TECHNOLOGY

Melanoma Oncolytic Virotherapy by the HSV-2 Mutant delta-PK

OVERVIEW

Oncolytic viruses are replication-conditional viruses with relative tumor selectivity and are a therapeutic strategy designed to reduce tumor burden by direct cell lysis; however, their modest clinical efficacy may be related to poor virus replication within the tumors. The present invention is based on the hypothesis that virotherapy strategies that function by inducing multiple non-redundant pathways of programmed cell death can selectively kill cancer cells and increase virus spread through the tumor mass, while avoiding the limitations of conventional oncolytic viruses. The HSV type 2 gene ICP10 has a protein kinase (PK) function that overrides multiple PCD pathways in cultured cell and animal models, suggesting these pathways are activated when this gene is deleted. The inventors demonstrated that the growth-compromised HSV-2 mutant delta-PK has strong oncolytic activity against melanoma in vitro and in vivo. For melanoma xenografts in mice, complete remission was seen for 7 of 8 tumors followed for 5 months after the last delta-PK injection. Compared to mock-treated animals, survival was significant, ranging between 80 to 100%. Analysis of the xenografts showed activation of calpain and caspases-7 and -3, with upregulation of Beclin-1 and H11/HspB. This virus has the distinct advantage of being well tolerated in humans, as evidenced by Phase I and Phase II clinical trials in patients with genital herpes. Melanoma comprises just 5% of all skin cancers, but it is the most deadly. High unmet needs persist for treating melanoma - despite three decades of extensive R&D, five-year survival of advanced patients remains below 20%. In the United States, the percentage of people who develop melanoma has more than doubled in the past 30 years. Although major pharmaceutical companies have melanoma therapies in late-stage clinical trials, a number of these agents have shown uncertain efficacy.

APPLICATIONS

Oncolytic therapy, in particular against melanoma

ADVANTAGES

-Research demonstrates high oncolytic activity for the delta-PK mutant against melanoma in vitro and in mouse xenograft models -The same mutant virus shown to be well tolerated in humans during Phase I and Phase II clinical trials for HSV

STAGE OF DEVELOPMENT

Proof of concept as oncolytic virus obtained in animal models of melanoma AND same product previously demonstrated as safe in humans.

R&D REQUIRED

Clinical development as new oncolytic therapy

LICENSING POTENTIAL

UMB seeks partners to further advance this technology in the healthcare field.

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Additional Information

INSTITUTION

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PATENT STATUS

U.S. Patent 8,414,885 issued 4/9/2013

LICENSE STATUS

Available for licensing

CATEGORIES

- Therapeutics
- Biologics

INVESTIGATOR(S)

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ATTACHMENTS

- Download document(45).pdf

EXTERNAL RESOURCES

- Oncolytic viruses as immunotherapy: progress and remaining challenges
- The oncolytic virus ?PK has multimodal anti-tumor activity

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