Oncolytic virotherapy for cancer treatment utilizes naturally occurring or engineered viruses for selective infection and death of cancer cells without any adverse effect on normal cells. Raccoonpox virus (RCN) is a member of the Orthopoxvirus genus of Parapoxviridae, with no known pathogenicity in any mammalian species so far. Raccoonpox virus has already been used as oncolytic virus in human cancer models (3,4). This study explores the potential of modified RCN armed with a suicide gene as an oncolytic vector for cancer treatment. We have generated a TK deleted recombinant Raccoonpox virus expressing the suicide gene FCU1 fused with Green fluorescent protein (RCNtk/gfp::fcu1). The FCU1 gene encodes a bifunctional chimeric protein that efficiently catalyses the direct conversion of the nontoxic 5-fluorouracil (5-FC) into the toxic metabolites 5-fluorouracil (5-FU), an anti-cancer chemotherapy drug, and 5-fluorouridine monophosphate (5-FdUMP) (5).

The combined FCU1/5-FC treatment has proven to be successful in various resistant human cancer cells. The RCNtk/gfp::fcu1 vector has been evaluated in numerous therapeutic human cancer cells, where it demonstrated significant tumor selectivity and retained full replication efficiency and its ability to kill human cancer cells. In vitro studies also demonstrated that the TK deleted Raccoonpox virus expressing FCU1 (RCN tk/gfp::fcu1) displayed reduced replication properties in primary non-transformed human liver cells but still lysed hepatocarcinoma. The results demonstrate the increased antitumoral activity of this new modified virus armed with FCU1 and its promising future for cancer treatment.

### Evaluation of a novel oncolytic Raccoonpox virus expressing the bifunctional FCU1 suicide gene

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**CONCLUSION**

We have shown that RCNtk/gfp::fcu1 can replicate in vitro in a large panel of human tumoral cells without any impact on its therapeutic index. We also have demonstrated that the expression of the FCU1 gene with addition of 5-FC prodrug can increase the antitumoral activity of RCNtk/gfp::fcu1 vector in the infected tumor cells. Our data showed a clear benefit in combining the oncolytic virotherapy using RCNtk/gfp::fcu1 and the prodrug 5-FC for treatment of resistant tumor model. Future development will focus on the in vivo therapeutic activity of RCNtk/gfp::fcu1 on a panel of human tumor in murine model in order to confirm these in vitro results.