cima
CENTER FOR APPLIED MEDICAL RESEARCH
UNIVERSITY OF NAVARRA

Cancer Virotherapy

Semliki Forest Virus: An efficient self-replicative RNA vector for cancer therapy

- **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 constitutes a promising tool for cancer therapy due to several intrinsic properties that include high expression levels, induction of type I interferon (IFN) responses and apoptosis in tumor cells.
- SFV vectors able to express immunostimulatory proteins, such as **interleukin-12** (IL-12) or **IFNα,** have been developed**.**
- Primary indication: **Cancer.**

Medical Need

Despite remarkable advances in cancer therapy based on the use of oncolytic vectors and immunomodulatory antibodies:

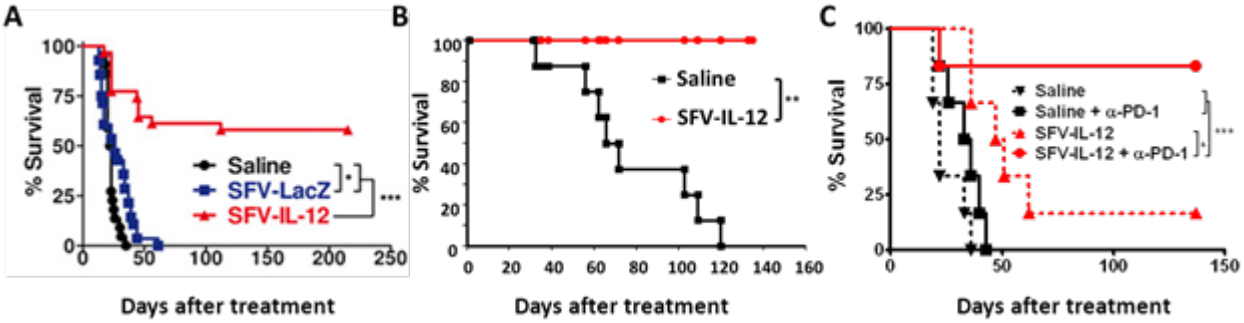
- Immunomodulatory antibodies do not work in all patients, show toxicity, and are not effective in some tumor types, such as pancreatic cancer, colorectal cancer or hepatocellular carcinoma.
- Oncolytic vectors are limited by the induction of anti-virus immune responses

Product profile:

- SFV vectors can be easily engineered to express immunostimulatory proteins.
- When given intratumorally, SFV vectors express locally high levels of immunostimulatory molecules, resulting in strong antitumor responses with low toxicity.
- The replication of SFV RNA within tumor cells induces potent type I interferon reponses that enhance immune responses.
- SFV vectors also induce apoptosis in tumor cells, favoring the release of tumor antigens and epitope spreading.
- SFV do not propagate and their expression is transient, lasting for only 2-3 days, reducing possible toxicity.
- Combination of SFV vectors expressing cytokines with immunomodulatory antibodies has shown potent synergistic effects.
- SFV vectors are poorly immunogenic, allowing repetitive administrations.
- SFV vectors can be used as viral particles, but also directly as RNA. This last possibility facilitates the production of the vector and increases its biosafety.

Proof of concept

- Antitumor effects *in vivo* 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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