

INTRODUCTION

Oncolytic virotherapy is a promising and fast emerging anti-cancer strategy. To date, herpes virus: Talimogene laherparepvec is the only FDA approved oncolytic virus (OV). However, many other types of OVs are showing promising results in clinical studies. One example is chimeric oncolytic adenovirus ONCOS-102, expressing GM-CSF as a transgene, which recently reported 33% ORR in advanced anti-PD1 refractory melanoma phase I study (NCT03003676).

Genetically modified OVs can be armed with different co-stimulatory molecules in order to boost the anti-tumour immune responses. Based on the ONCOS-102 backbone, we have engineered next generation ONCOS virus, ONCOS-214, expressing novel double transgenes designed to enhance apoptosis of the cancer cells, leading to increased release of tumour antigens and thereby enhancement of cross presentation of tumour antigens and priming of cancer specific T cells.

Fig. 1. ONCOS-102 backbone – matrix for the development of ONCOS-214.

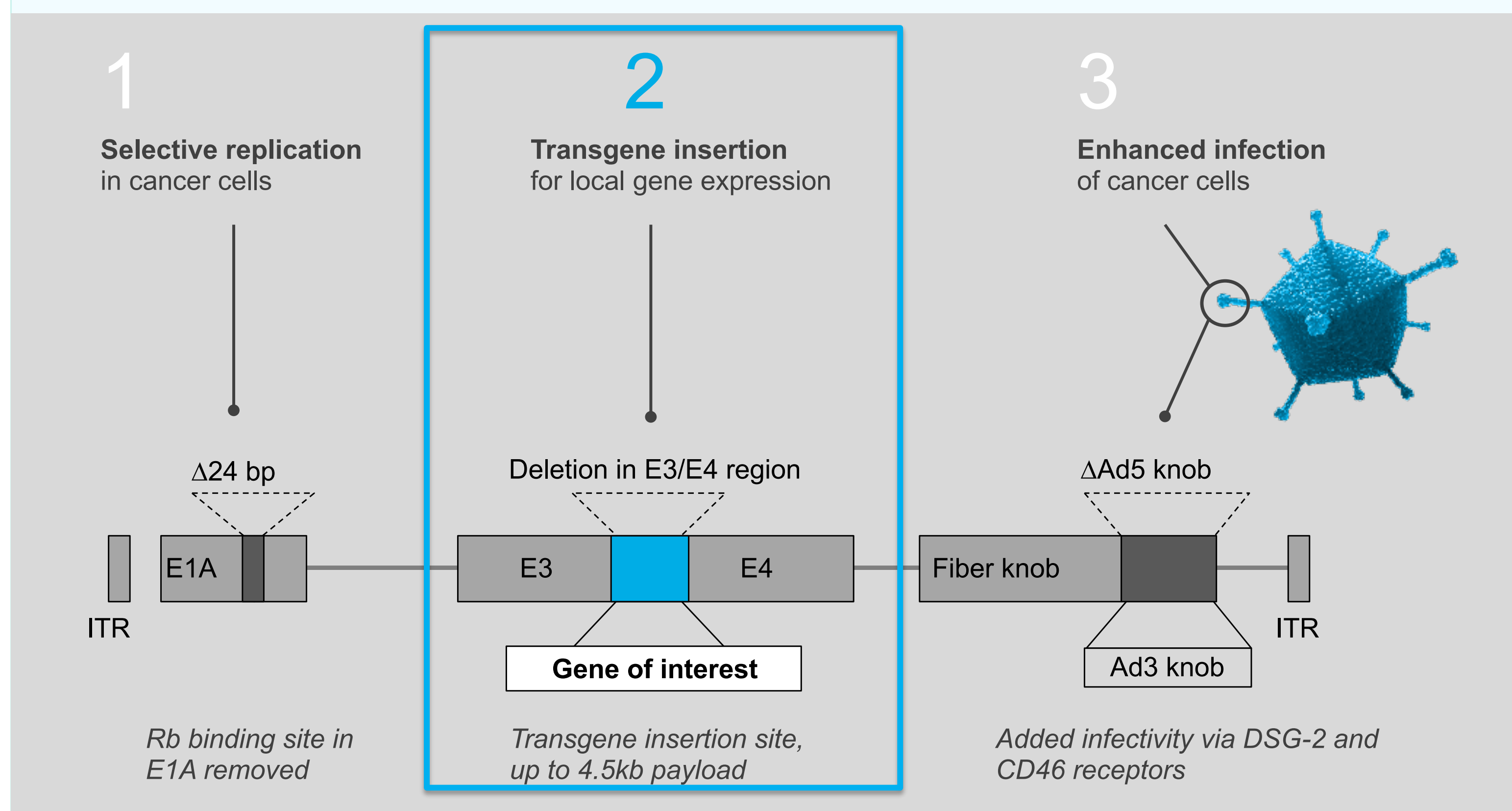


Fig. 2. Advantages of ONCOS-backbone.

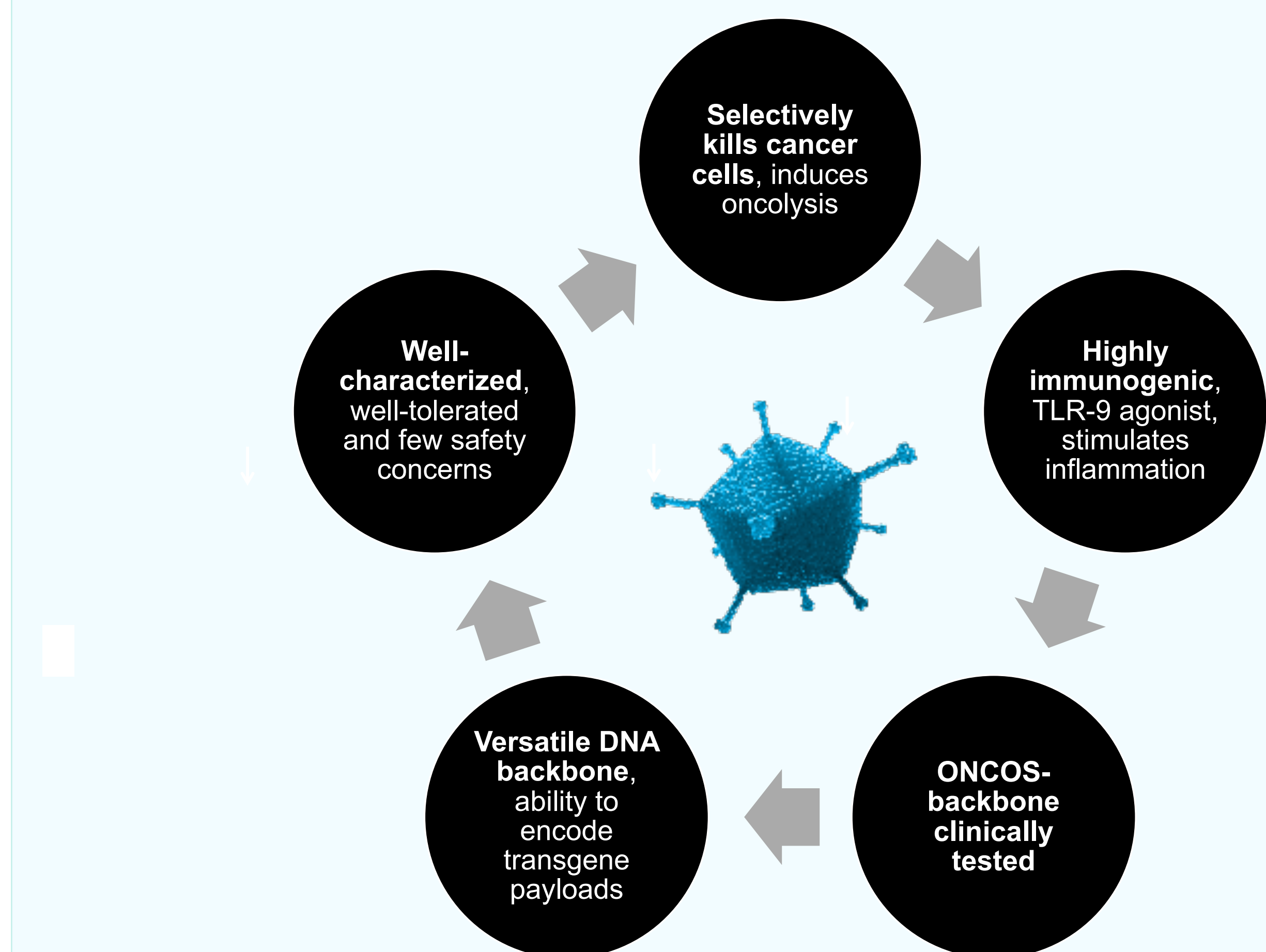
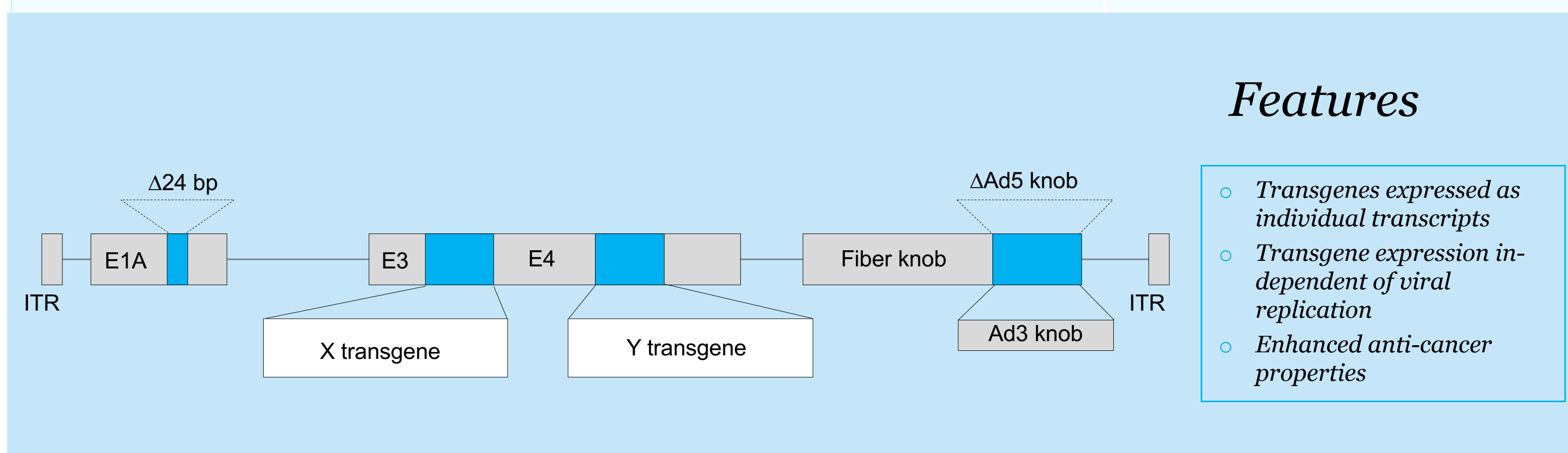


