Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Conditionally Replication Deficient Herpes Virus and Use Thereof in Vaccines

Product

Conditional mutant shingles vaccine

Indication

Zoster (shingles) vaccine

Value Propositions

- Prevents spontaneous Zoster reactivation
- Protects elderly and immunocompromised individuals

Market

- $1.08 billion—Global shingles vaccine market (5.22% CAGR 2019-2024)

Intellectual Property

- Issued US patent*
- Available for licensing

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Ref# CU3061H

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Background on CU3061H

Varicella zoster virus (VZV) causes varicella (chickenpox) in 4 million children annually. After varicella, VZV typically becomes latent but can spontaneously reactivate and result in zoster (shingles), characterized by pain and rash. This reaction is especially problematic in elderly or immunocompromised patients and can lead to complications such as postherpetic neuralgia, stroke, paralysis, or blindness.

Technical Innovation

Drs. Ravi Mahalingam and Donald Gilden have developed mutated viral strains that only replicate under explicitly defined conditions and can be utilized as shingles vaccines. The inventors discovered that VZV ORF 63 or 70 protein expression is a requirement for varicella virus expression. Using a rhesus macaques model, mutant strains were developed as simian varicella virus (SVV), the primate version of VZV that closely parallels VZV infection in humans. Within the SVV mutant, ORF 63 is deleted and ORF 70 is fused to a destabilization domain. In the presence of the antibiotic trimethoprim (TMP), ORF 70 is stabilized and promotes virus replication.

The ablity of TMP to drive SVV-GFP (green fluorescent protein) mutant replication in a reversible manner is shown in **Figure 1**. These results suggest a vaccine comprised of conditional SVV or analogous VZV mutants administered in conjunction with TMP will elicit a protective immune response that can be reversibly “turned off” by antibiotic removal, potentially preventing development of complications from zoster as well as other neurotropic herpesviruses.

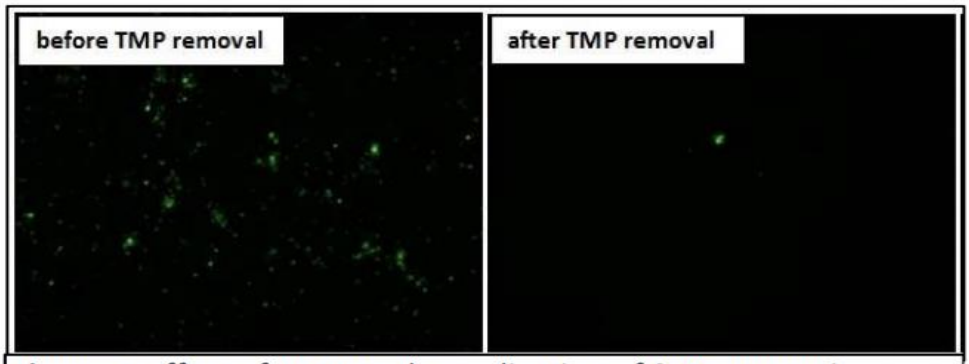

Figure 1. Effect of TMP on the replication of SVV mutant is reversible. SVV mutant-infected cells were cultured with 100nM TMP. Active virus replication was confirmed by GFP expression. After TMP removal minimal GFP was detected.

Resources & Documents:

**Issued US patent 10,232,035—"Conditionally Replication Deficient Herpes Viruses and Use Thereof in Vaccines"*