cima
CENTER FOR APPLIED MEDICAL RESEARCH
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Cancer Virotherapy

Semliki Forest Virus (SFV) vector: An efficient self-replicative RNA

- The **combination** of **immunotherapy and virotherapy,** using oncolytic viruses, has shown great promise in **cancer therapy**.
- **Semliki Forest virus** (SFV) **vectors** are based on a **self-replicating RNA** that constitute a very promising tool for cancer therapy due to several properties that include high expression levels, **induction of type I interferon responses** and apoptosis in tumor cells.
- Several **SFV vectors** have been developed which are able **to express** immunostimulatory proteins such as **interleukin-12** (IL-12) or **IFNα.**
- **SFV vectors** are **poorly immunogenic**
- Primary indication: **Cancer.**

Medical Need

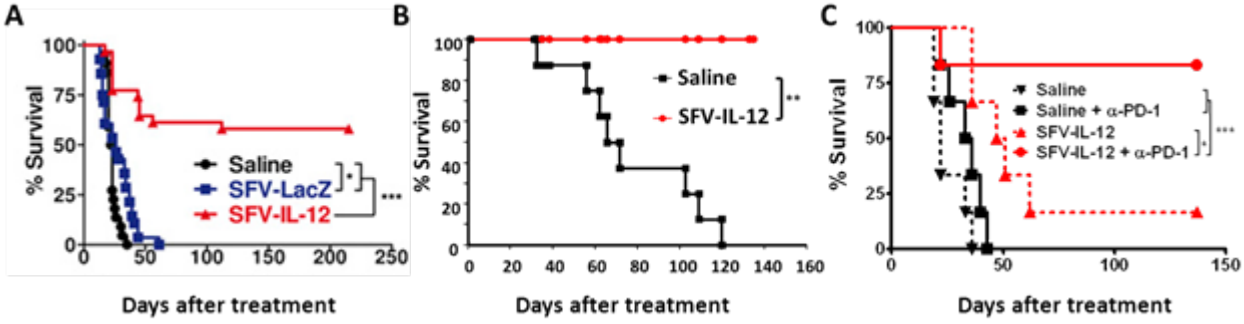
- Immunotherapeutical approaches based on immunomodulatory antibodies do not work in all cancer patients, show some degree of toxicity, and are not effective in some tumor types, such as pancreatic cancer, colorectal cancer or hepatocellular carcinoma.
- Oncolytic vectors are limited by the induction of anti-virus immune responses

Product profile:

- SFV vectors are based on a self-replicating RNA that induces potent type I interferon responses, enhancing immune responses.
- SFV vectors induce apoptosis in tumor cells, favoring the release of tumor antigens and epitope spreading.
- SFV vectors do not propagate and their expression is transient, lasting for only 2-3 days, reducing possible toxicity.
- SFV vectors are poorly immunogenic, allowing repetitive administrations.
- SFV vectors can be used as viral particles, but also directly as RNA or DNA. These last two formats increase the biosafety of the system, facilitate its production, and reduce immunogenicity.
- Intratumoral administration of SFV vectors can mediate very high local expression of immunostimulatory molecules, resulting in strong antitumor responses.
- Combination of SFV vectors expressing cytokines with immunomodulatory antibodies has shown potent synergistic effects.

Proof of concept

- ***In vivo,*** *a*ntitumor effects with SFV vectors:



The administration of SFV vectors expressing pro-inflammatory cytokines, like IL-12, induced potent antitumor responses in immunocompetent mice using transplantable colon adenocarcinoma (A) or spontaneous hepatocellular carcinoma (B) tumor models. In addition, this vector showed a potent antitumor synergy when used at a suboptimal dose in combination with immunomodulatory antibodies, like anti-PD-1 (α-PD-1), in colon adenocarcinoma tumors (C).

References

1. Quetglas JI *et al*. J. Immunology. 2013. 190:2994-3004
2. Rodriguez-Madoz JR *et al*. Human Gene Therapy. 2014. 25(2):132-143
3. Quetglas JI *et al*. Cancer Immunology Research. 2015. 3(5):449-454

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