Fig. 3. ONCOS-214 structure (transgenes undisclosed).



PURPOSE OF THE STUDY

The purpose of this study was to engineer next generation ONCOS-based virus with enhanced anti-cancer properties and assess its efficacy in pre-clinical studies.

METHODS

Next generation double transgene ONCOS-214 was engineered using standard cloning tools. Two single transgene vectors containing either transgene X or Y were also cloned. Anti-cancer properties of the tested virus were assessed both *in vitro* and *in vivo*. The oncolytic properties of ONCOS-214 were confirmed in 4 melanoma cell lines *in vitro*. Anti-cancer effects of the virus were also assessed in i) immunodeficient xenograft and ii) humanized xenograft melanoma mouse models to further understand the anti-cancer and immune stimulatory potency of the constructs.

RESULTS

The oncolytic properties of ONCOS-214 were confirmed in 4 melanoma cell lines *in vitro*, demonstrating robust cell lysis and anti-cancer properties. ONCOS-214 showed superior anti-cancer effect *in vitro* by enhancing cancer cell death (Fig. 4A and Fig. 4B).

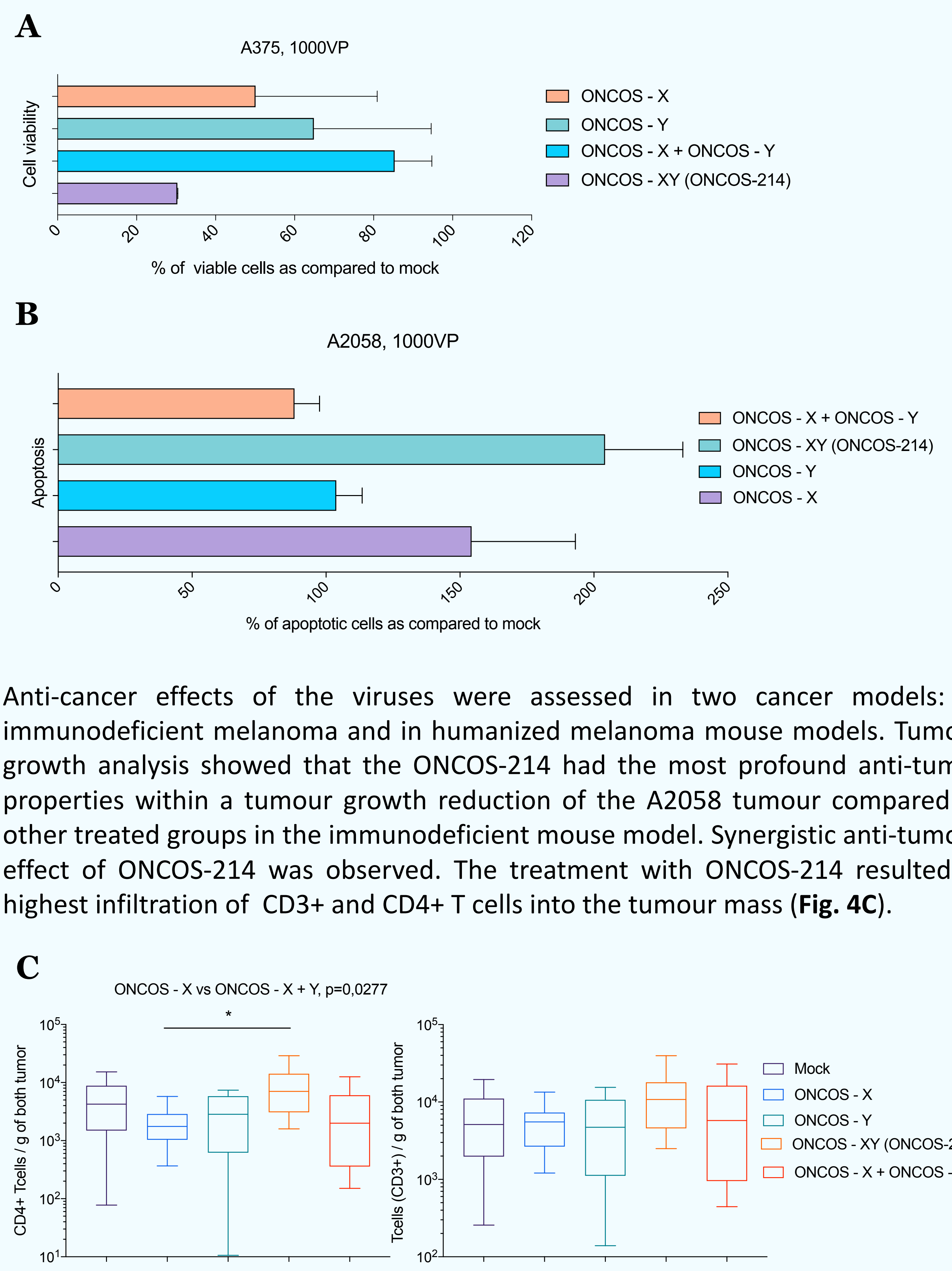


Fig. 4. A: Anti-cancer effect *in vitro* (cell viability assay). B: Apoptotic cell death analyses *in vitro*. C: Infiltration of human immune cells into the tumor mass post treatment (humanized melanoma mouse model). Results are expressed as mean +/- SEM and % of untreated cells. * p<0.05, ** p<0.01, ***p<0.001.

CONCLUSIONS

- These pre-clinical findings demonstrated that ONCOS-214 have anti-cancer properties
- These encouraging preclinical findings will be further investigated to elucidate the mode of action and to perform toxicological studies to bring ONCOS-214 towards clinical testing.