

## LINEAR DNA AMPLICONS AS A NOVEL ANTIVIRAL AND CANCER VACCINE STRATEGY

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**Background** DNA-based vaccines represent a simple, safe and promising strategy for harnessing the immune system to fight infectious diseases as well as various forms of cancer and thus are considered an important tool in the cancer immunotherapy toolbox. Nonetheless, the manufacture of plasmid DNA vaccines has several drawbacks, including long lead times and the need to remove impurities from bacterial cultures. Here we report the development of polymerase chain reaction (PCR)-produced amplicon expression vectors as DNA vaccines and their *in vivo* application to elicit antigen-specific immune responses in animal cancer models.<sup>1</sup>

**Methods** Plasmid DNA and amplicon expression was assessed both *in vitro*, by HeLa cells transfection, and *in vivo*, by evaluating luciferase expression in mice through optical imaging. Immunogenicity induced by DNA amplicons was assessed by vaccinating mice, cats and ferrets against SARS-CoV-2 Spike protein. Similarly, amplicons encoding a tumor-associated antigen (Telomerase Reverse Transcriptase, TERT) and neoantigens were tested to evaluate the antitumoral effect of DNA amplicons in murine cancer models in combination with immune-checkpoint inhibitors (ICIs).

**Results** Amplicons encoding Spike Receptor Binding Domain (RBD) were strongly immunogenic in all models and were able to confer antiviral effects. DNA vaccines encoding tumor-associated-antigens, such as telomerase reverse transcriptase or neoantigens expressed by murine tumor cell lines were able to elicit antigen-specific immune responses and proved to significantly impact tumor growth when administered in combination with ICIs.

**Conclusions** These results strongly support the further exploration of the use of PCR-based amplicons as an innovative immunotherapeutic approach to viral diseases and cancer treatment.

## REFERENCE

1. Conforti A, et al. Linear DNA amplicons as a novel cancer vaccine strategy. *J Exp Clin Cancer Res* 2022 Jun 6;**41**(1):195. doi: 10.1186/s13046-022-02402-5.

**Ethics Approval** All animal experiments were performed according to the guidelines for the care and use of laboratory animals and were approved by the ethical committee of the Italian Ministry of Health, with authorization #1166/2020-PR

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