# ONCOLYTIC VIRUSES ENCODING RECOMBINANT TRANSFORMING GROWTH FACTOR (TGF)-BETA MONOMERS AND USES THEREOF

## CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 63/070,965, filed August 27, 2020, which is herein incorporated by reference in its entirety.

## FIELD

This disclosure concerns oncolytic viruses encoding recombinant TGF-β monomers, which function as TGF-β signaling inhibitors. This disclosure further concerns use of the TGF-β monomer-encoding oncolytic viruses for cancer immunotherapy.

## ACKNOWLEDGMENT OF GOVERNMENT SUPPORT

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## BACKGROUND

TGF-β is a multifunctional cytokine with diverse biological effects on cellular processes, including cell proliferation, migration, differentiation, and apoptosis. The three mammalian TGF-β isoforms, TGF-β1, -β2 and -β3, exert their functions through a cell surface receptor complex composed of type I (TβRI) and type II (TβRII) serine/threonine kinase receptors. Receptor activation induces both SMAD proteins and other downstream targets, including Ras, RhoA, TAK1, MEKK1, PI3K, and PP2A, to produce the full spectrum of TGF-β responses (Roberts and Wakefield, *Proc Natl Acad Sci USA* 100:8621-8623, 2003; Derynck and Zhang, *Nature* 425:577-584, 2003; Massagué, *Cell* 134:215-230, 2008).

## SUMMARY

Oncolytic viruses encoding transforming growth factor (TGF)-β monomers engineered to prevent homodimerization and signaling are disclosed. Recombinant engineered monomeric TGF-β functions as an inhibitor of TGF-β signaling by preventing recruitment of TβRI and thereby blocking downstream signaling. Oncolytic virus, such as vaccinia virus, encoding monomeric TGF-β can be used, for example, as a cancer immunotherapeutic.