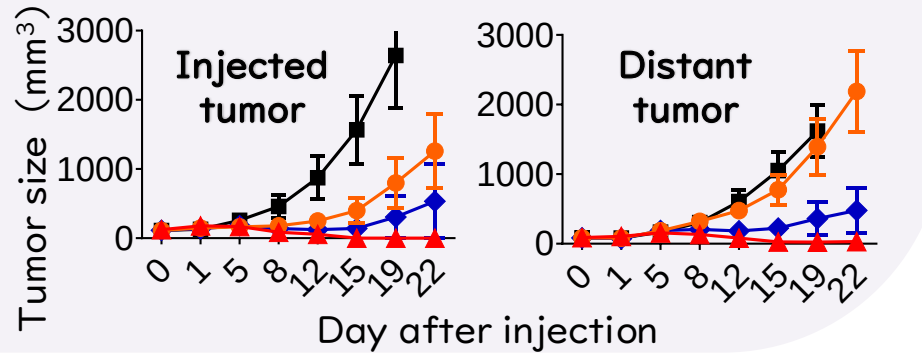
【Next-generation oncolytic virus to address the issues】

FUVAC121 has enhanced tumor lysis and antitumor immune responses via induction of cell-cell fusion and expressions of IL12 and CCL21.



Unilateral intratumoral injection of FUVAC121▲ exhibited higher antitumor effects than PBS■, FUVAC● and MDRW121◆ in mice bearing bilateral subcutaneous colorectal tumors. FUVAC121 achieved 86% complete response in both tumors compared to 0% for FUVAC and 33% for MDRW121.





【 Related publication 】

Nakatake M, et al. (2024) Cancer Sci. 115: 600-610.
Kurosaki H, , et al. (2021) Cells 10: 985.
Nakatake M, et al. (2021) Mol. Ther. 29: 1782-1793.
Nakatake M, et al. (2019) Mol. Ther. Oncolytics 14: 159-171.